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(54) **TREATMENTS AGAINST MOSQUITO-BORNE VIRUSES BASED ON MOSQUITO SALIVARY GLAND PROTEINS**

(71) Applicant: **YALE UNIVERSITY**, New Haven, CT (US)

(72) Inventors: **Erol FIKRIG**, Guilford, CT (US); **Ryuta URAKI**, New Haven, CT (US); **Andrew HASTINGS**, Hamden, CT (US)

(73) Assignee: **YALE UNIVERSITY**, New Haven, CT (US)

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§ 371 (c)(1),
(2) Date: **Mar. 5, 2021**

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A61K 38/17 (2006.01)

(52) **U.S. Cl.**
CPC ***A61K 38/1767*** (2013.01)

(57) **ABSTRACT**

The invention is directed to compositions comprising mosquito (e.g., *Aedes aegypti*) salivary polypeptides and related methods for preventing and/or treating mosquito-borne viral infections such as infections caused by flaviviruses and alphaviruses. The flavivirus that is prevented or treated includes Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, and yellow fever virus.

Specification includes a Sequence Listing.

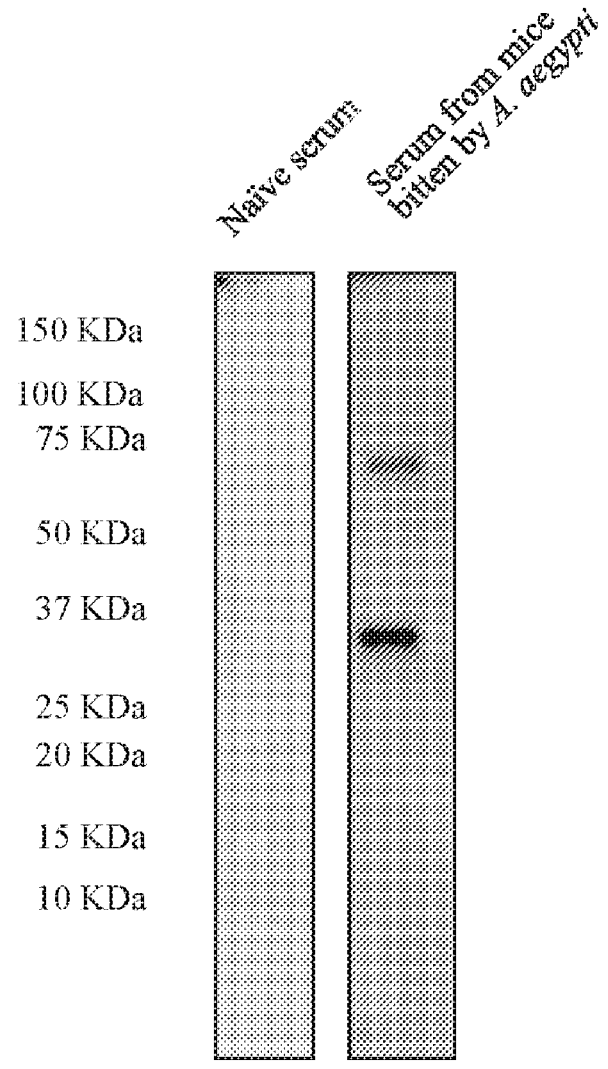


FIG. 1A

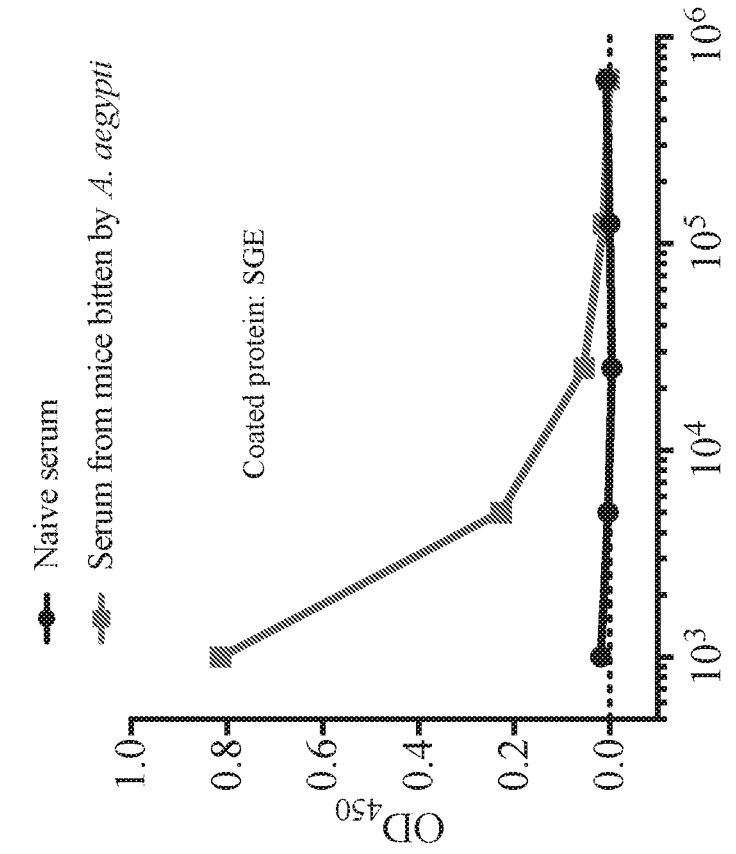

Naive serum
Serum from mice bitten by A. aegypti
Coated protein: SGE
OD450
1.0
0.8
0.6
0.4
0.2
0.0
10^3
10^4
10^5
10^6
Serum dilution

FIG. 1B

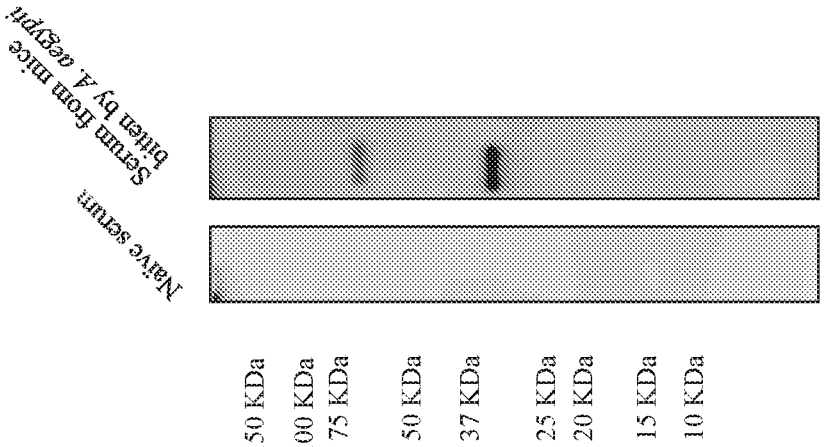

Naive serum
Serum from mice bitten by A. aegypti
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa

FIG. 2A

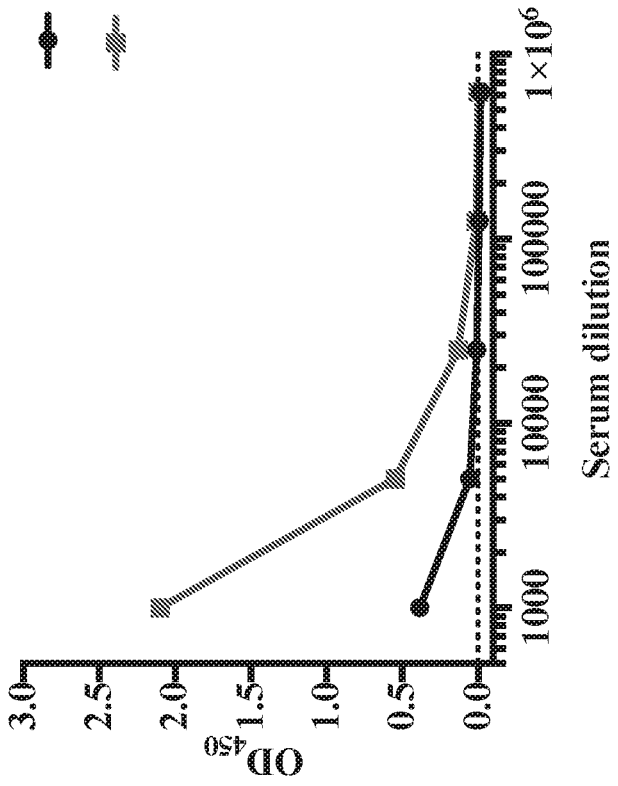

Naive serum
Serum from human bitten by A. aegypti
OD_{450}
3.0
2.5
2.0
1.5
1.0
0.5
0.0
1000
10000
100000
1×10^6
Serum dilution

FIG. 2B

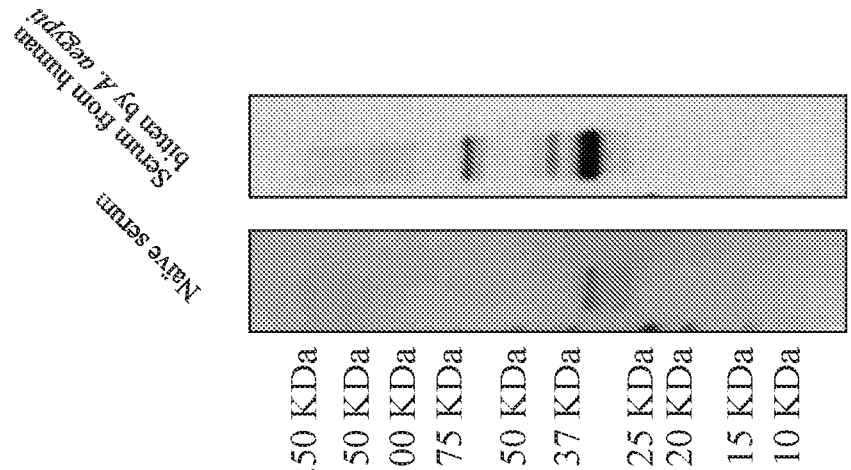

Naive serum
Serum from human bitten by A. aegypti
250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa

FIG. 3A

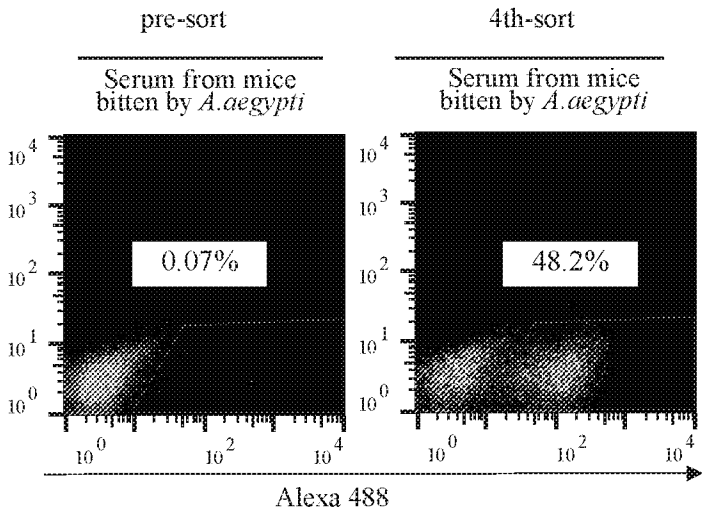


FIG. 3B

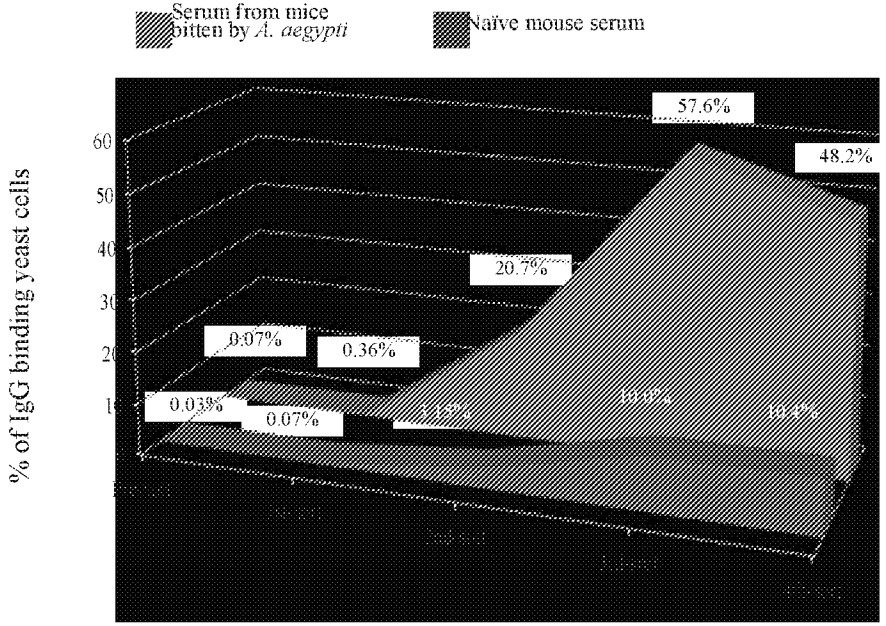


FIG. 3C

Clone	Serum used in screen	Number of times identified in the screen	Gene Identity	Protein name	Abbreviation in this study	Sinal peptide	MW (KDa) (including signal peptode)
1	mouse	19	LOC5578630	Putative 34 kDa family secreted salivary protein	SP	Yes	36
2	mouse	12	LOC5578631	Putative 34 kDa secreted protein	Nest1	Yes	36
3	mouse	11	LOC5567956	Long form D7Bclu1 salivary protein	D7Bclu	Yes	39
4	mouse	7	LOC5580038	Putative 30 kDa allergen-like protein	AILP	Yes	24
5	mouse	1	LOC5573204	Bacteria-responsive protein 1	AgBR1	Yes	49

FIG. 4A

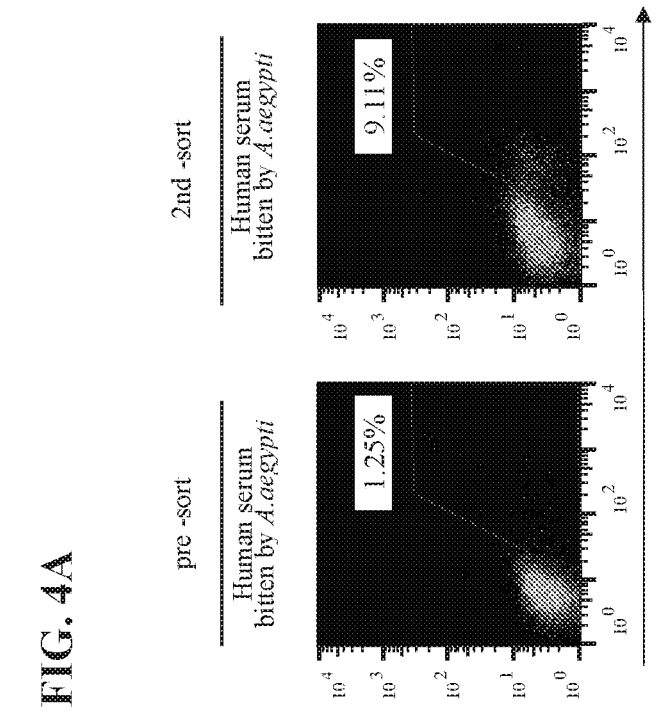


FIG. 4B

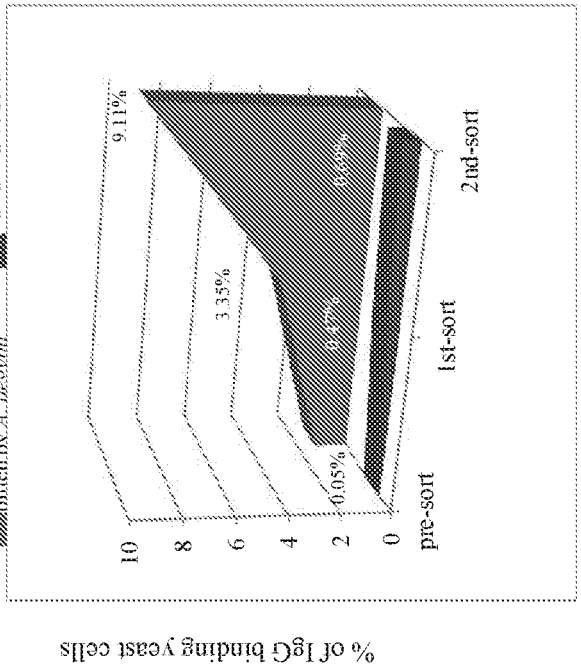


FIG. 4C

Clone	Serum used in screen	Number of times identified in the screen	Gene Identity	Protein name	Abbreviation in this study	Sinal peptide	MW (KDa) (including signal peptide)
6	human	1	LOC5566287	Fibrinogen-related protein	FbRP	Yes	34
7	human	1	LOC5567958	37 kDa salivary gland allergen Aed a 2 Precursor	Aada2	Yes	37
8	human	1	LOC5568702	Lipase	Lipase	Yes	37
9	human	7	LOC110675548	Angiopoietin-like protein	AnLP	Yes	34

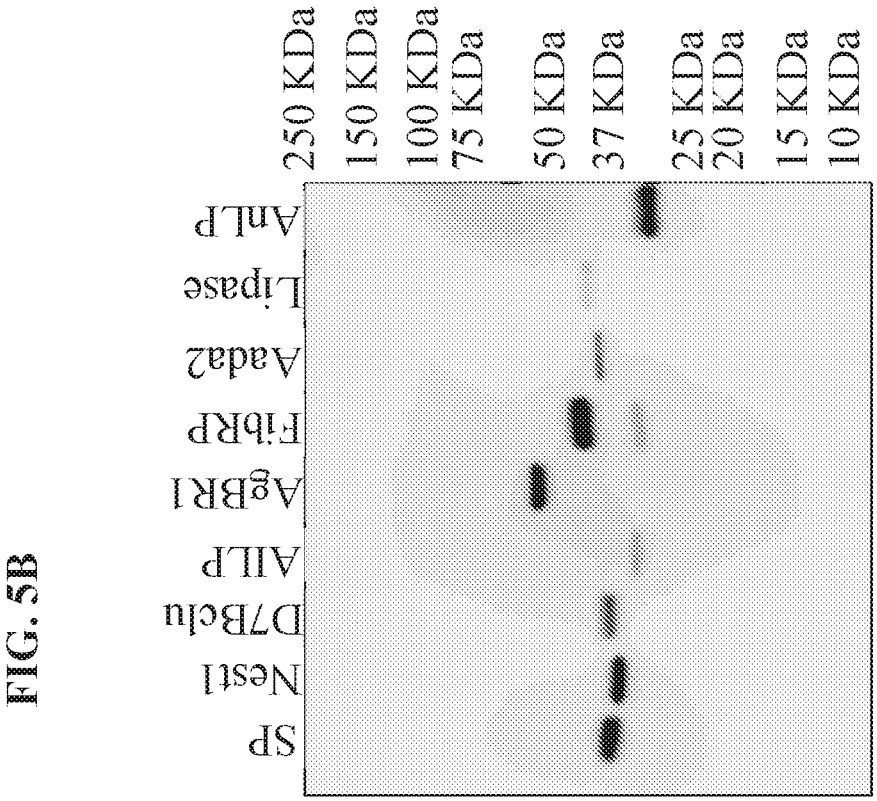

250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa
SP
Nest1
D7Bclu
AILP
AgBR1
FibRP
Aada2
Lipase
AnLP

FIG. 5B

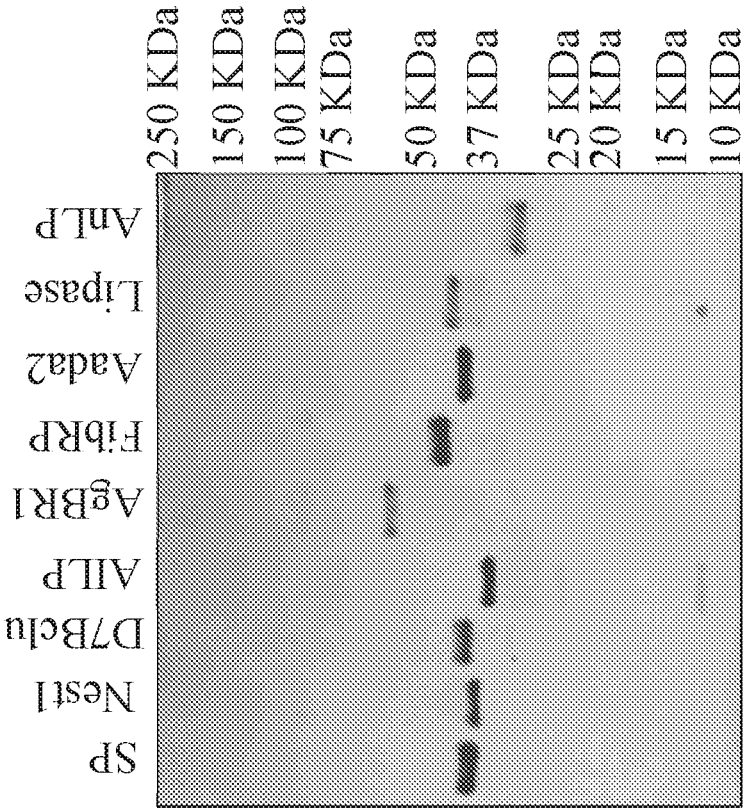

250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa
SP
Nest1
D7Bclu
AILP
AgBR1
FibRP
Aada2
Lipase
AnLP

FIG. 5A

FIG. 5C

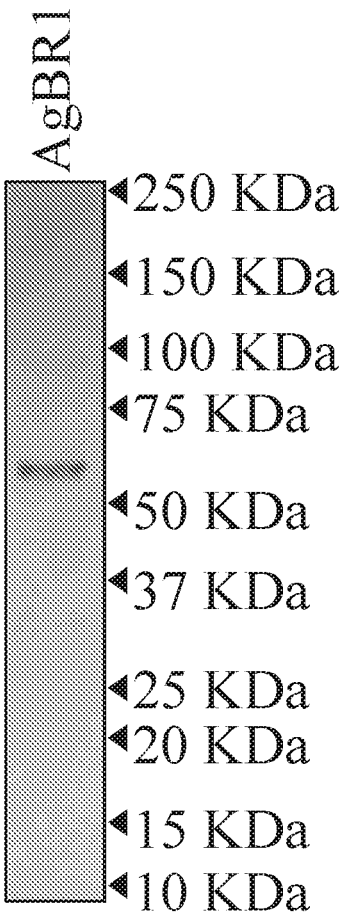

AgBR1
250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa

FIG. 5D

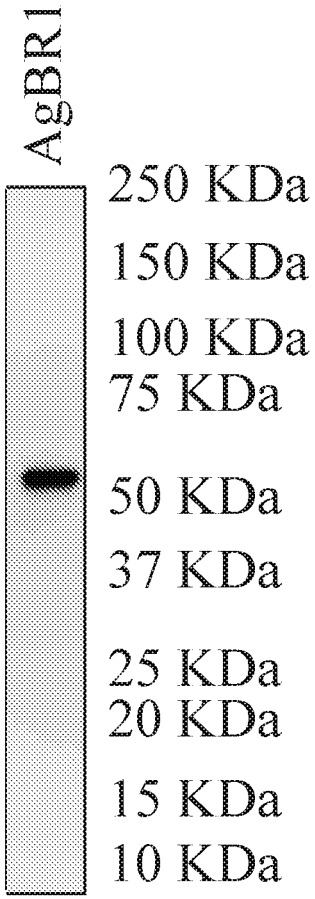

AgBR1
250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa

FIG. 6A anti-SP serum

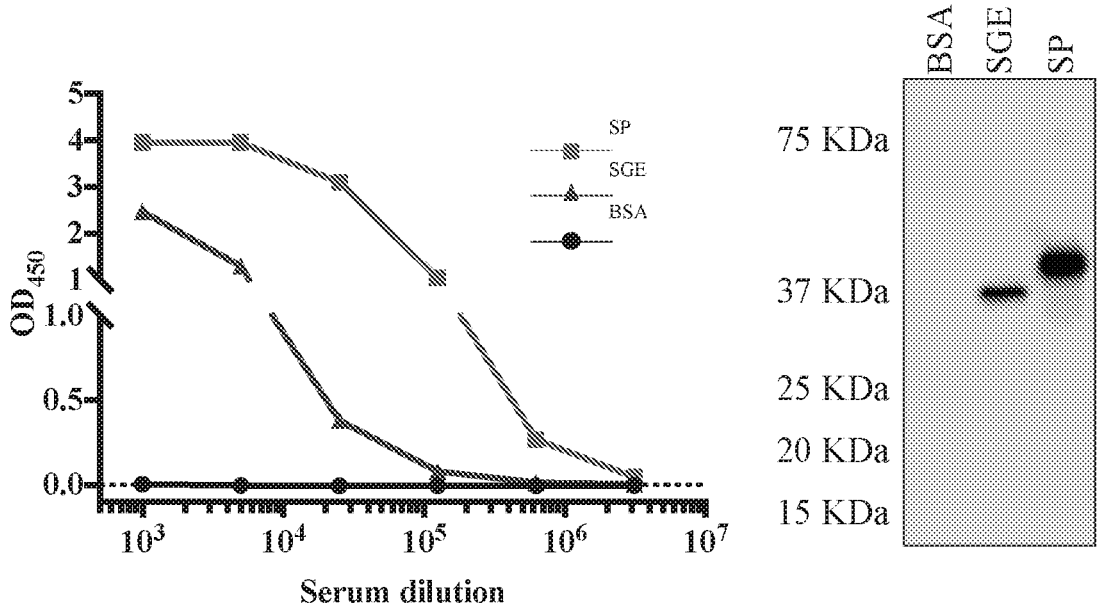


FIG. 6B anti-Nest1 serum

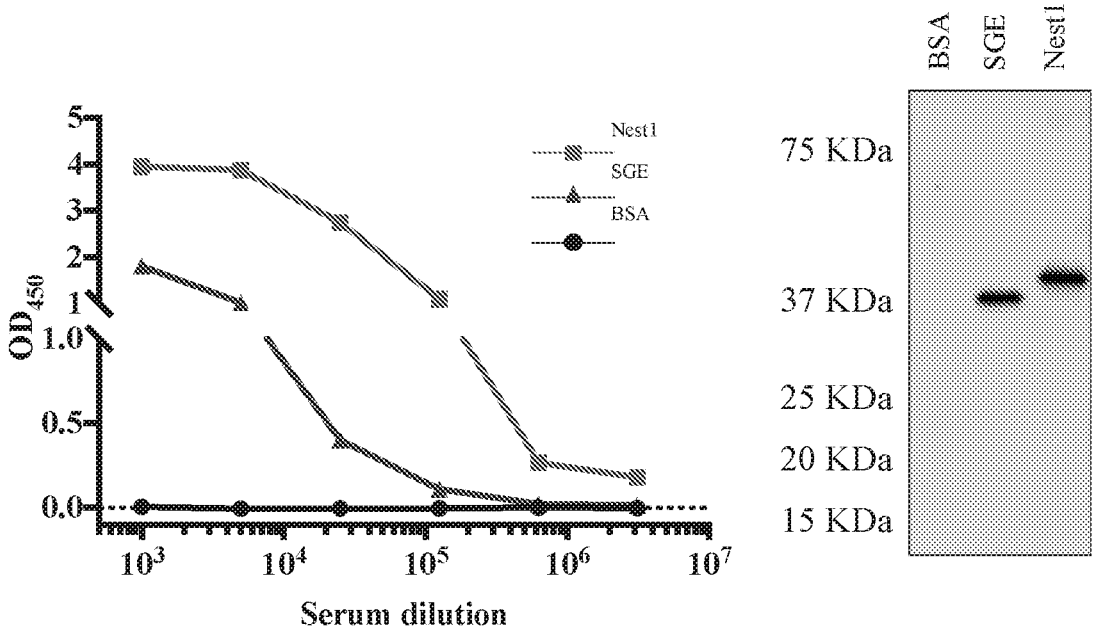


FIG. 6C anti-D7Bclu serum

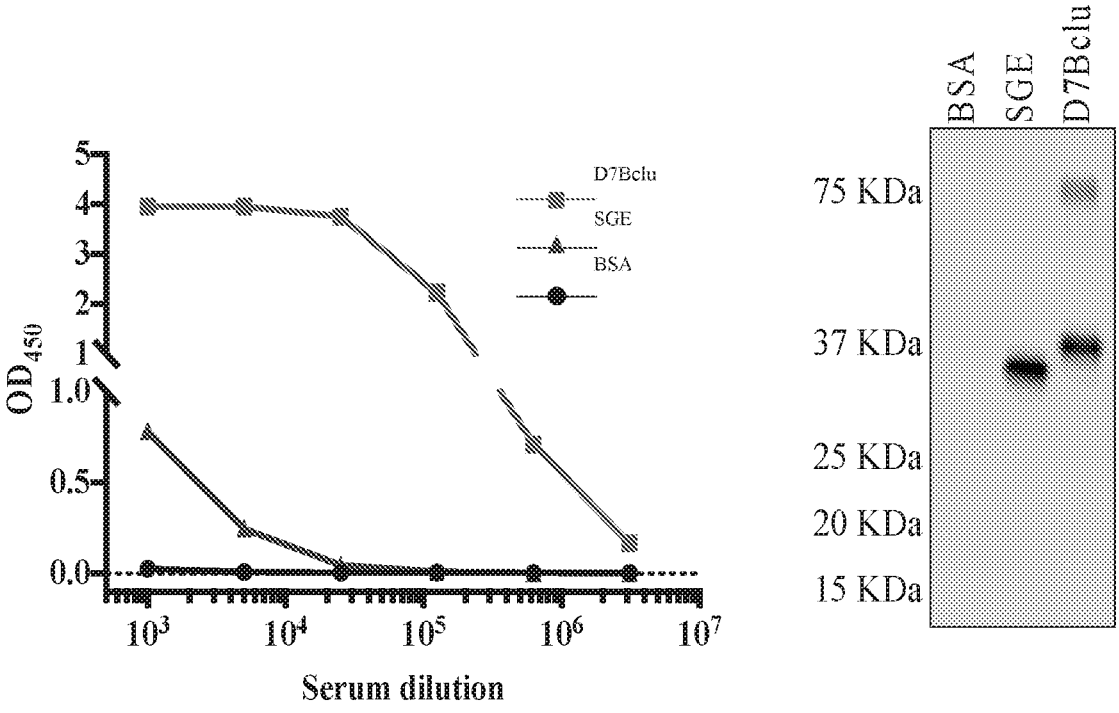


FIG. 6D anti-AILP serum

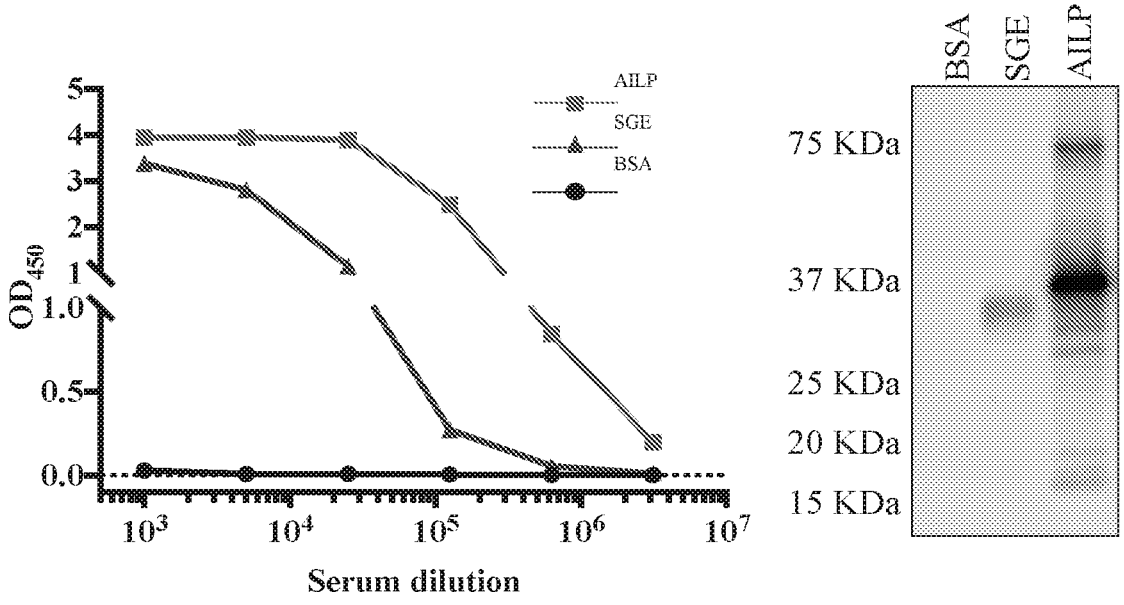


FIG. 6E anti-AgBR1 serum

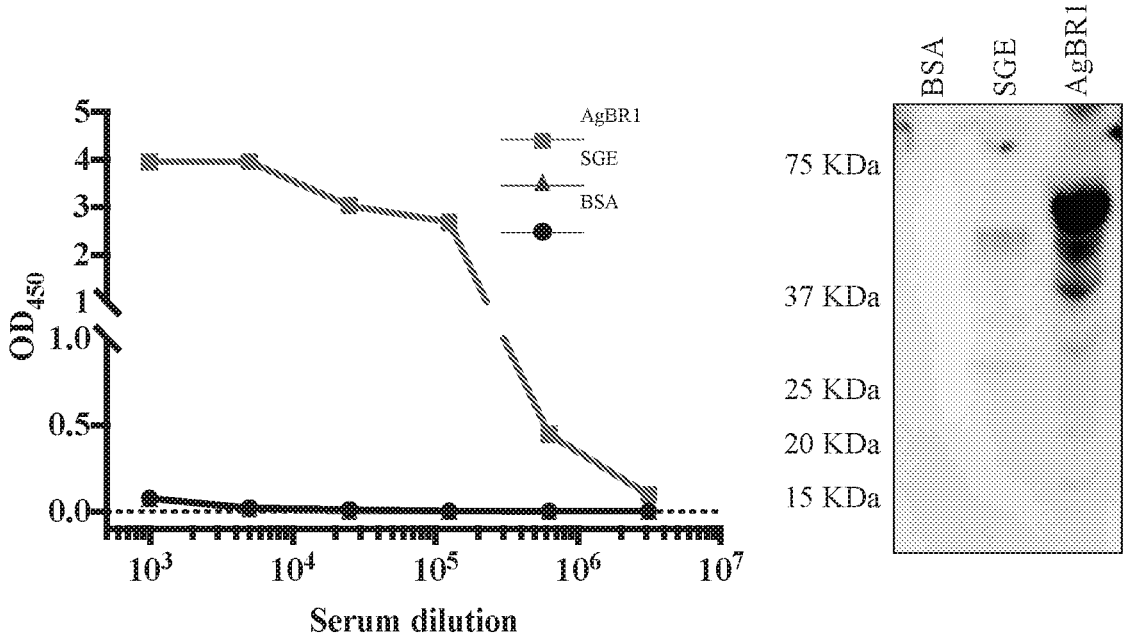


FIG. 6F anti-FibRP serum

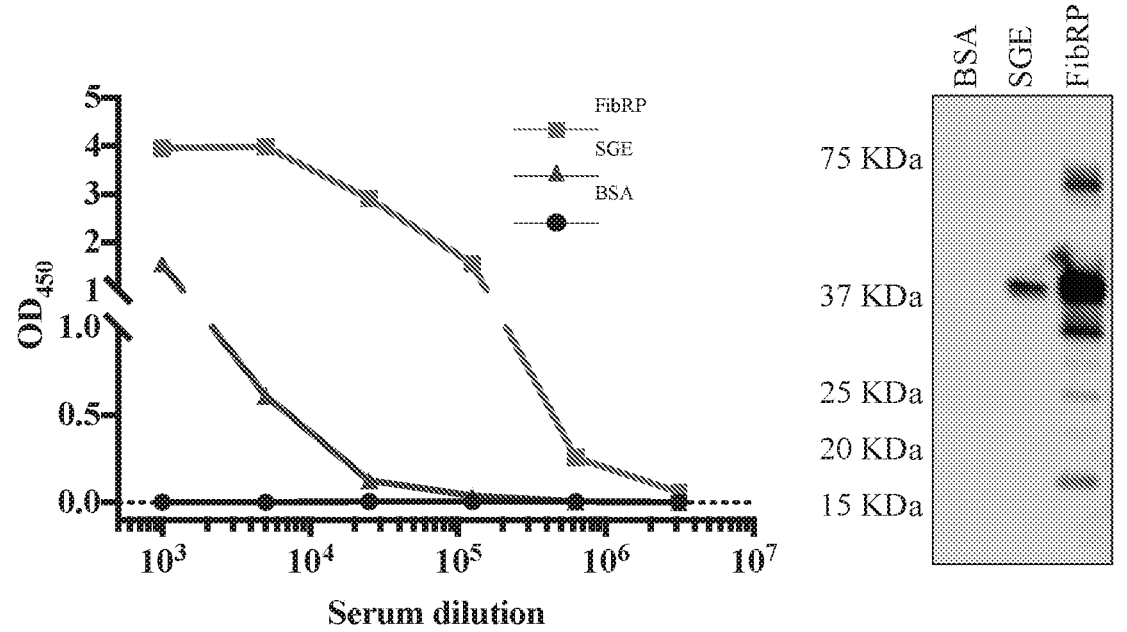


FIG. 6G anti-Aada2 serum

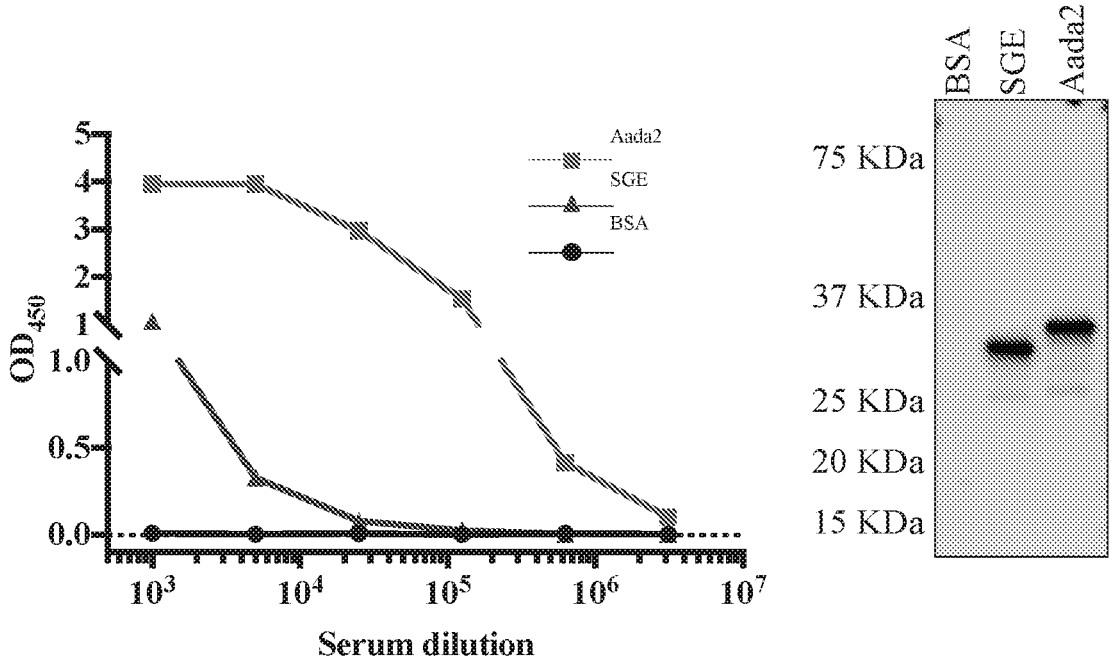


FIG. 6H anti-Lipase serum

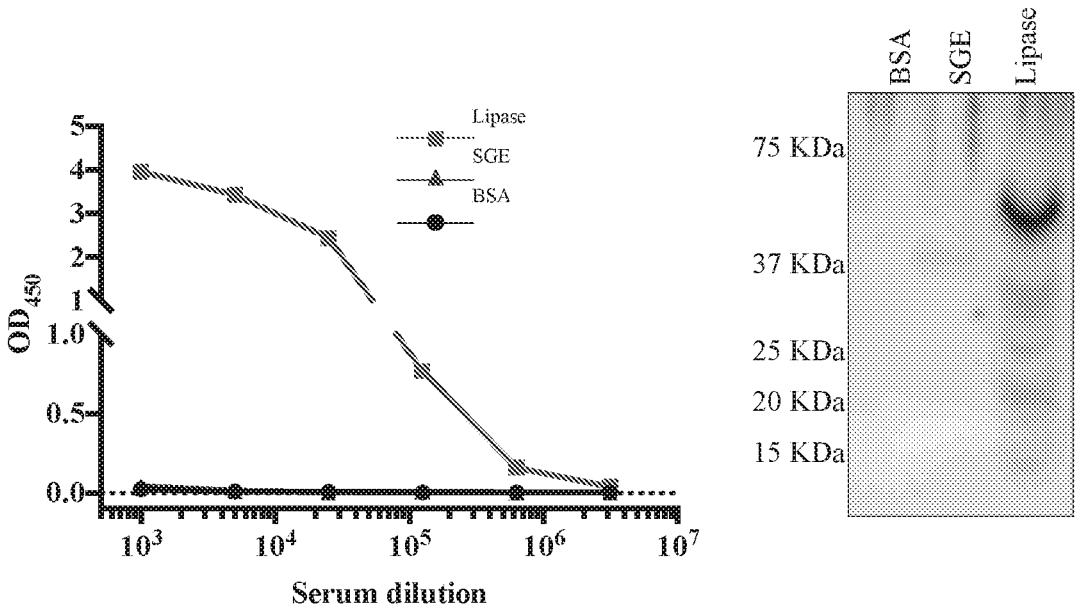


FIG. 6I anti-AnLP serum

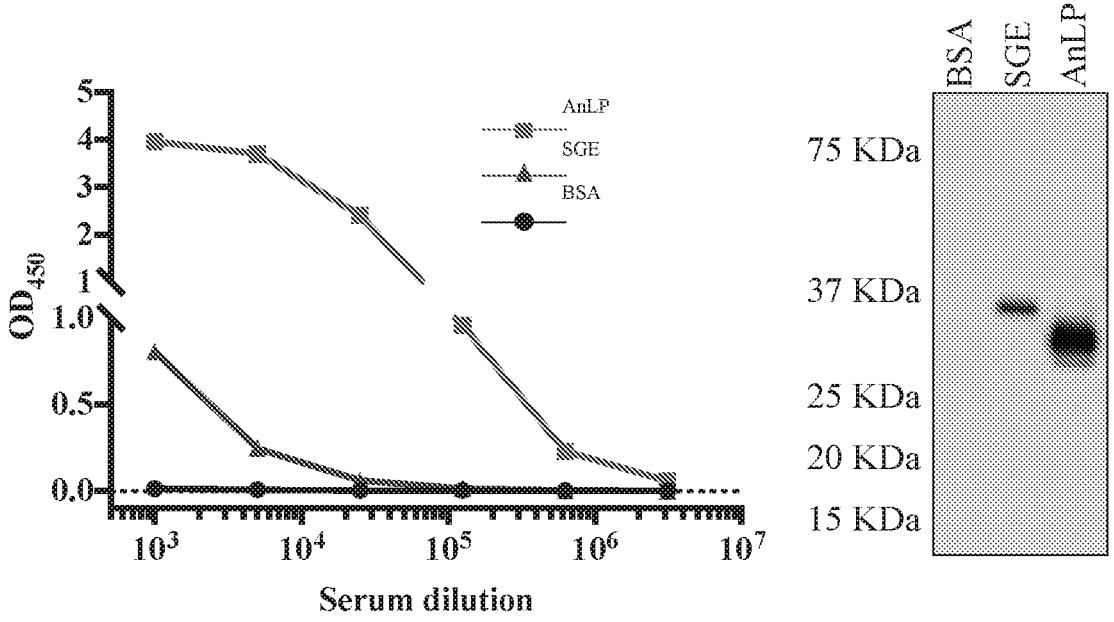


FIG. 6J naïve serum

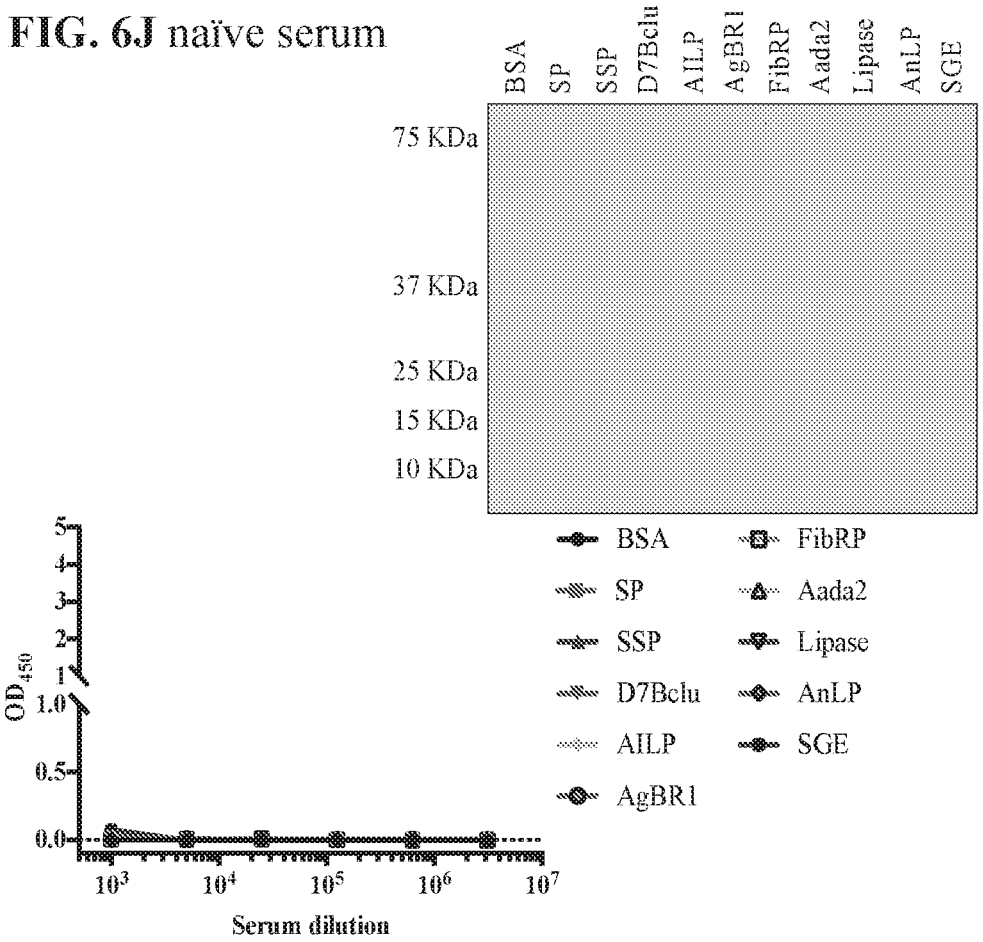


FIG. 7A

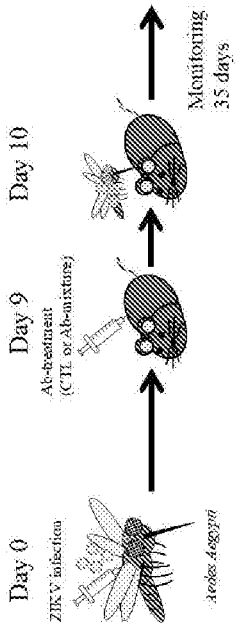


FIG. 7B

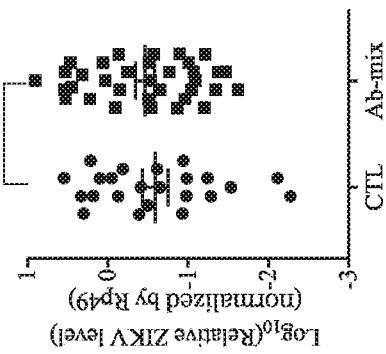


FIG. 7C

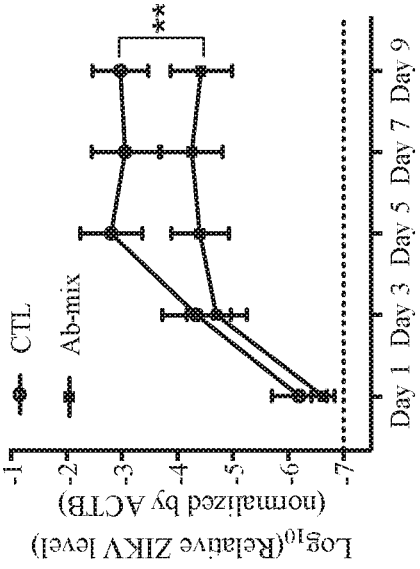


FIG. 7D

FIG. 7E

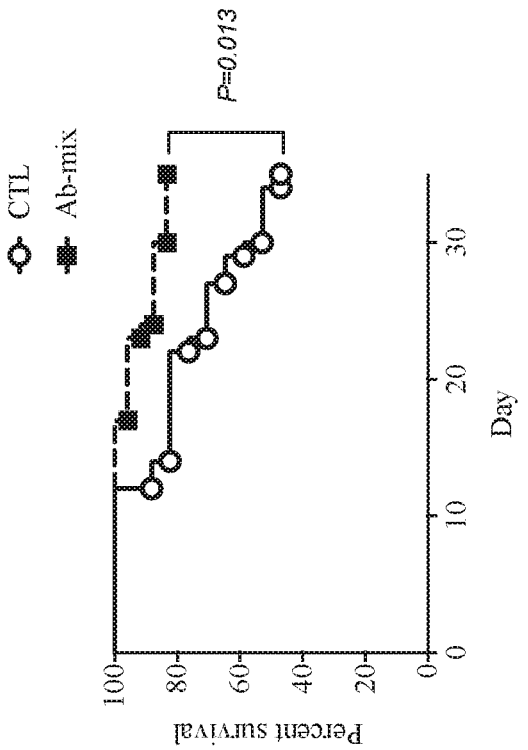


FIG. 8A

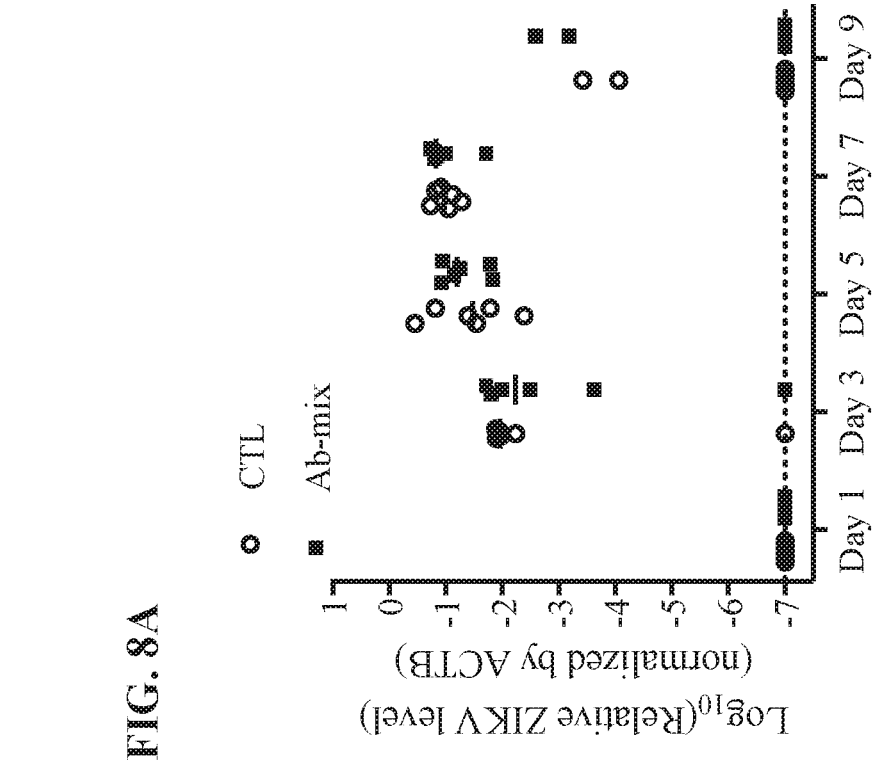
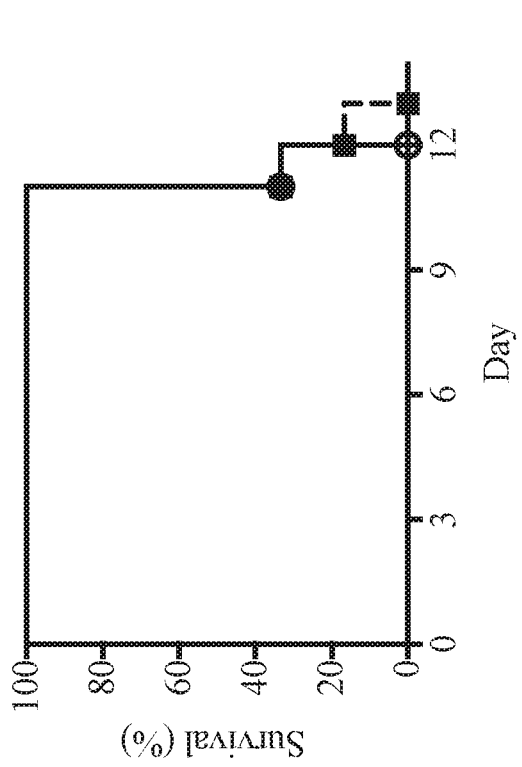

CTL
Ab-mix
Log10(Relative ZIKV level)
(normalized by ACTB)
1
0
-1
-2
-3
-4
-5
-6
-7
Day 1
Day 3
Day 5
Day 7
Day 9

FIG. 8B


CTL
Ab-mix
Survival (%)
100
80
60
40
20
0
0
3
6
9
12
Day

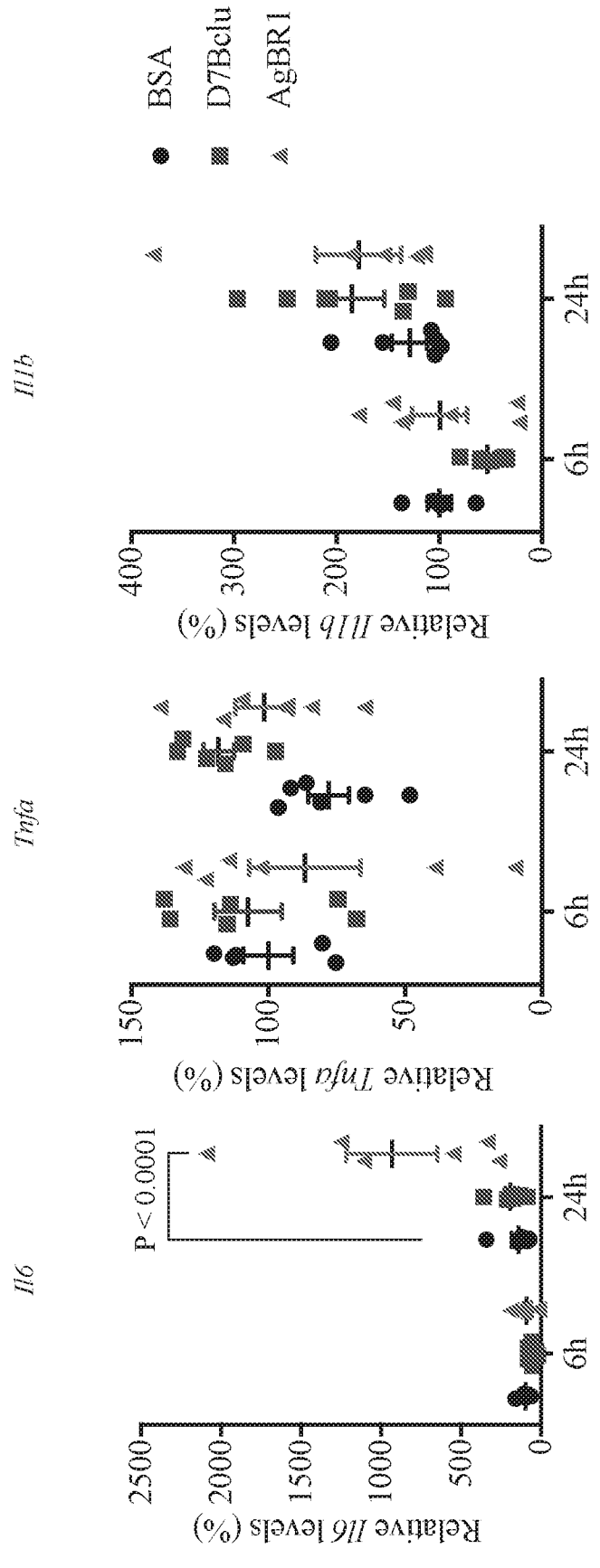

BSA
D7Bclu
AgBR1
Il6
Tnfa
Il1b
Relative Il6 levels (%)
Relative Tnfa levels (%)
Relative Il1b levels (%)
P < 0.0001
6h
24h
0
500
1000
1500
2000
2500
50
100
150
200
300
400

FIG. 9

FIG. 10A

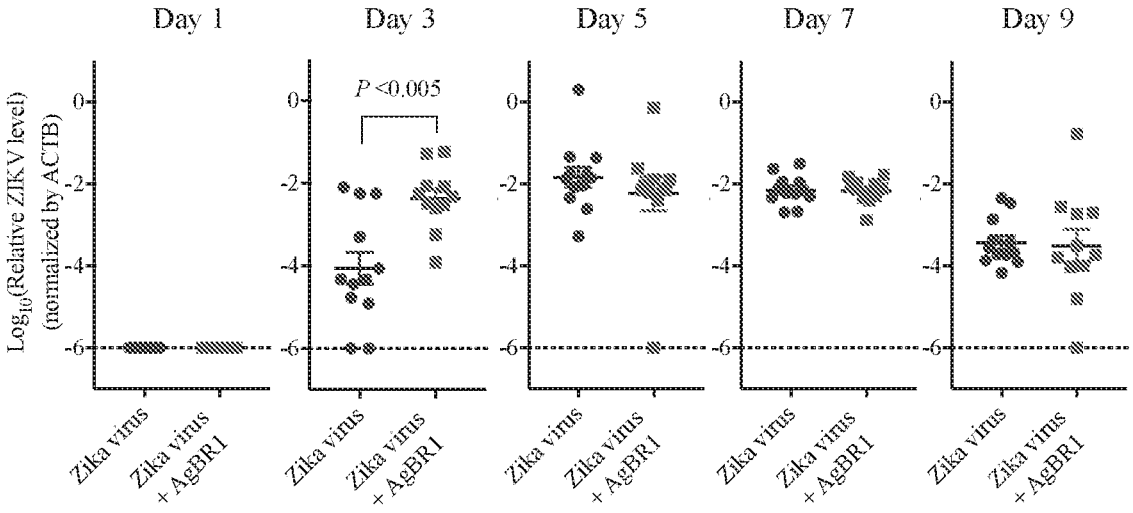
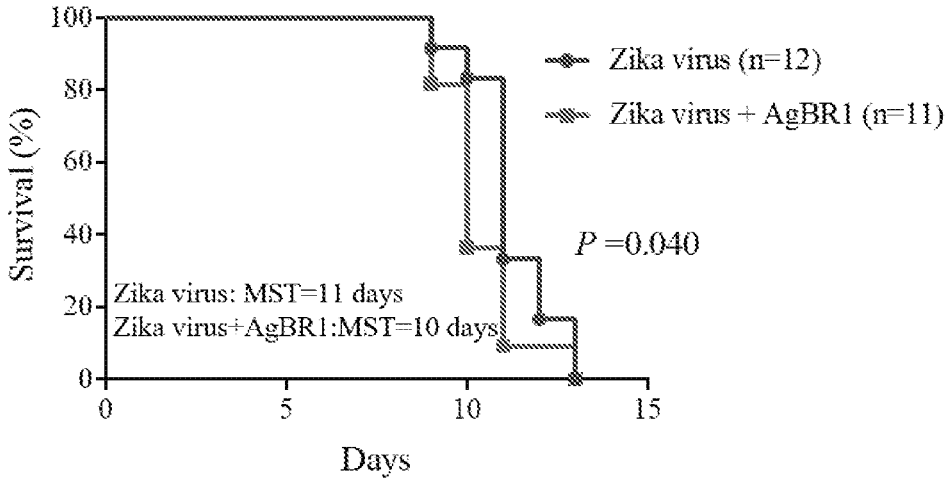


FIG. 10B



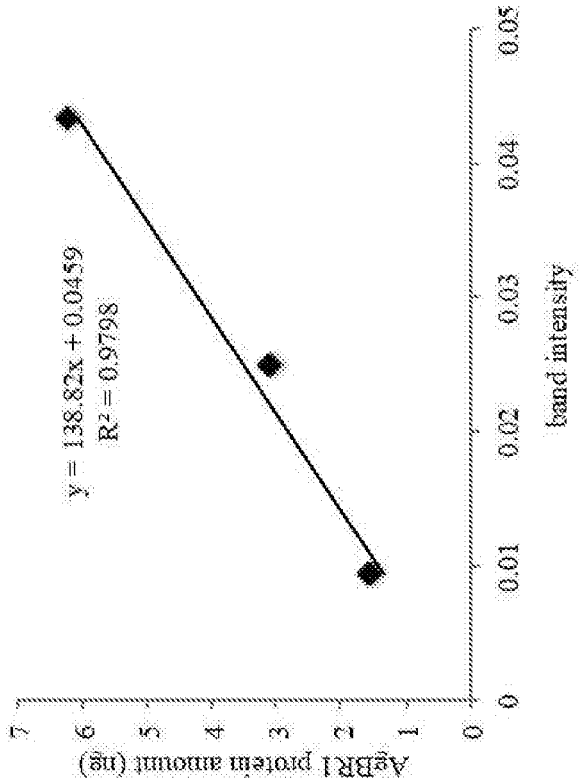
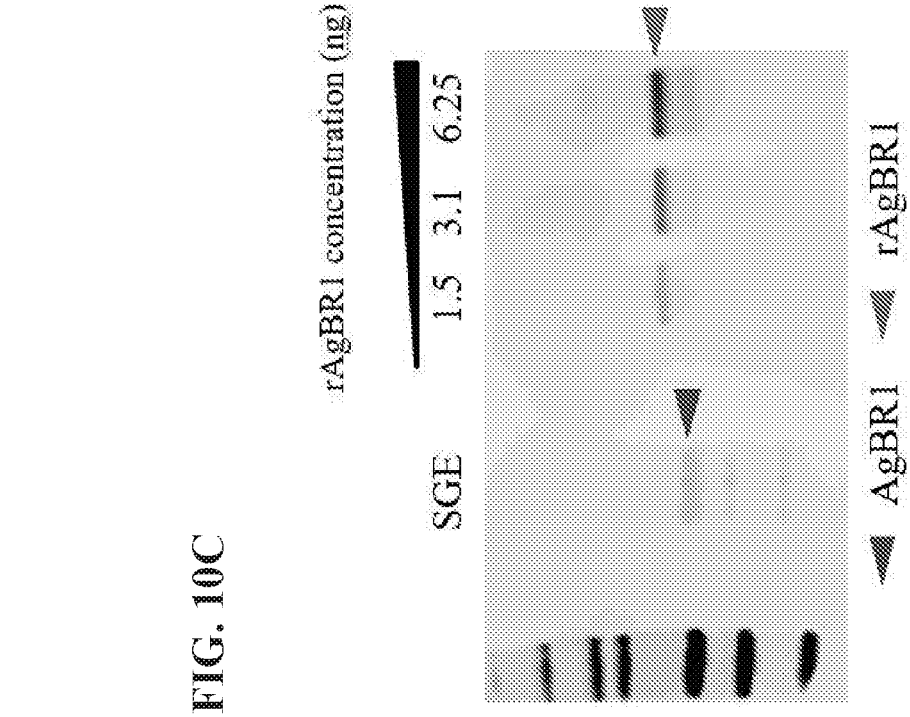

AgBR1 protein amount (ng)
0
1
2
3
4
5
6
7
y = 138.82x + 0.0459
R² = 0.9798
0
0.01
0.02
0.03
0.04
0.05
band intensity

FIG. 10C


rAgBR1 concentration (ng)
SGE
1.5
3.1
6.25
AgBR1
rAgBR1

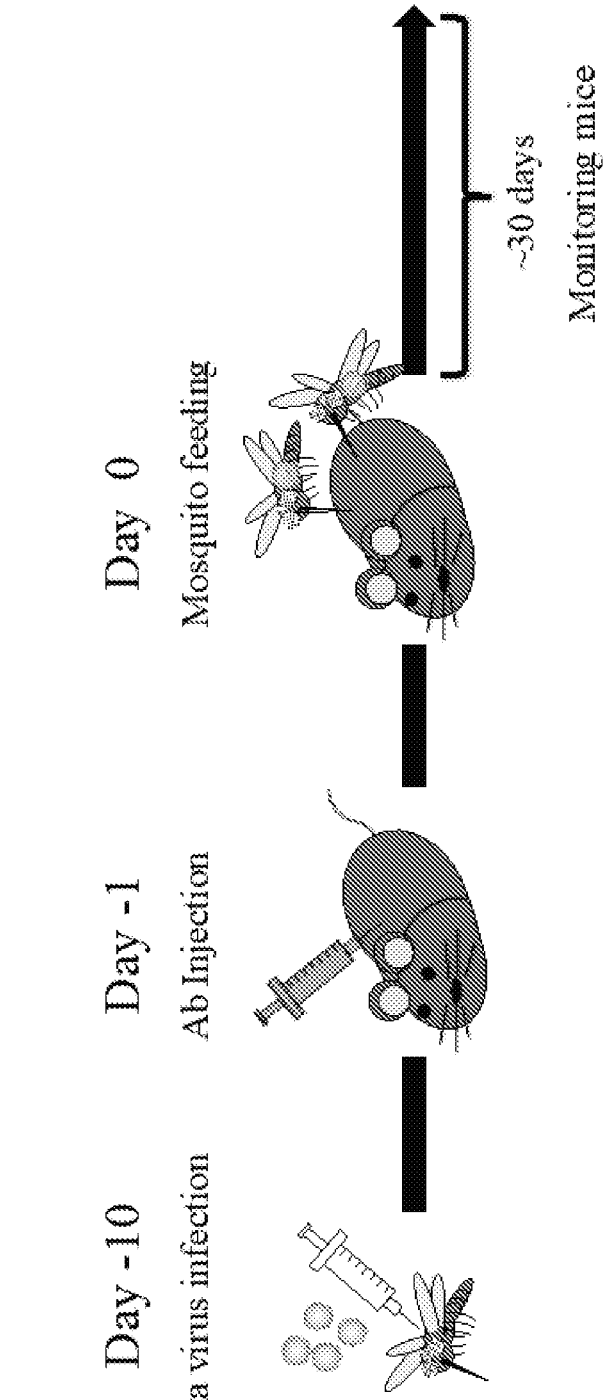

Day -10
Zika virus infection
Day -1
Ab Injection
Day 0
Mosquito feeding
~30 days
Monitoring mice

FIG. 11A

FIG. 11B

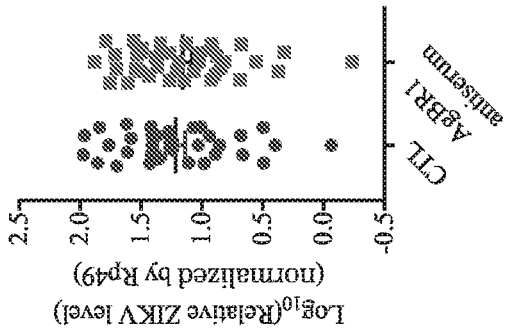


FIG. 11C

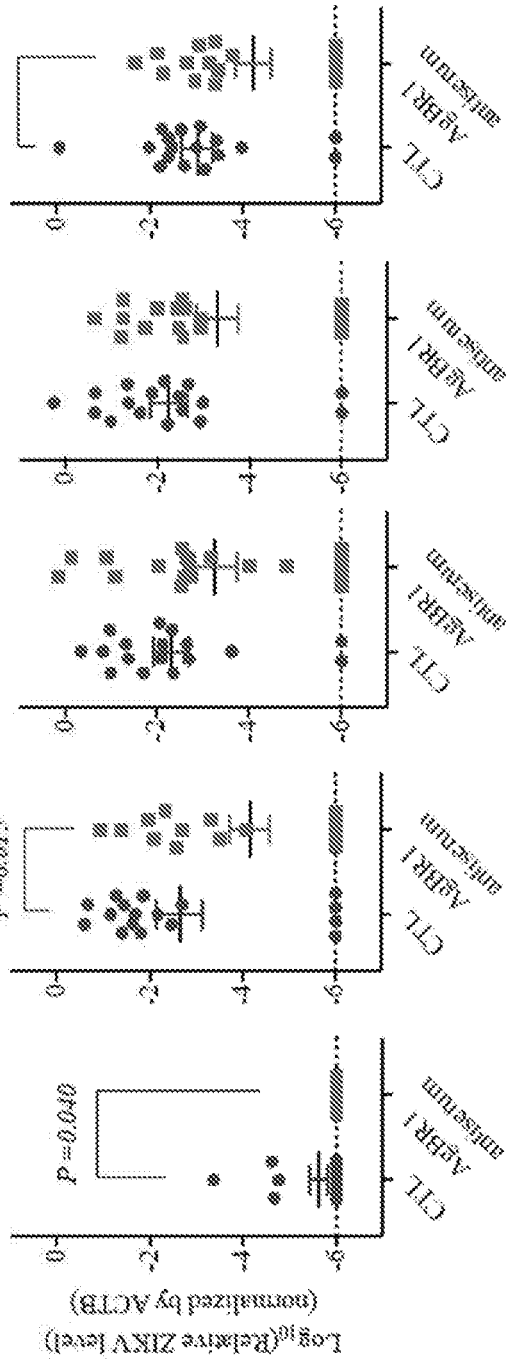


FIG. 11D

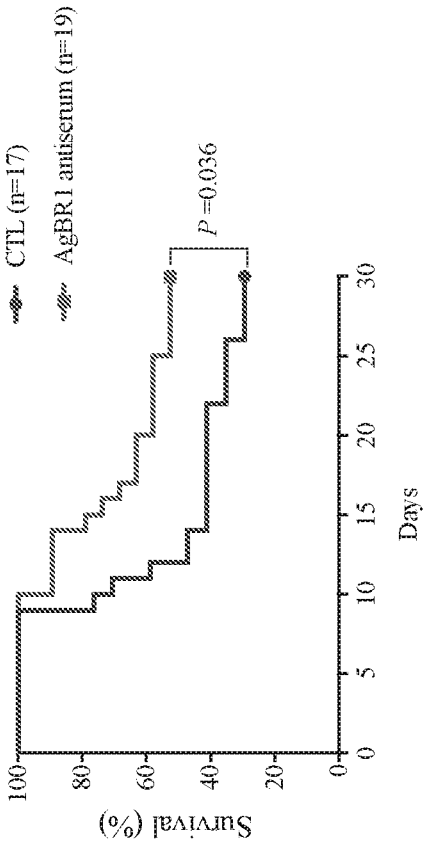
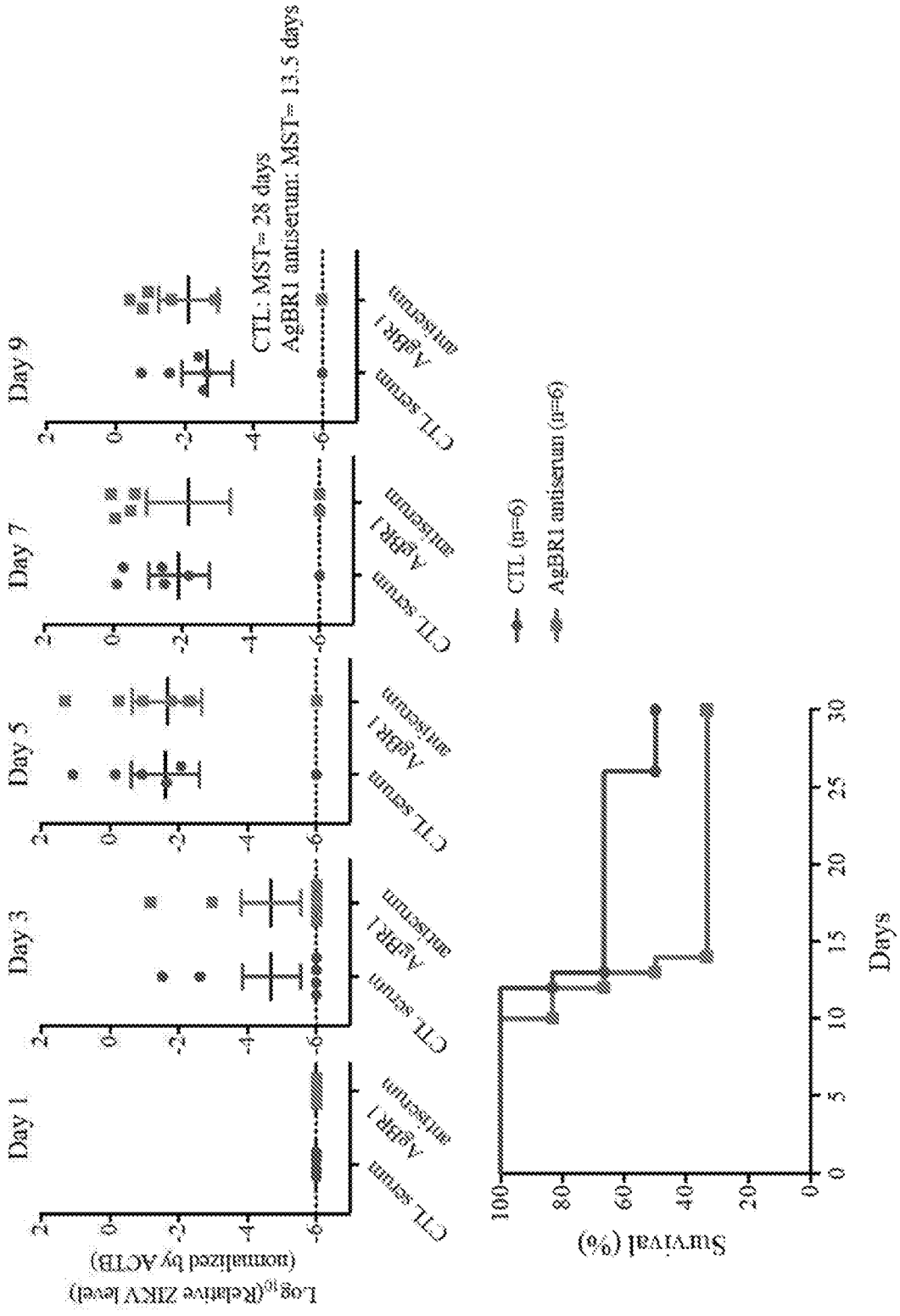


FIG. 11E


Log10(Relative ZIKV level)
(normalized by ACTB)
Day 1
Day 3
Day 5
Day 7
Day 9
CTL serum
AgBR1 antiserum
CTL: MST= 28 days
AgBR1 antiserum: MST= 13.5 days
CTL (n=6)
AgBR1 antiserum (n=6)
Survival (%)
Days

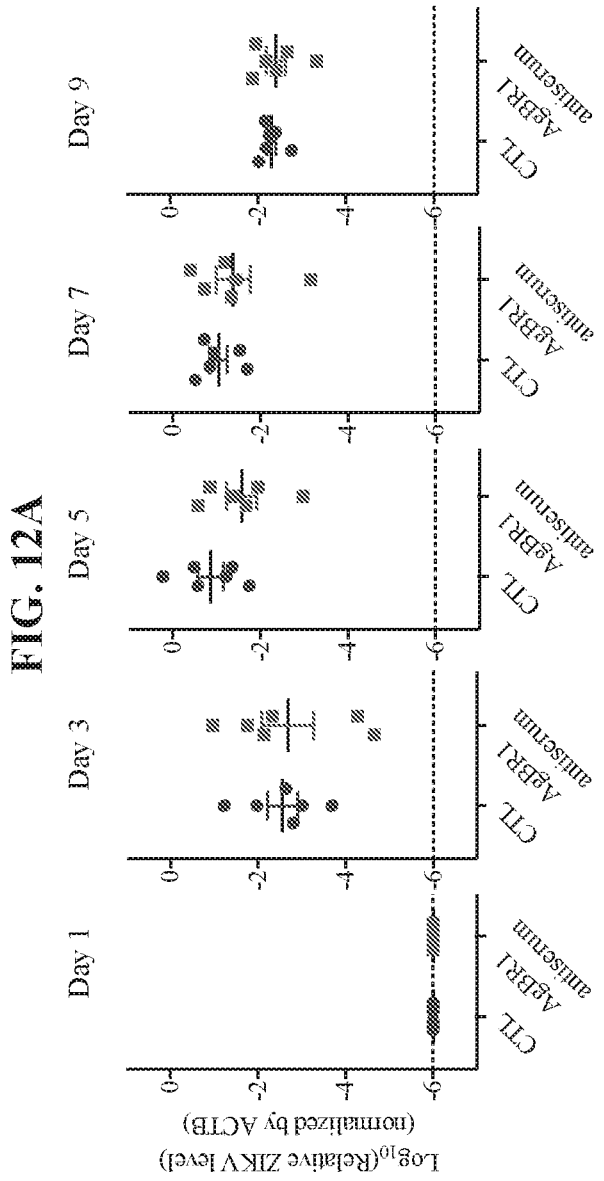


FIG. 12A

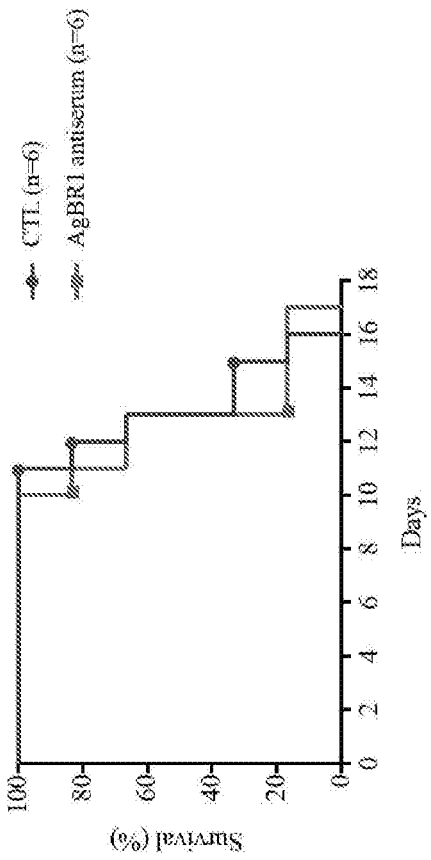


FIG. 12B

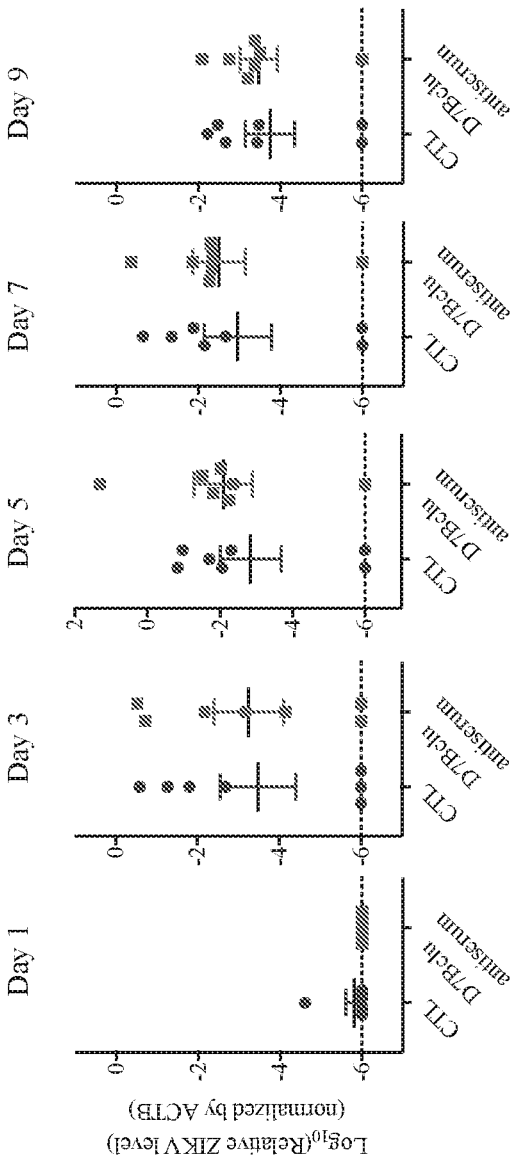


FIG. 13A CTL vs D7Bclu

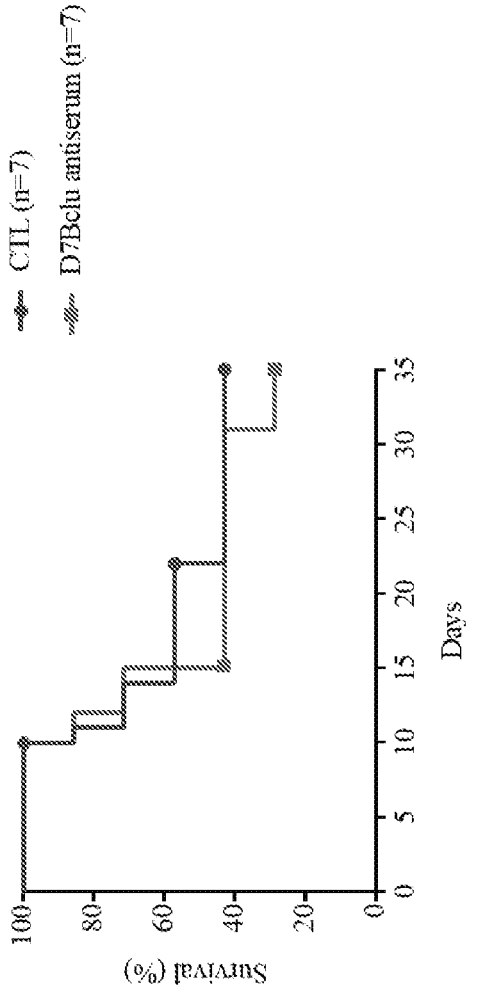


FIG. 13B

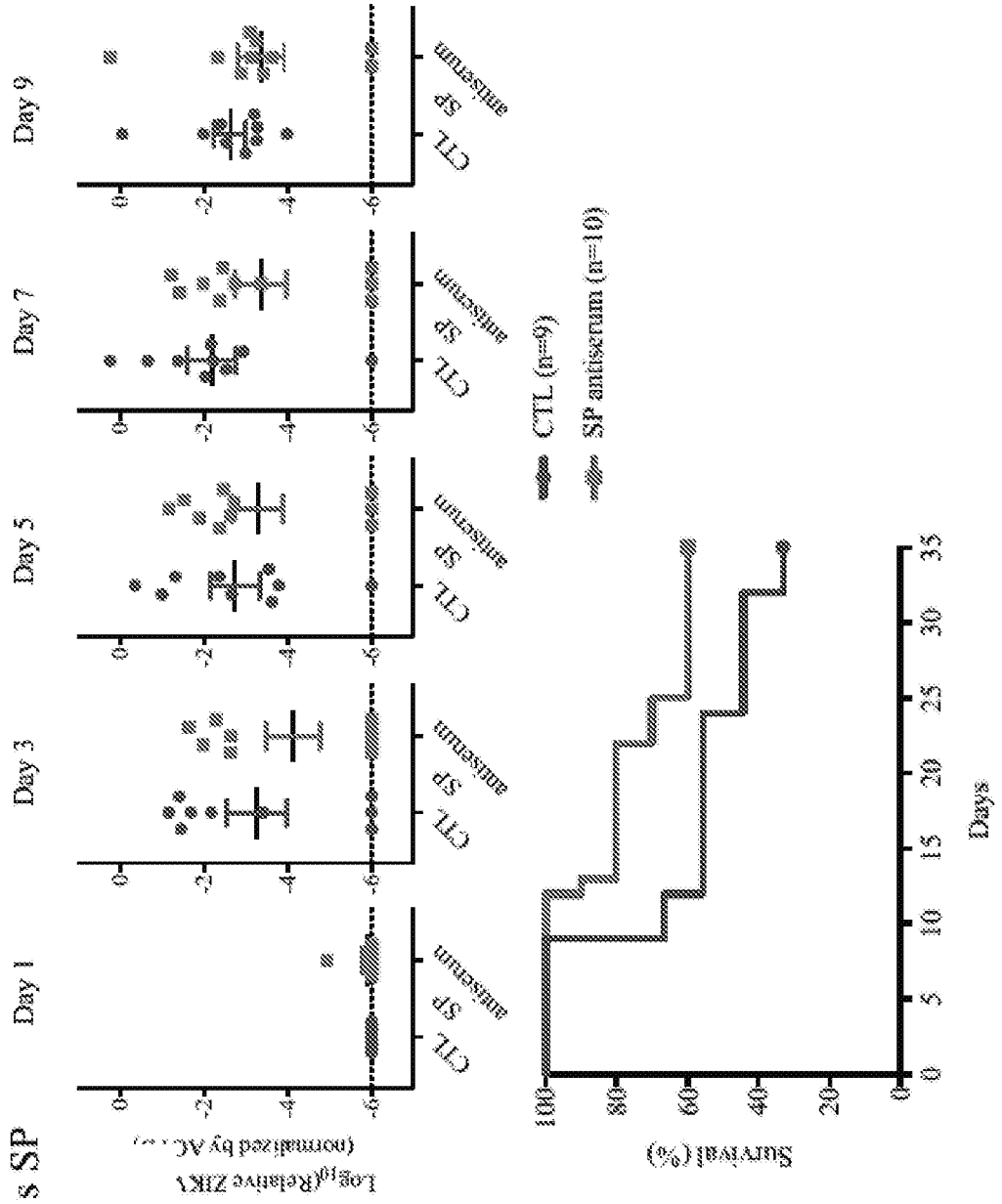


FIG. 13C CTL vs SP

FIG. 13D

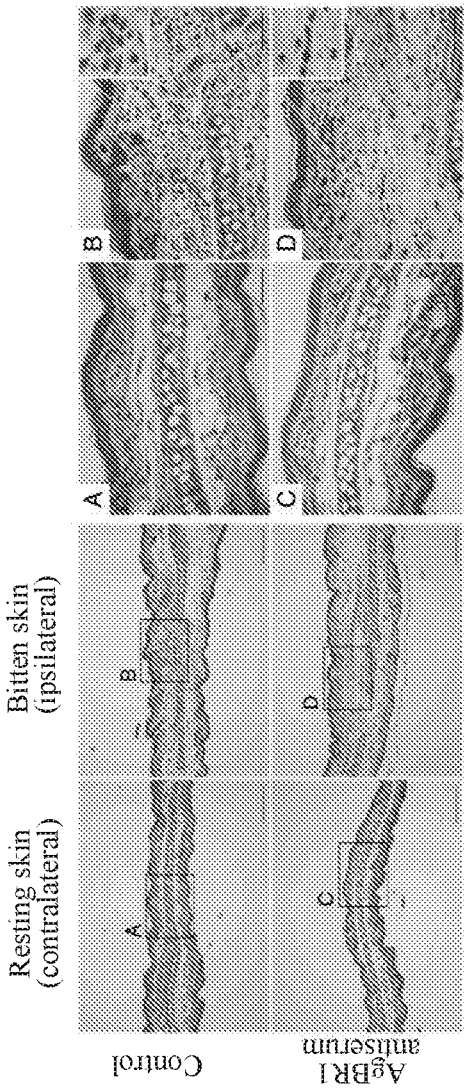


FIG. 14A

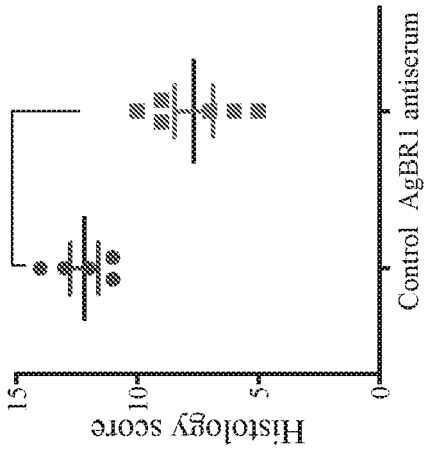


FIG. 14C

FIG. 14B

	Mock	Abx
Inflammation	3.6 ± 0.24	2.0 ± 0.26**
Neutrophils	3.6 ± 0.24	1.7 ± 0.21***
Mononuclear cells	2.4 ± 0.24	1.5 ± 0.22*
Edema	2.6 ± 0.40	2.5 ± 0.34

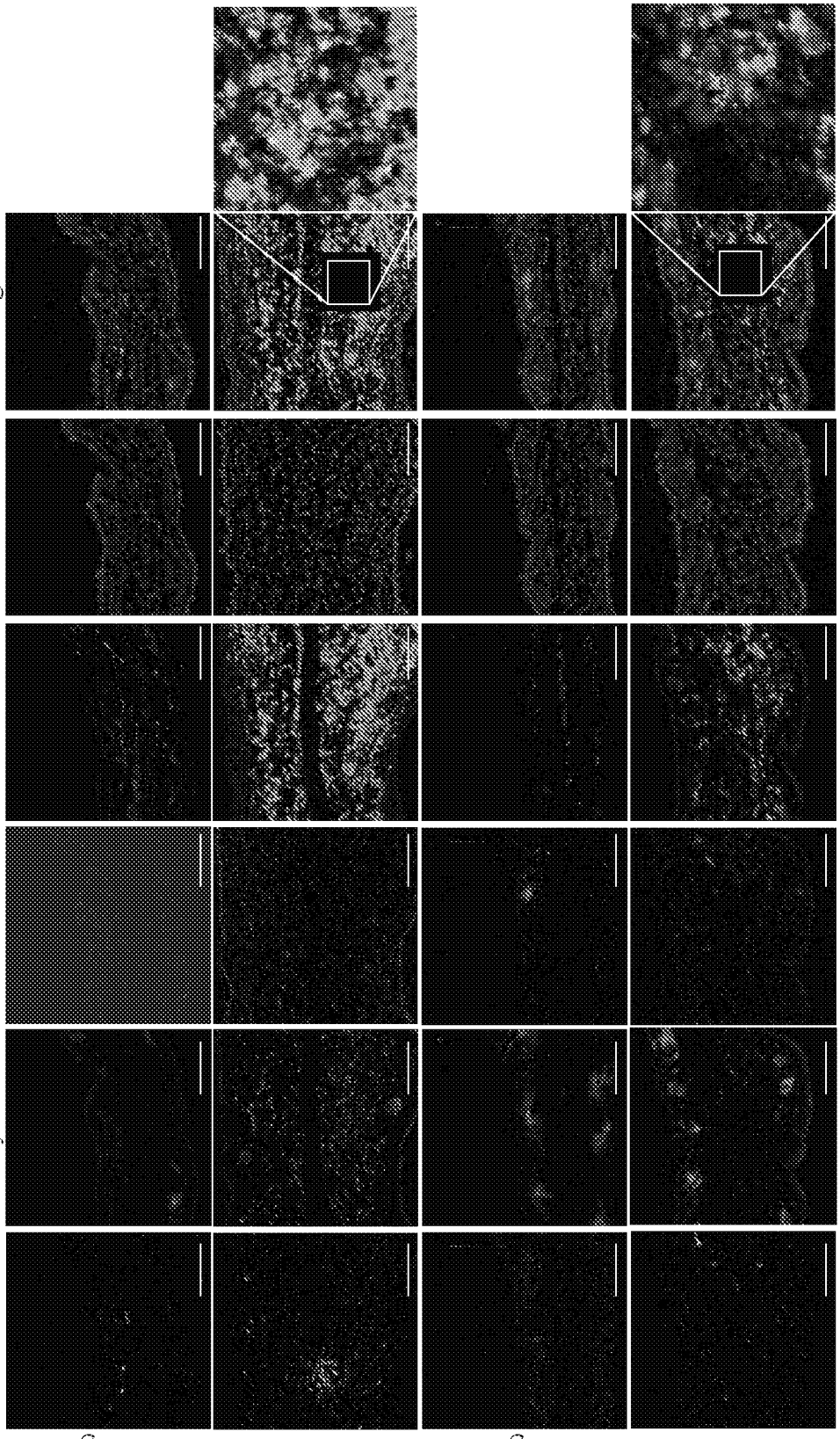

Merge
DNA
CD11b
MHCII
Ly6G
CD3
Resting skin
Bitten skin
Control
Resting skin
Bitten skin
AgBR1 antiserum

FIG. 14D

FIG. 14E

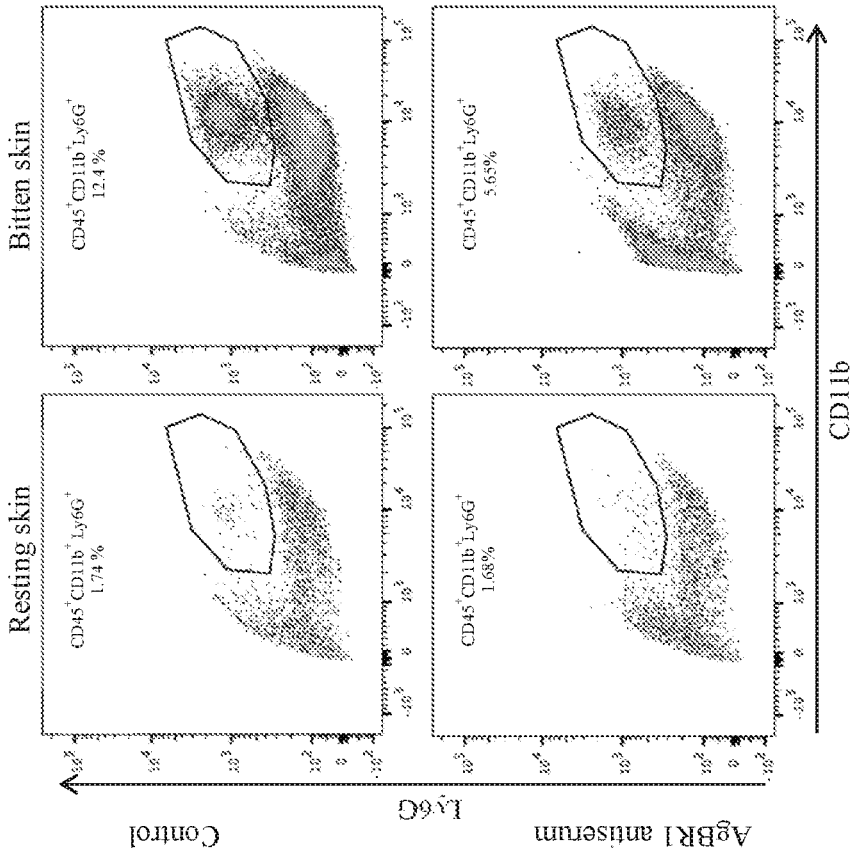
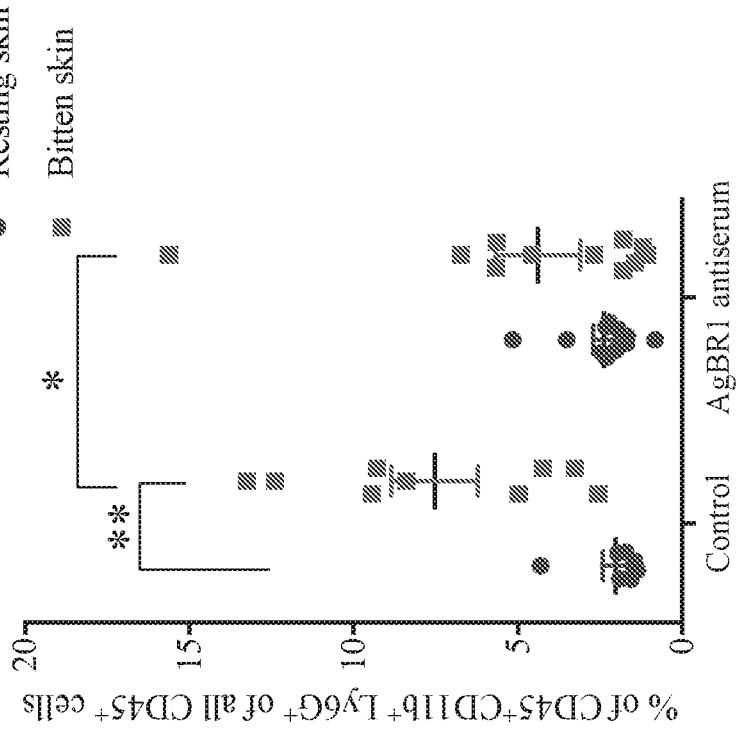


FIG. 14F



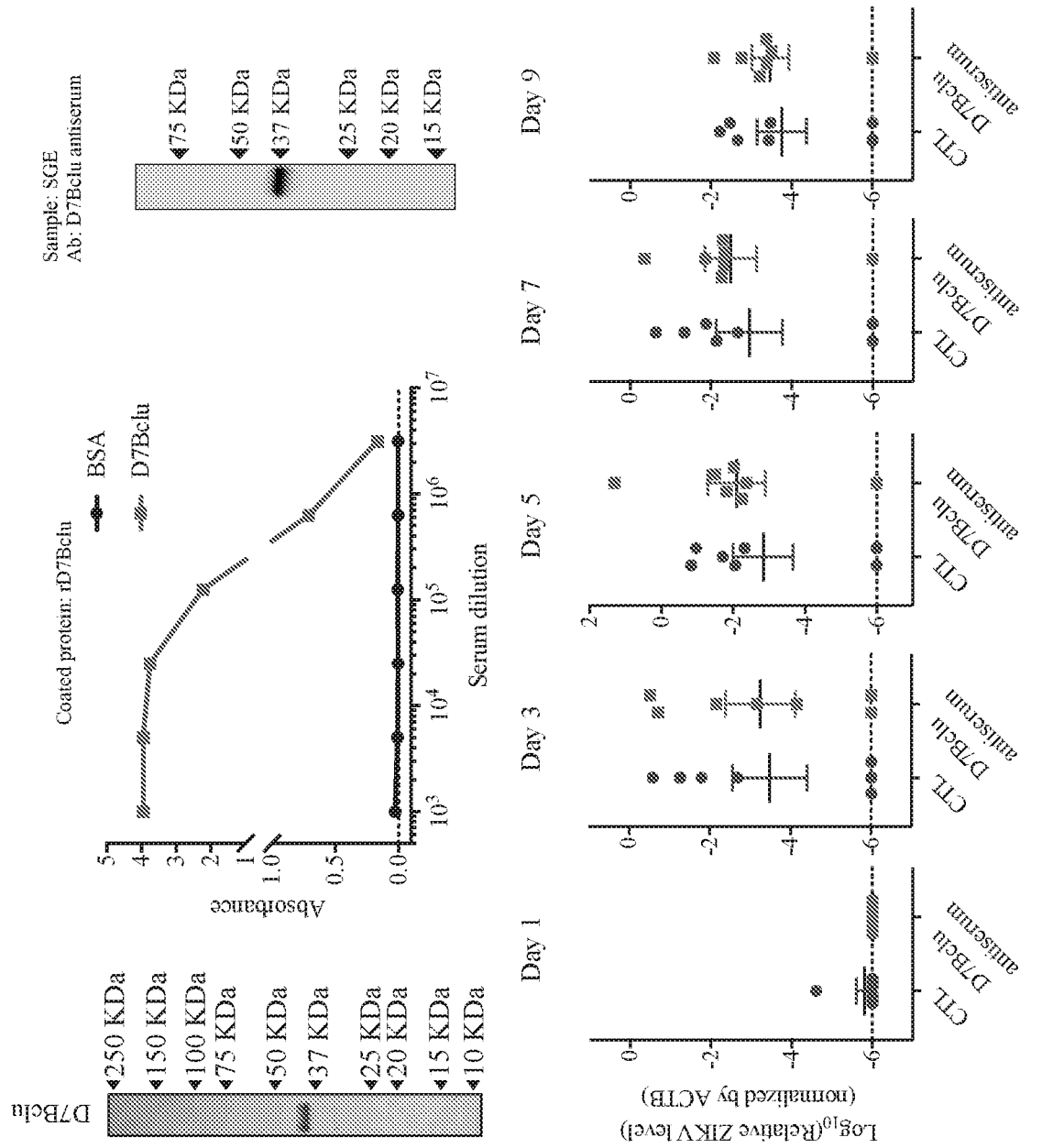

D7Bclu
250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa
Coated protein: rD7Bclu
BSA
D7Bclu
Absorbance
Serum dilution
Sample: SGE
Ab: D7Bclu antiserum
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
Day 1
Day 3
Day 5
Day 7
Day 9
CTL
D7Bclu antiserum
Log10(Relative ZIKV level)
(normalized by ACTB)

FIG. 14G

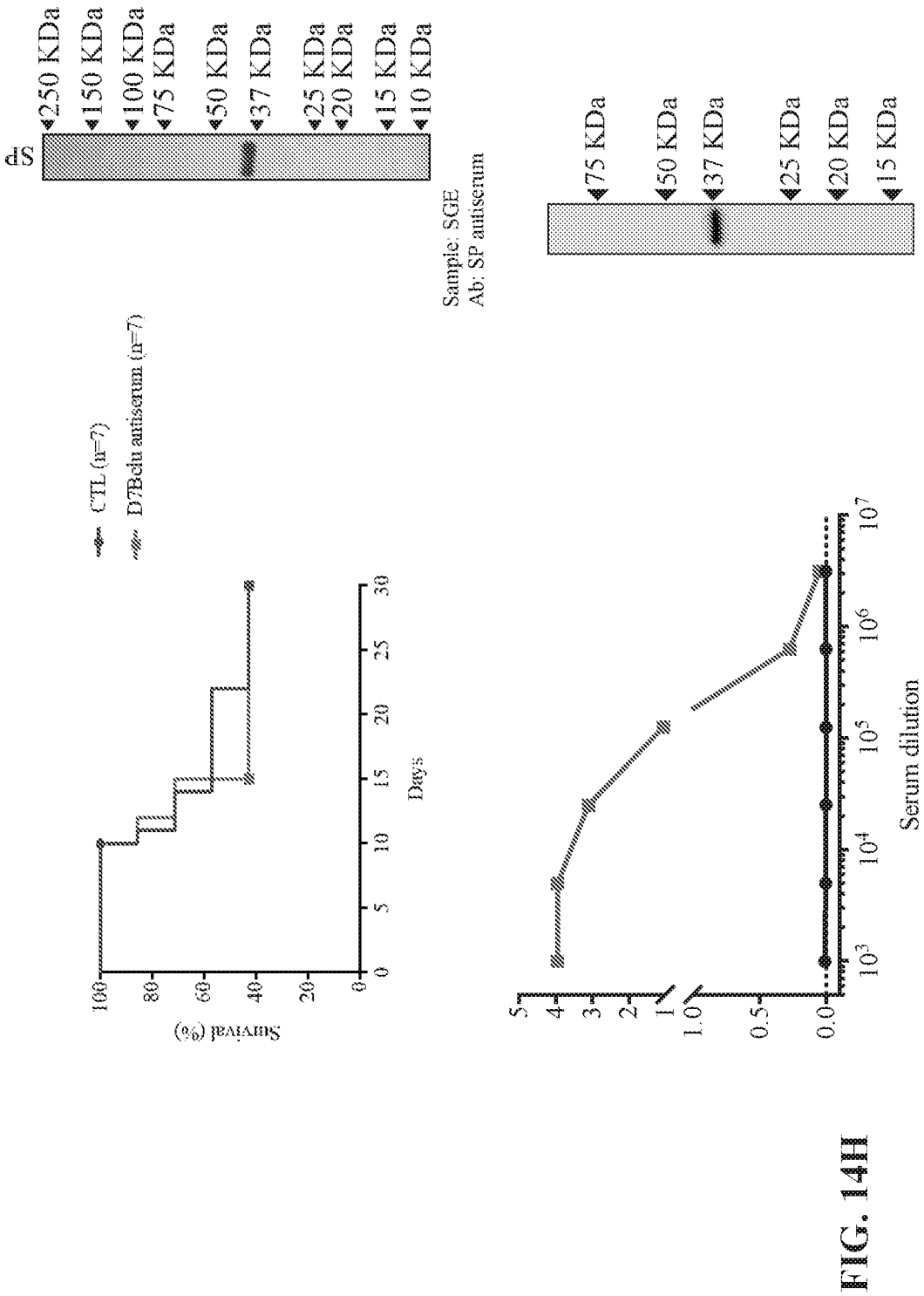

SP
250 KDa
150 KDa
100 KDa
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
10 KDa
Sample: SGE
Ab: SP antiserum
75 KDa
50 KDa
37 KDa
25 KDa
20 KDa
15 KDa
CTL (n=7)
D7Bclu antiserum (n=7)
Survival (%)
Days
Serum dilution

FIG. 14H

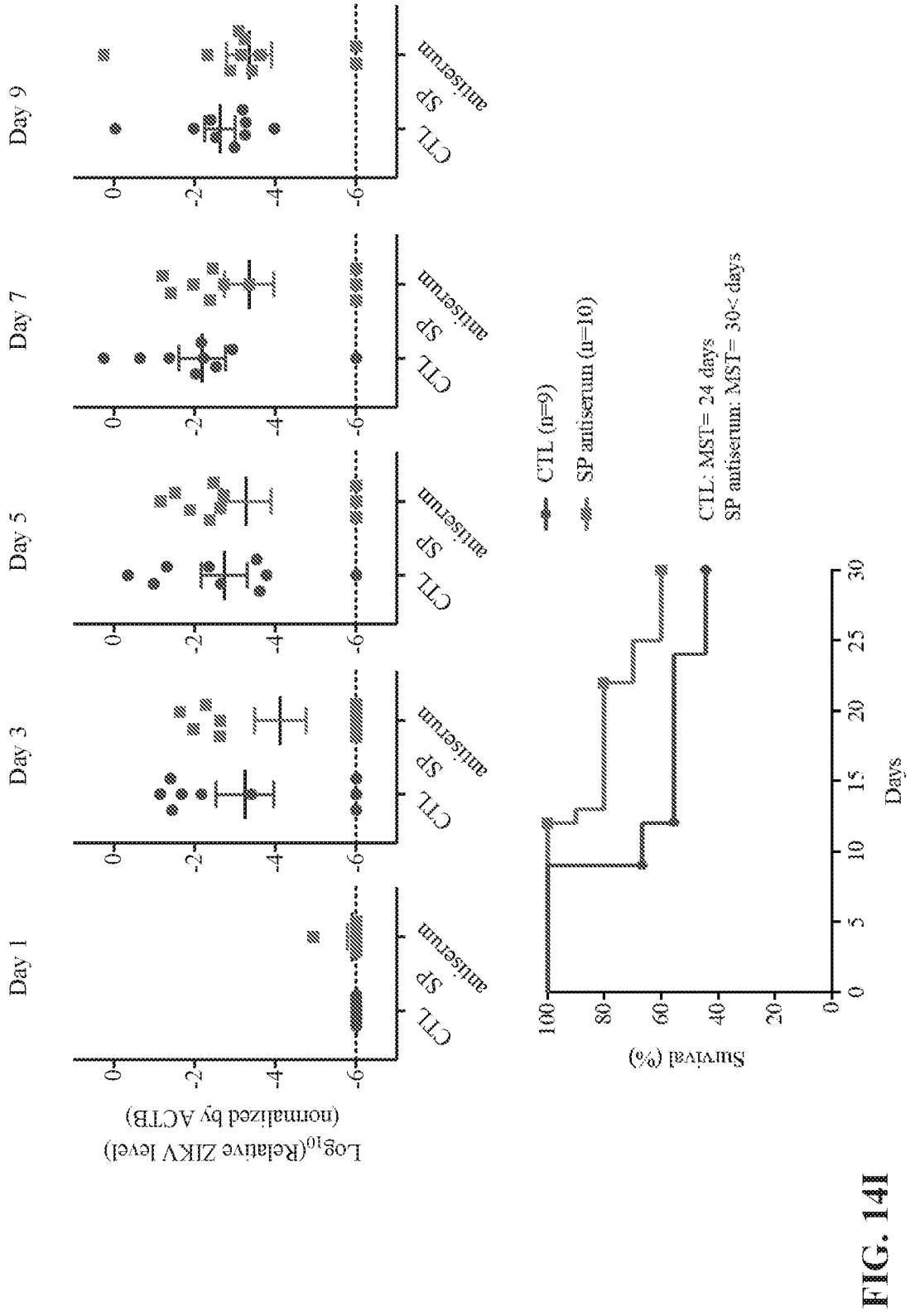
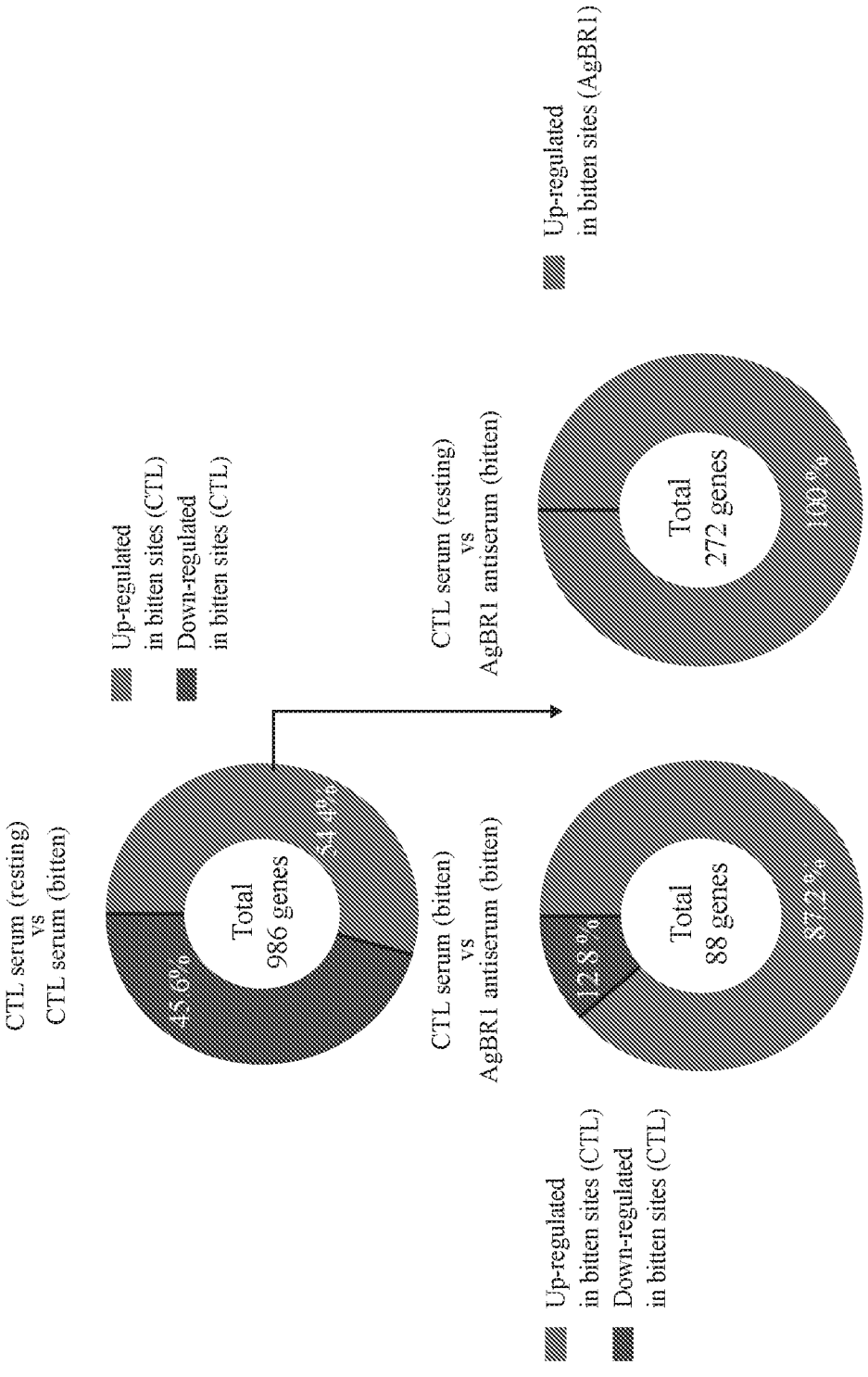

Day 1
Day 3
Day 5
Day 7
Day 9
CTL
SP antiserum
Log10(Relative ZIKV level)
(normalized by ACTB)
0
-2
-4
-6
CTL (n=9)
SP antiserum (n=10)
CTL: MST= 24 days
SP antiserum: MST= 30< days
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
Days

FIG. 14I

FIG. 15A


CTL serum (resting)
vs
CTL serum (bitten)
Up-regulated
in bitten sites (CTL)
Down-regulated
in bitten sites (CTL)
Total
986 genes
45.6%
54.4%
CTL serum (bitten)
vs
AgBR1 antiserum (bitten)
Up-regulated
in bitten sites (CTL)
Down-regulated
in bitten sites (CTL)
Total
88 genes
12.8%
87.2%
CTL serum (resting)
vs
AgBR1 antiserum (bitten)
Up-regulated
in bitten sites (AgBR1)
Total
272 genes
100%

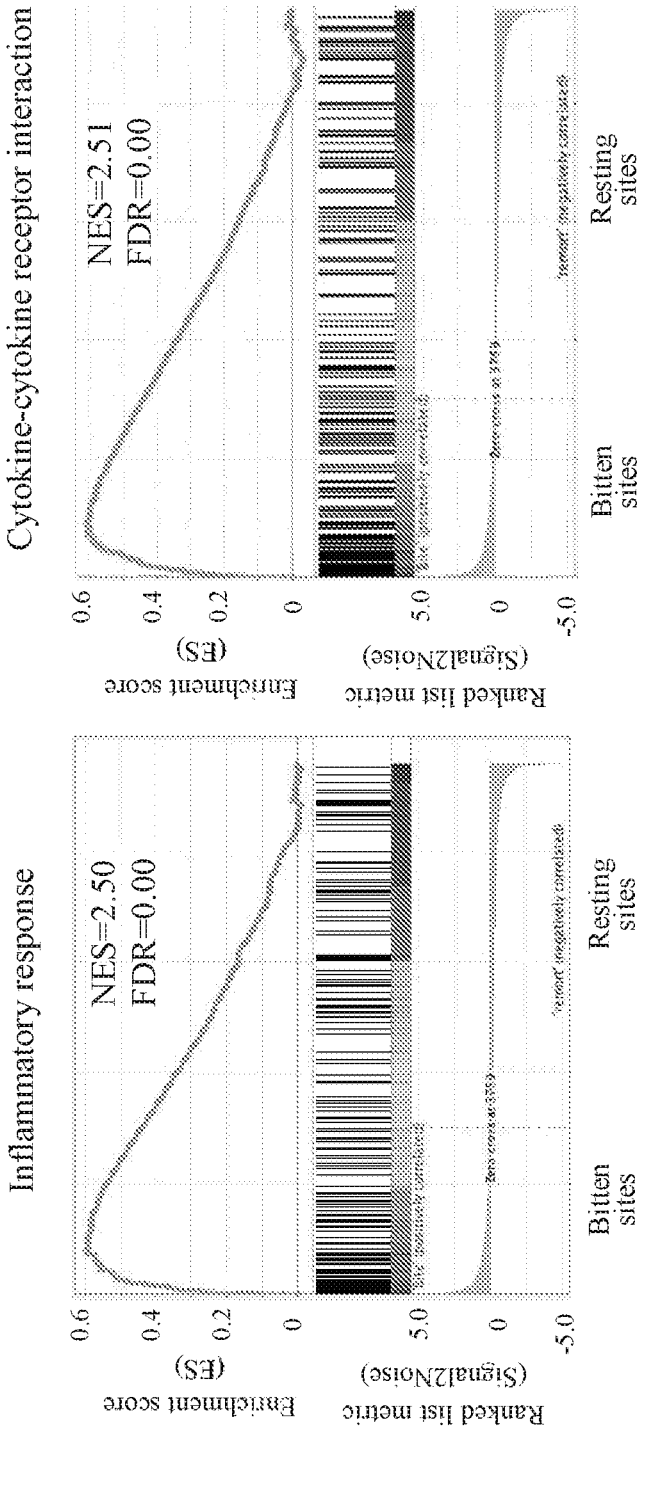

Inflammatory response
NES=2.50
FDR=0.00
Enrichment score (ES)
Ranked list metric (Signal2Noise)
Bitten sites
Resting sites
Cytokine-cytokine receptor interaction
NES=2.51
FDR=0.00
Enrichment score (ES)
Ranked list metric (Signal2Noise)
Bitten sites
Resting sites

FIG. 15B

FIG. 15C

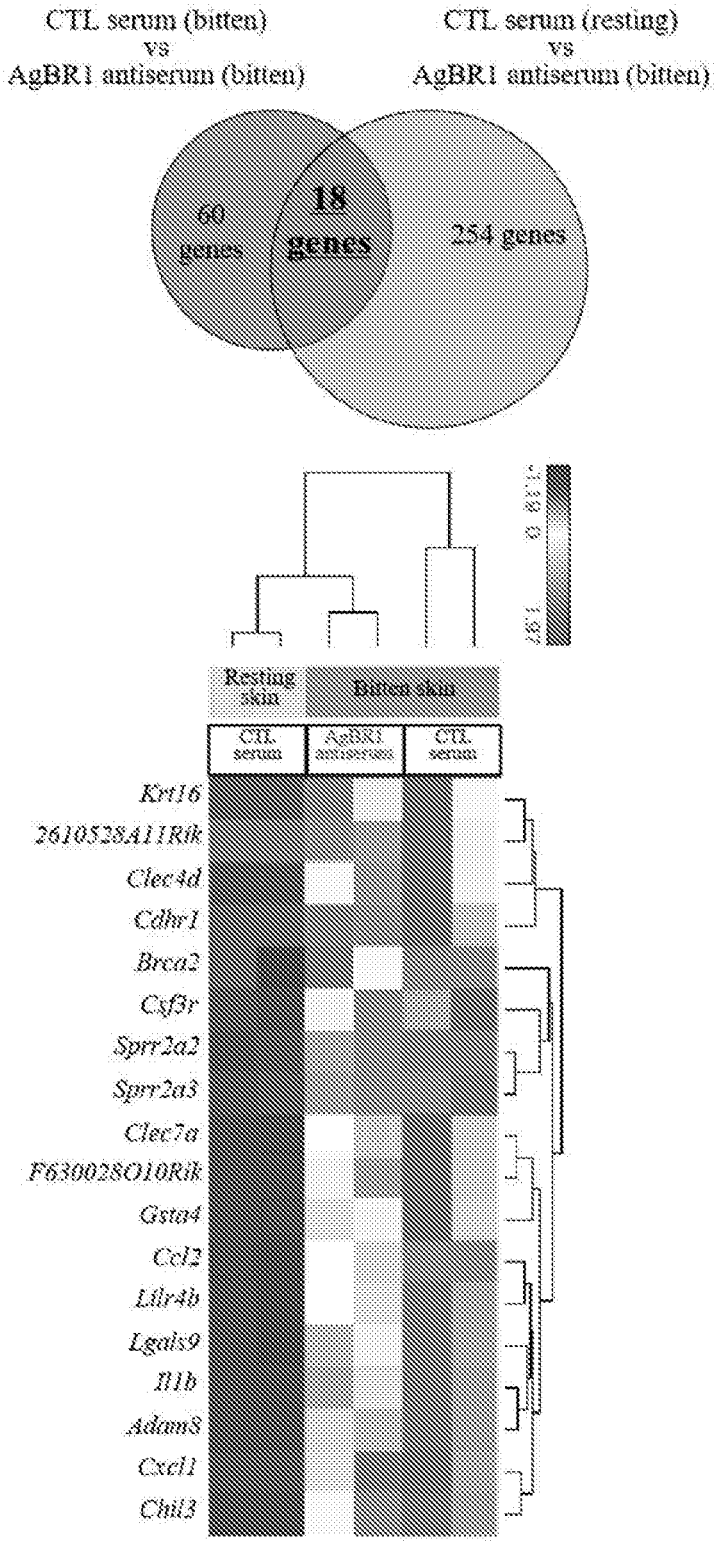

CTL serum (bitten)
vs
AgBR1 antiserum (bitten)
CTL serum (resting)
vs
AgBR1 antiserum (bitten)
60 genes
18 genes
254 genes
1.39
0
-1.39
Resting skin
Bitten skin
CTL serum
AgBR1 antiserum
CTL serum
Krt16
2610528A11Rik
Clec4d
Cdhr1
Brca2
Csf3r
Sprr2a2
Sprr2a3
Clec7a
F630028O10Rik
Gsta4
Ccl2
Lilr4b
Lgals9
Il1b
Adam8
Cxcl1
Chil3

FIG. 15D

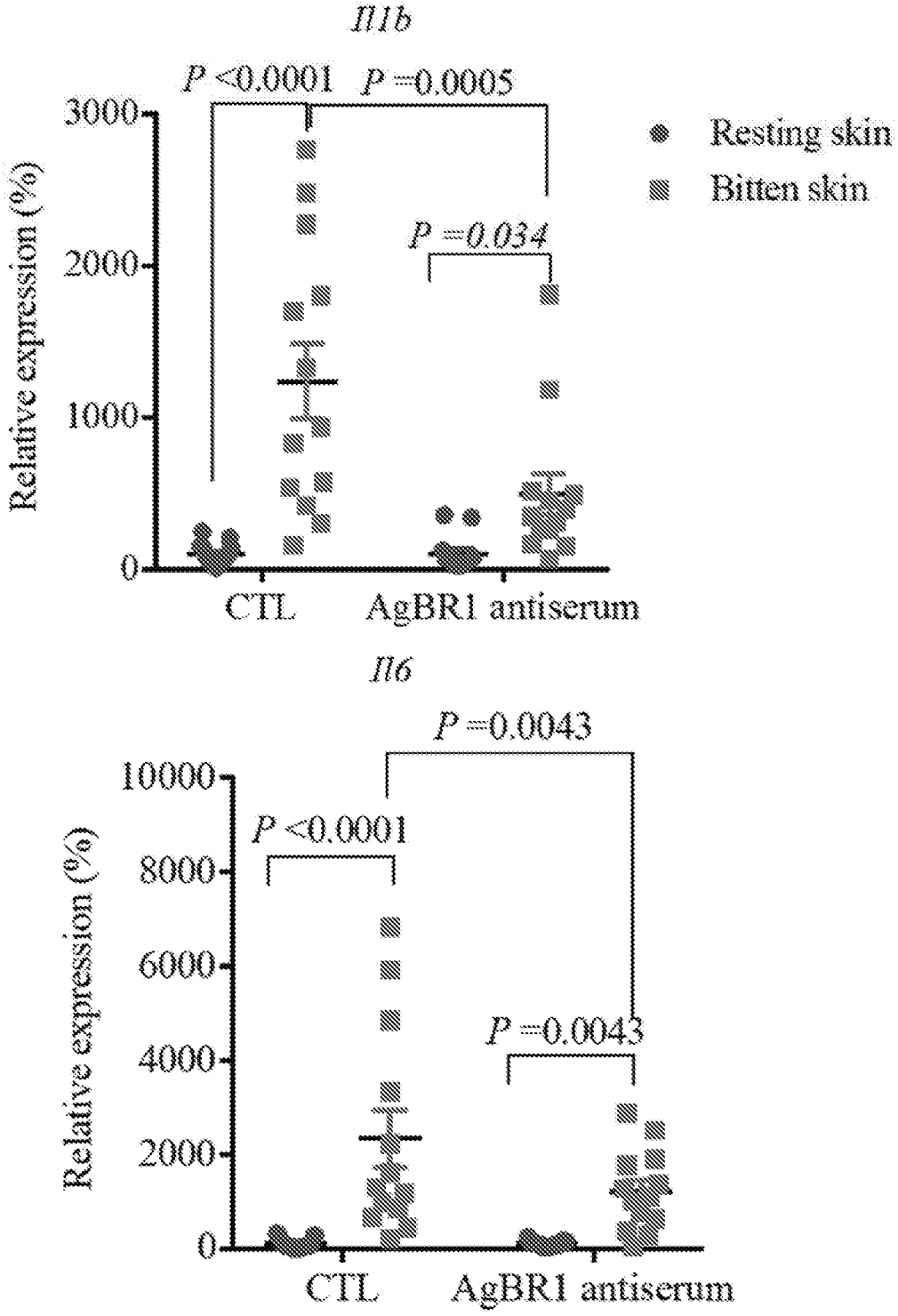
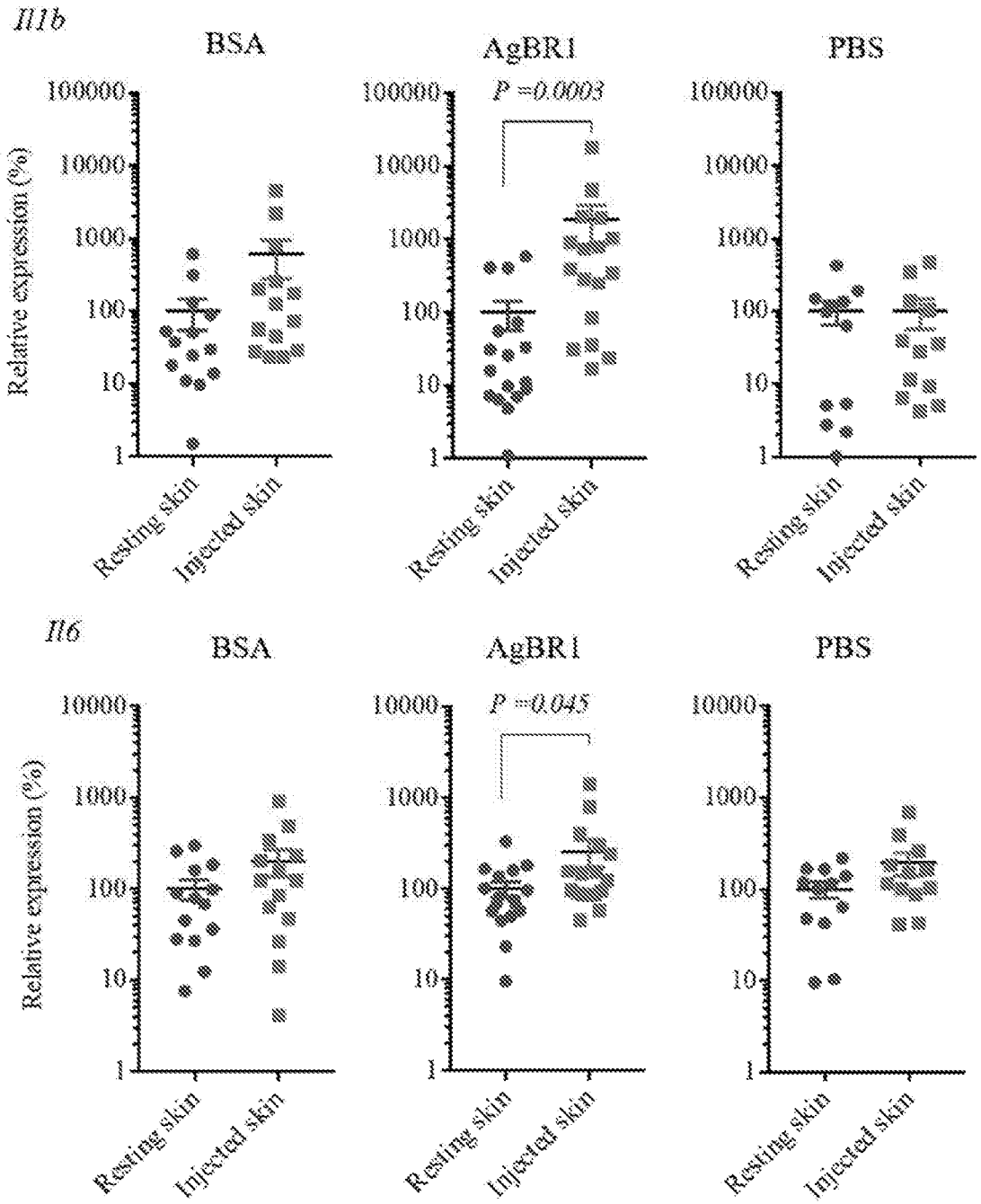

Il1b
P <0.0001
P =0.0005
P =0.034
Resting skin
Bitten skin
Relative expression (%)
3000
2000
1000
0
CTL
AgBR1 antiserum
Il6
P =0.0043
P <0.0001
P =0.0043
Relative expression (%)
10000
8000
6000
4000
2000
0
CTL
AgBR1 antiserum

FIG. 15E


Il1b
BSA
AgBR1
PBS
P =0.0003
Relative expression (%)
100000
10000
1000
100
10
1
Resting skin
Injected skin
Il6
BSA
AgBR1
PBS
P =0.045
Relative expression (%)
10000
1000
100
10
1
Resting skin
Injected skin

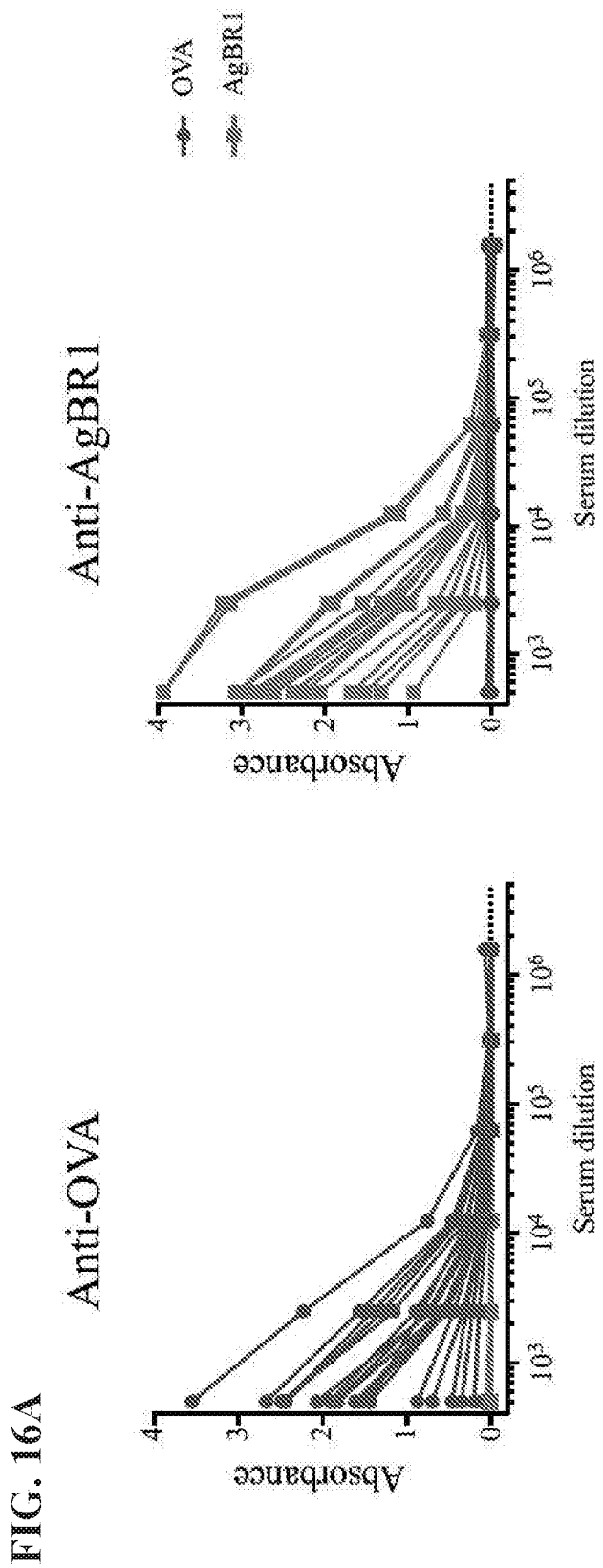

Anti-AgBR1
OVA
AgBR1
Absorbance
0
1
2
3
4
10^3
10^4
10^5
10^6
Serum dilution
Anti-OVA
Absorbance
0
1
2
3
4
10^3
10^4
10^5
10^6
Serum dilution

FIG. 16A

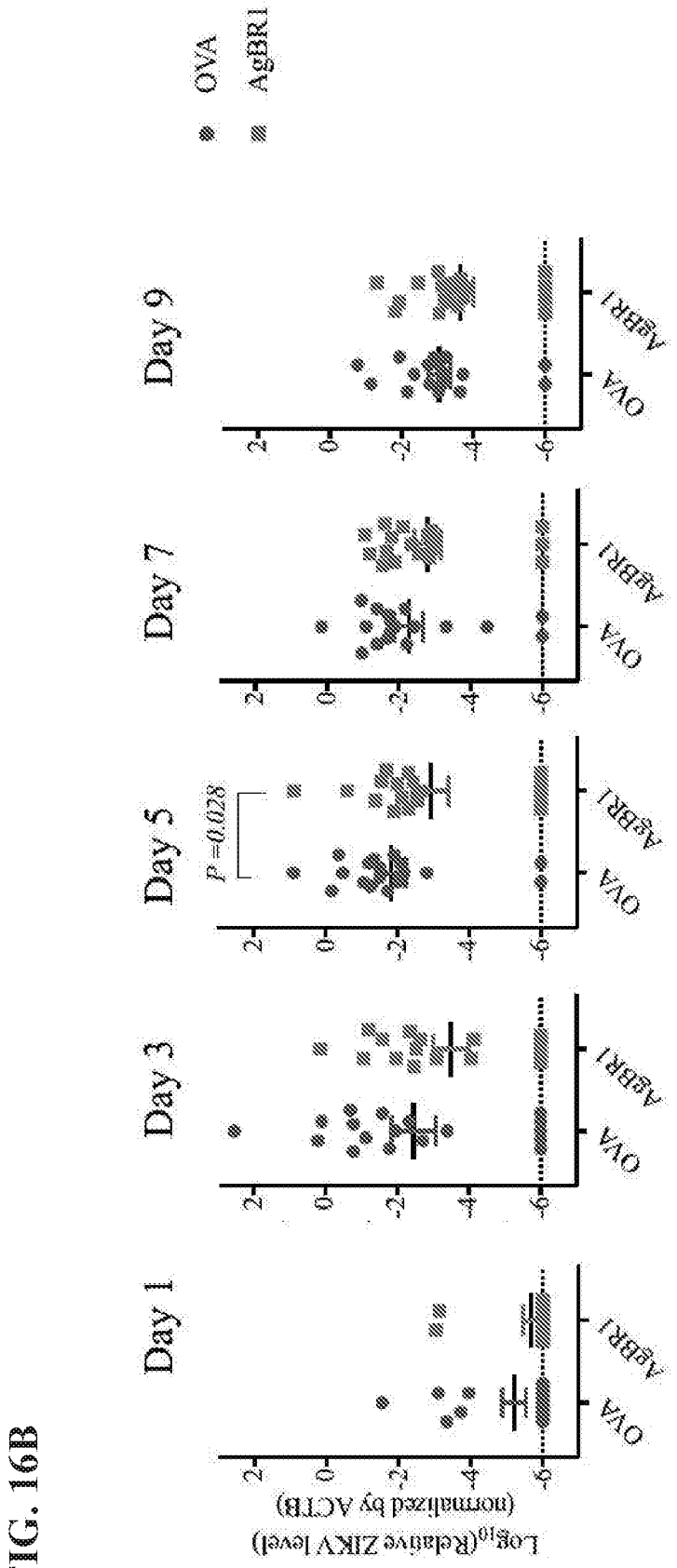

OVA
AgBR1
Day 1
Day 3
Day 5
Day 7
Day 9
P =0.028
Log10(Relative ZIKV level)
(normalized by ACTB)
2
0
-2
-4
-6

FIG. 16B

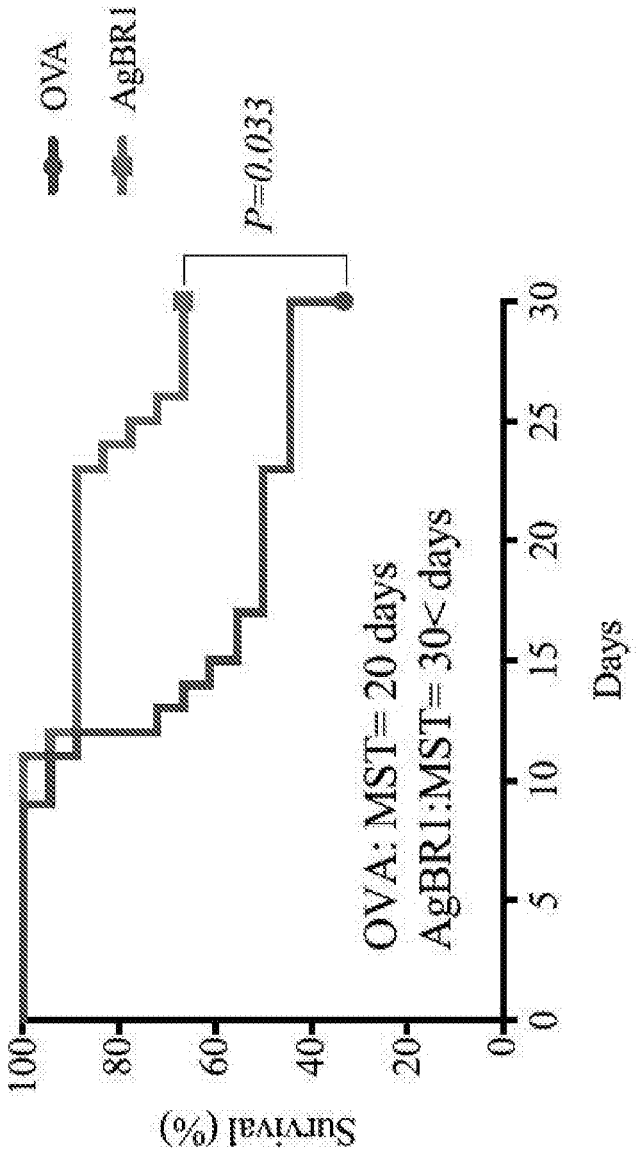

OVA
AgBR1
P=0.033
OVA: MST= 20 days
AgBR1:MST= 30< days
Survival (%)
100
80
60
40
20
0
0
5
10
15
20
25
30
Days

FIG. 16C

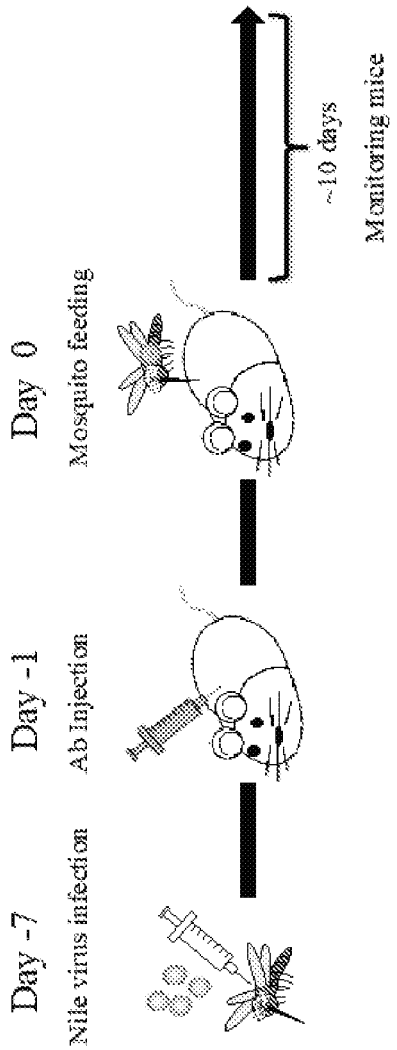


FIG. 17A

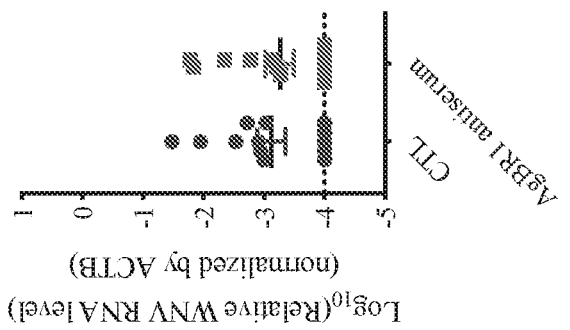


FIG. 17B

FIG. 17C

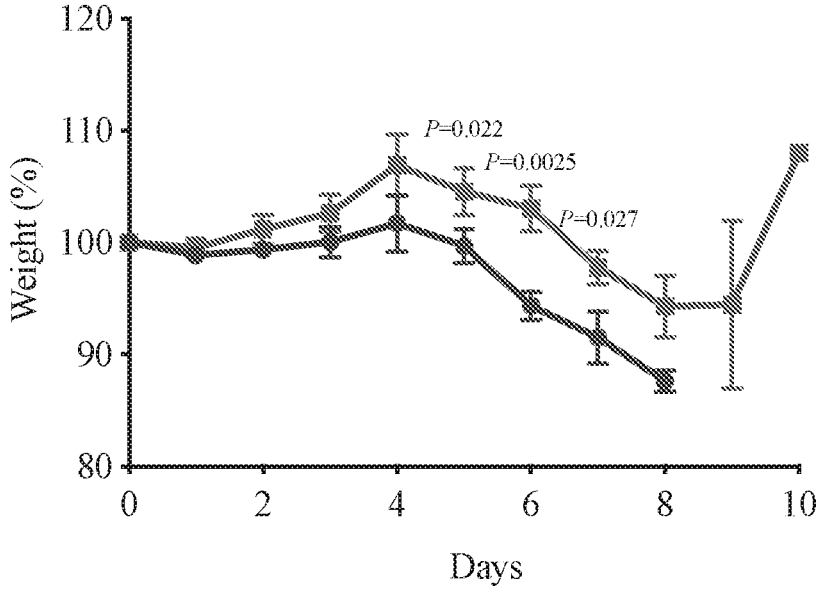
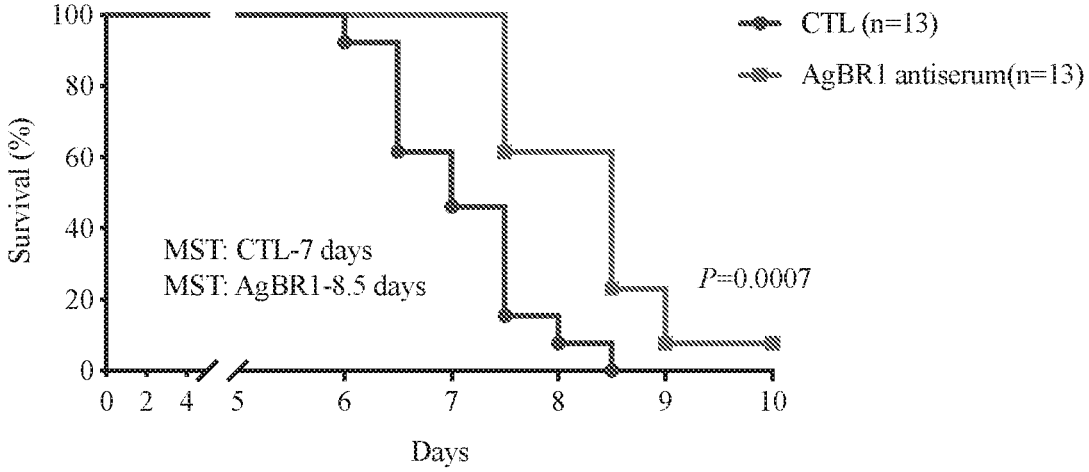


FIG. 17D



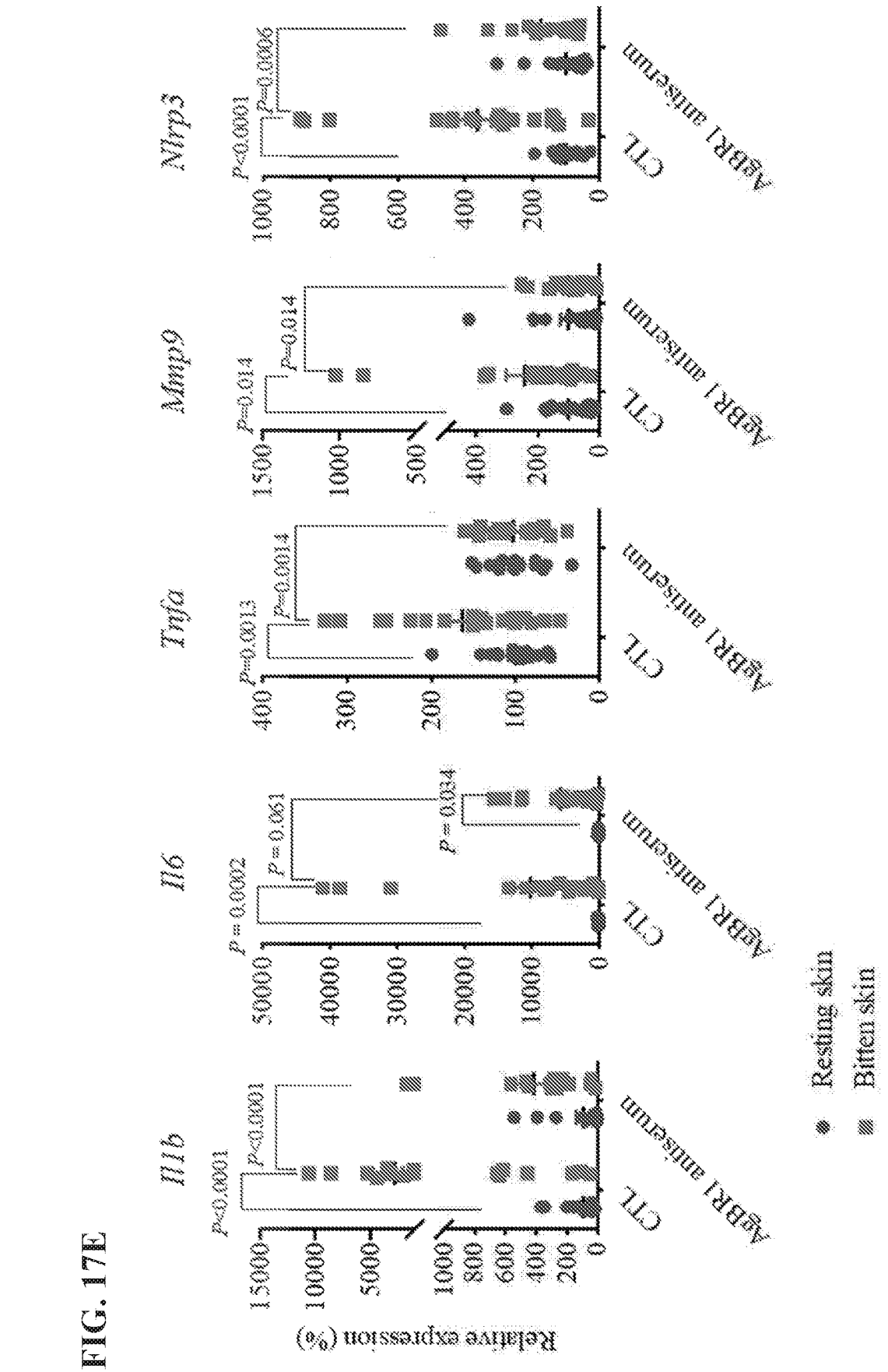

Il1b
Il6
Tnfa
Mmp9
Nlrp3
Relative expression (%)
P<0.0001
P<0.0001
P = 0.0002
P = 0.061
P = 0.034
P=0.0013
P=0.0014
P=0.014
P=0.014
P<0.0001
P=0.0006
CTL
AgBR1 antiserum
Resting skin
Bitten skin

FIG. 17E

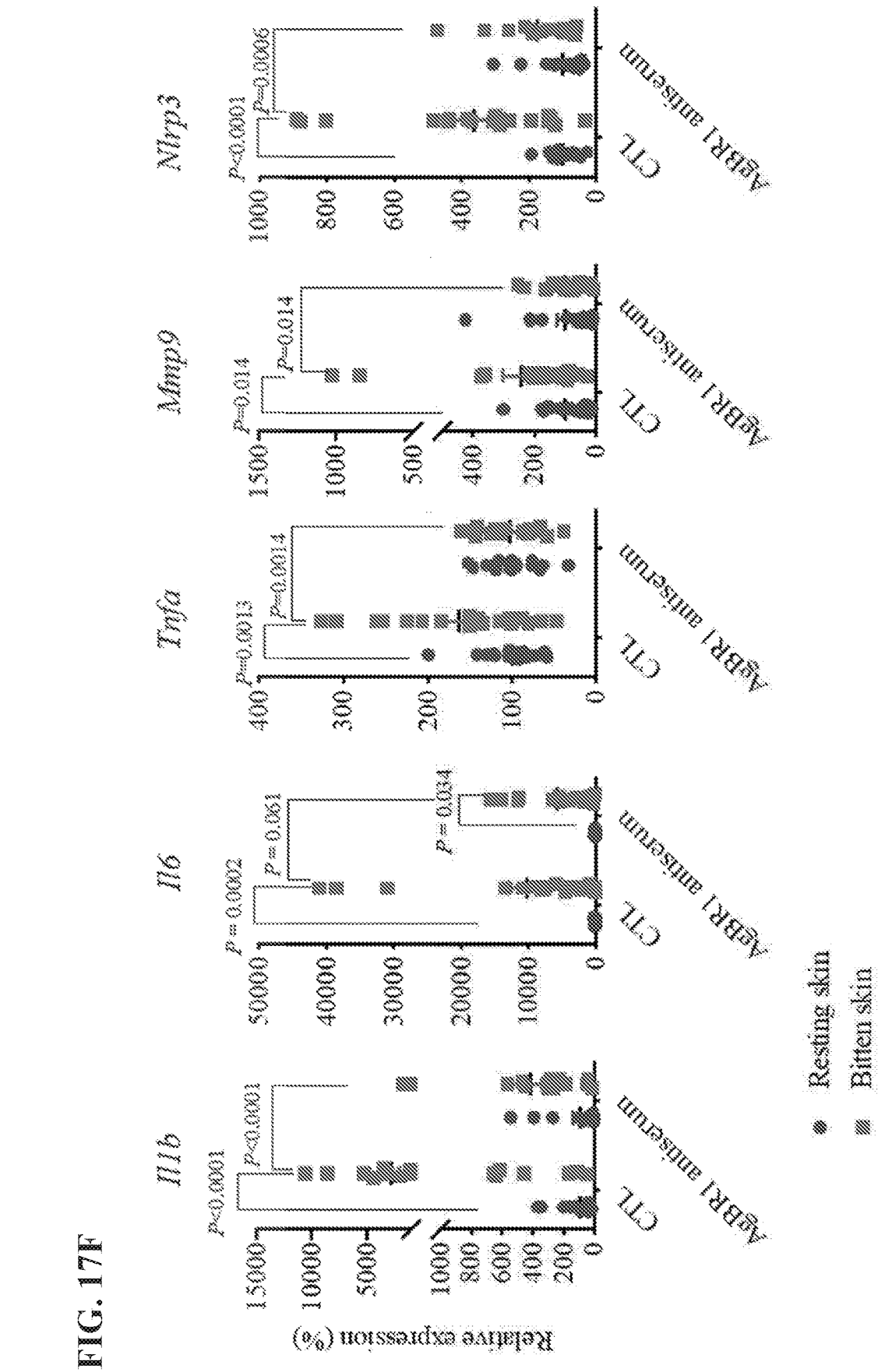

Il1b
Il6
Tnfa
Mmp9
Nlrp3
Relative expression (%)
P<0.0001
P<0.0001
P = 0.0002
P = 0.061
P = 0.034
P=0.0013
P=0.0014
P=0.014
P=0.014
P<0.0001
P=0.0006
CTL
AgBR1 antiserum
Resting skin
Bitten skin

FIG. 17F

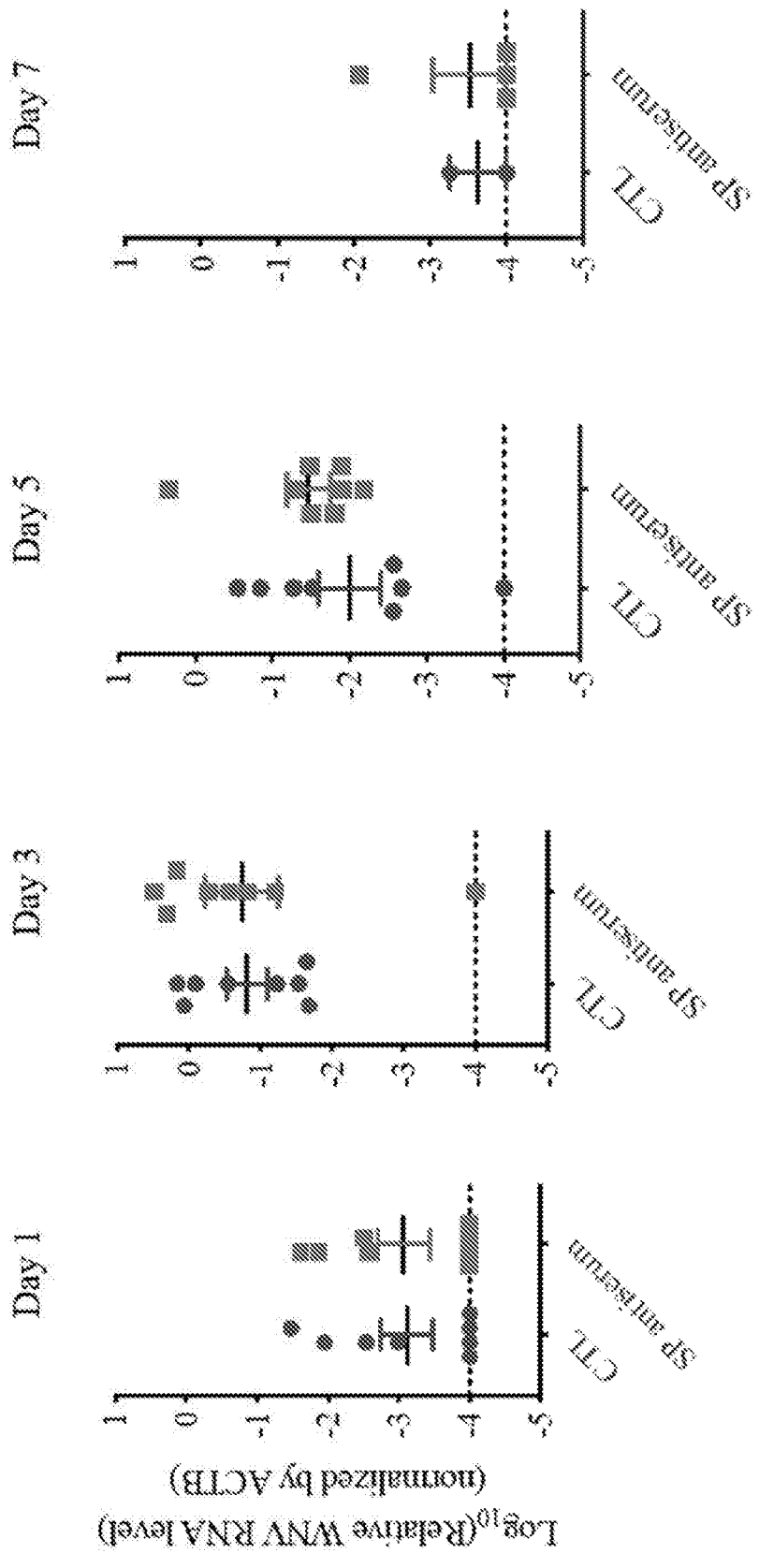

Day 1
Day 3
Day 5
Day 7
CTL
SP antiserum
1
0
-1
-2
-3
-4
-5
Log10(Relative WNV RNA level)
(normalized by ACTB)

FIG. 17G

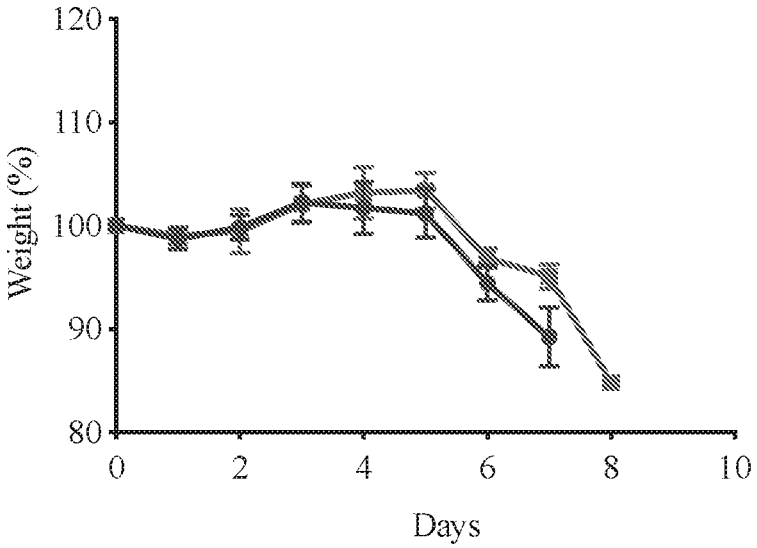


FIG. 17H

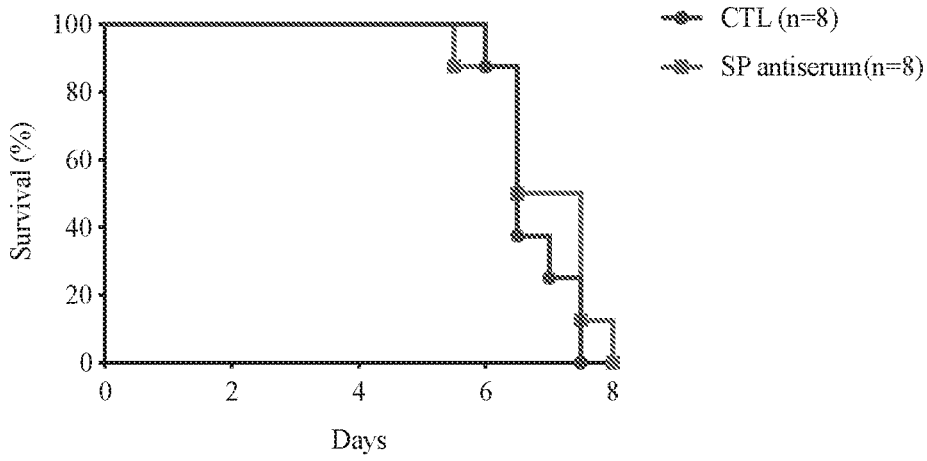


FIG. 17I

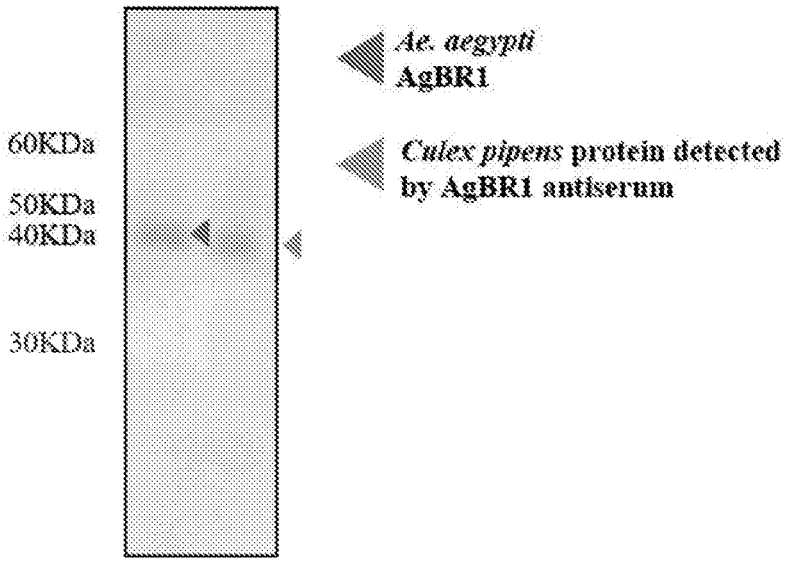


FIG. 17J

FIG. 18A

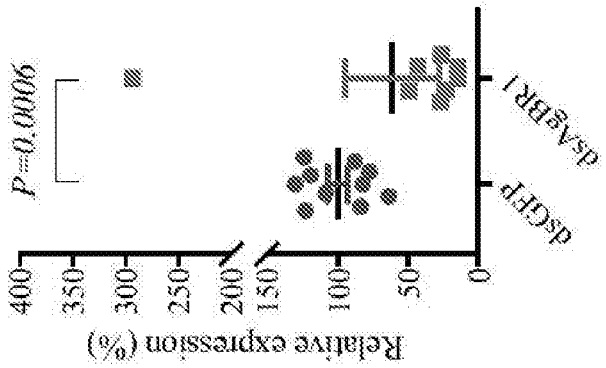


FIG. 18B

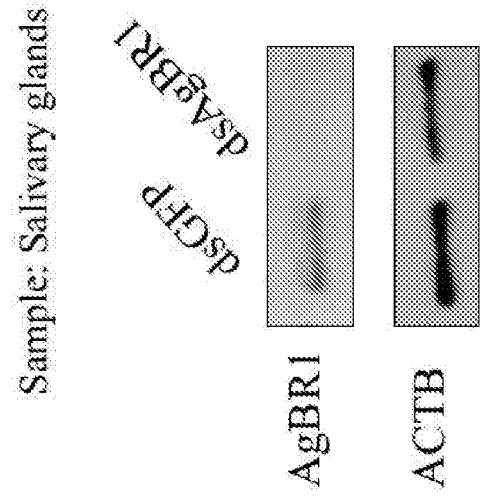


FIG. 18C

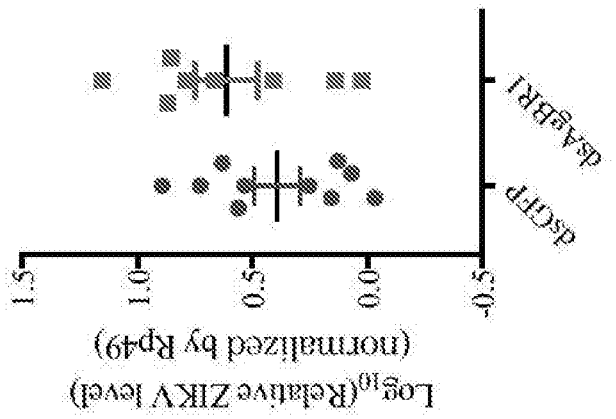


FIG. 18D

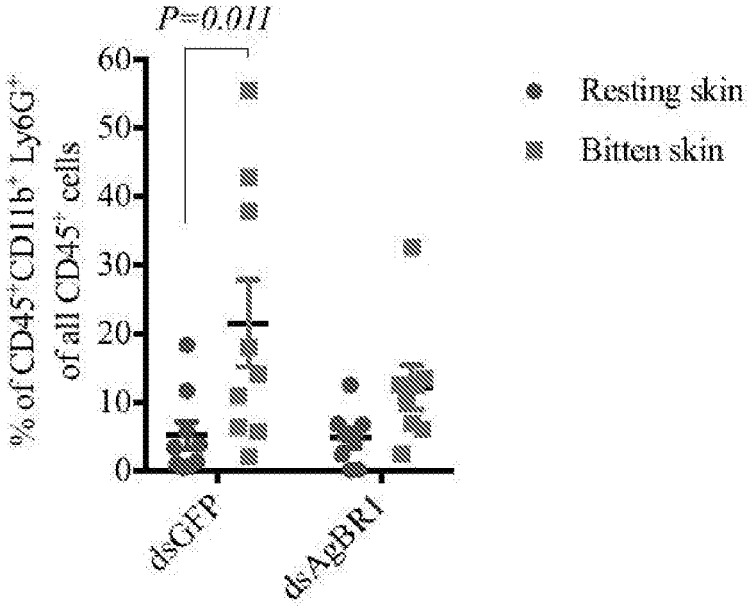


FIG. 19

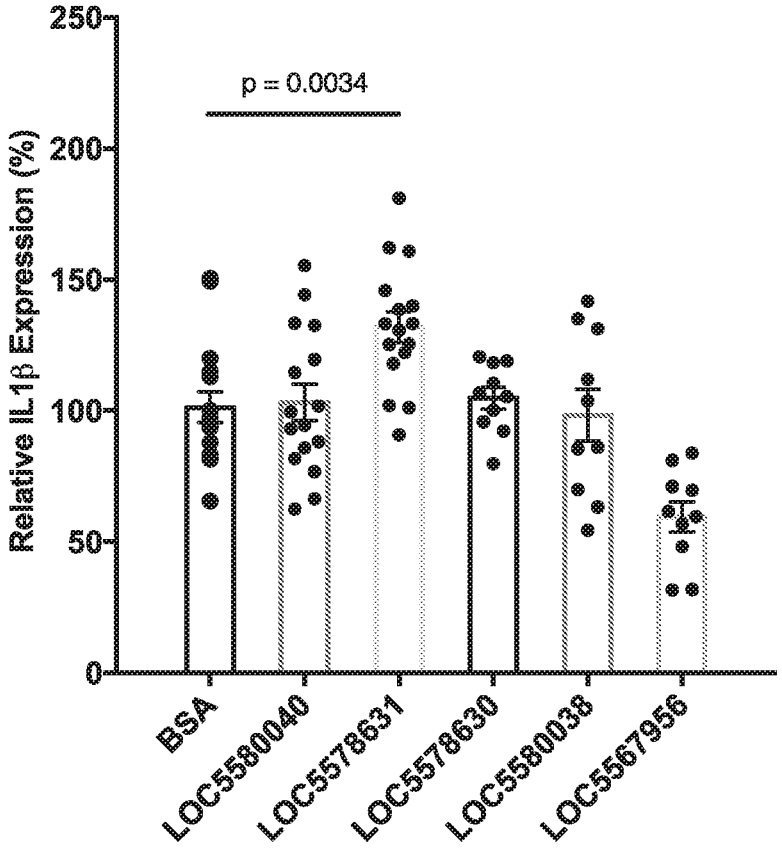


FIG. 20

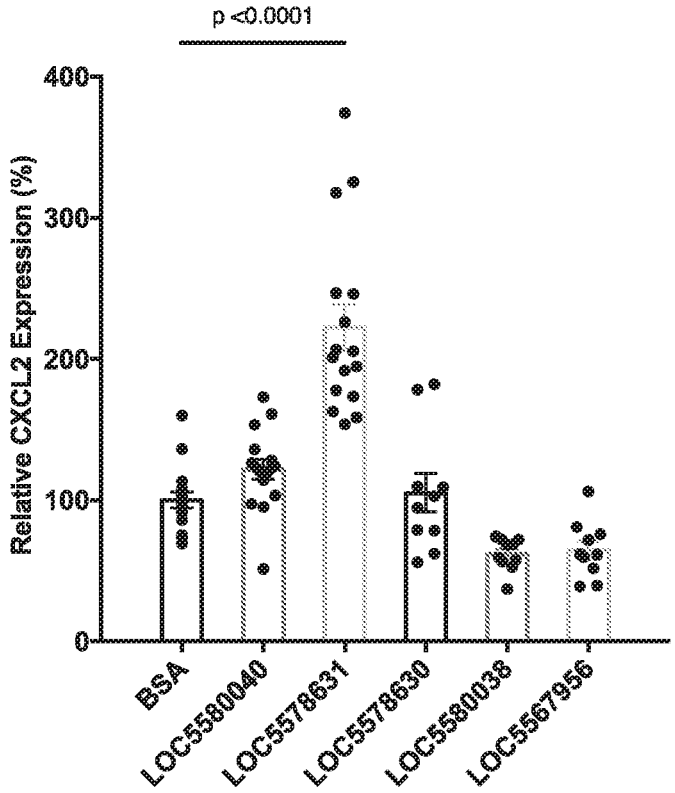

p <0.0001
Relative CXCL2 Expression (%)
400
300
200
100
0
BSA
LOC5580040
LOC5578631
LOC5578630
LOC5580038
LOC5567956

FIG. 21

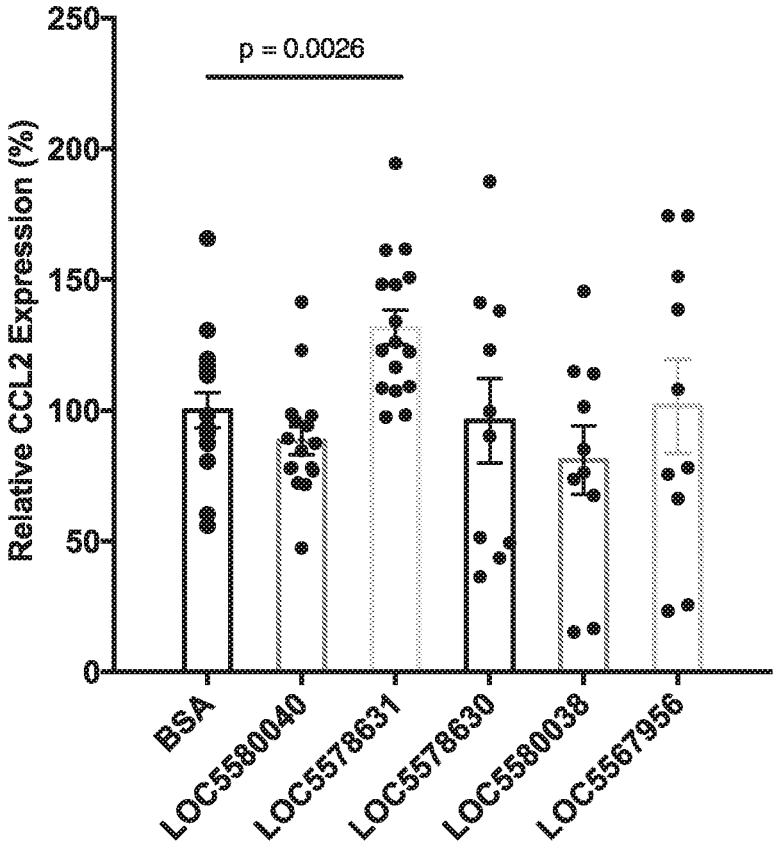

p = 0.0026
Relative CCL2 Expression (%)
250
200
150
100
50
0
BSA
LOC5580040
LOC5578631
LOC5578630
LOC5580038
LOC5567956

FIG. 22

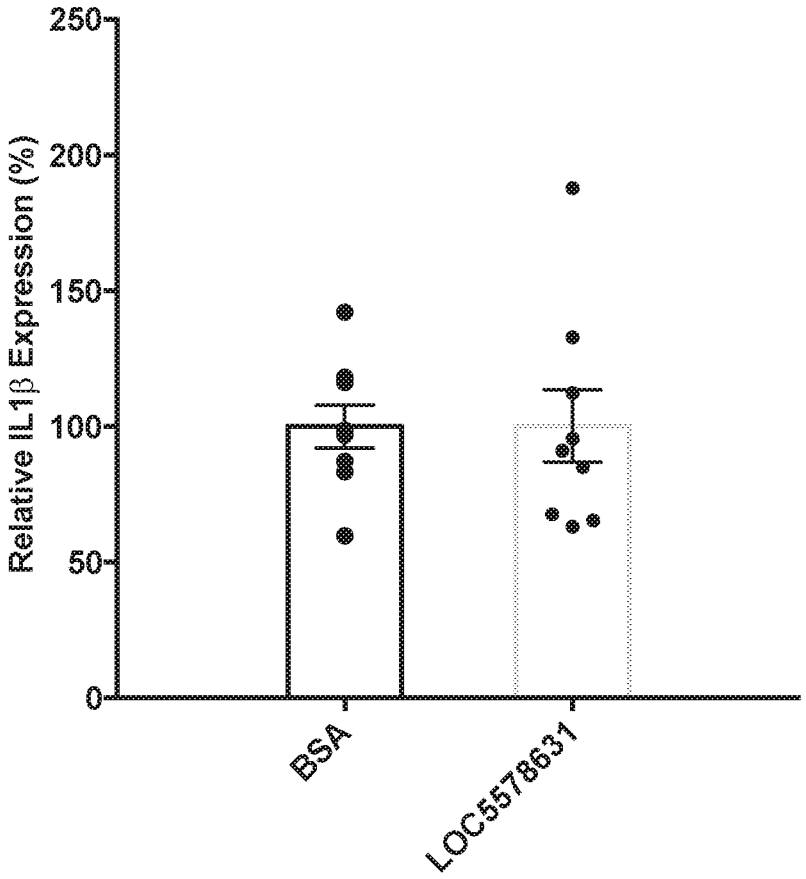

250
200
150
100
50
0
Relative IL1β Expression (%)
BSA
LOC5578631

FIG. 23

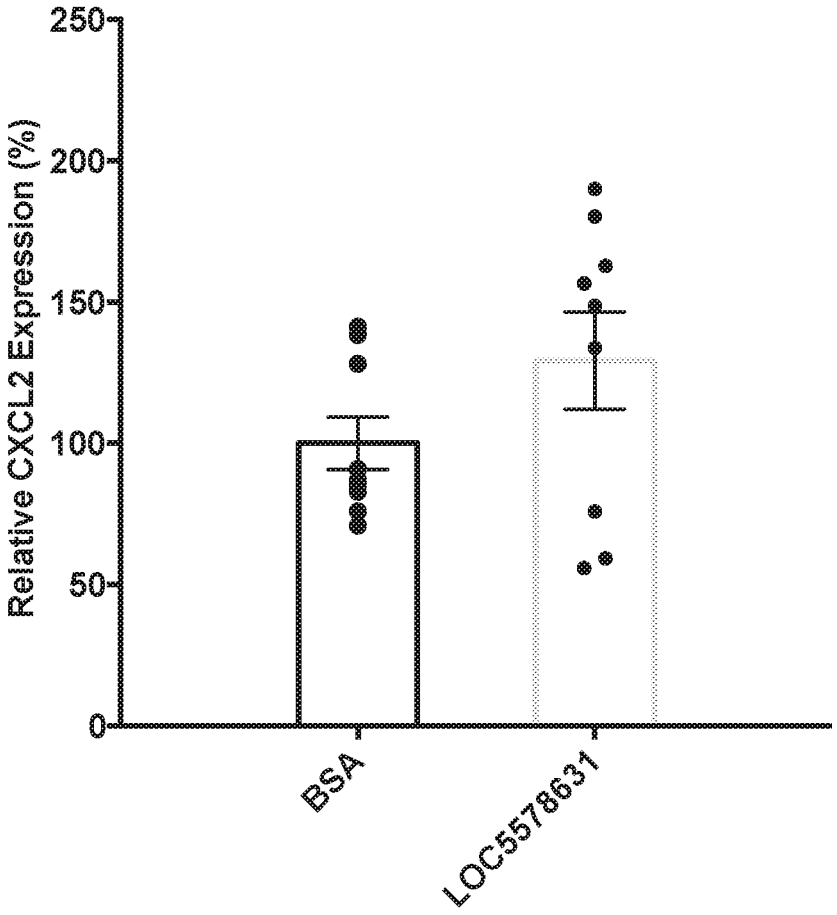

Relative CXCL2 Expression (%)
250
200
150
100
50
0
BSA
LOC5578631

FIG. 24

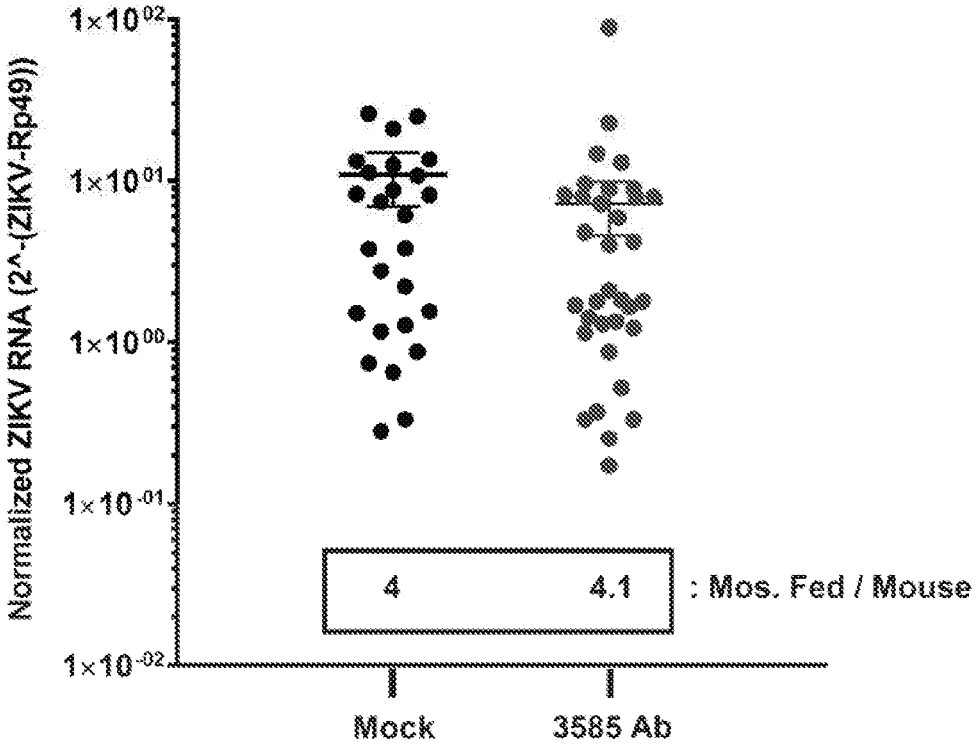

Normalized ZIKV RNA (2^-(ZIKV-Rp49))
1×10^02
1×10^01
1×10^00
1×10^-01
1×10^-02
4
4.1
: Mos. Fed / Mouse
Mock
3585 Ab

FIG. 25

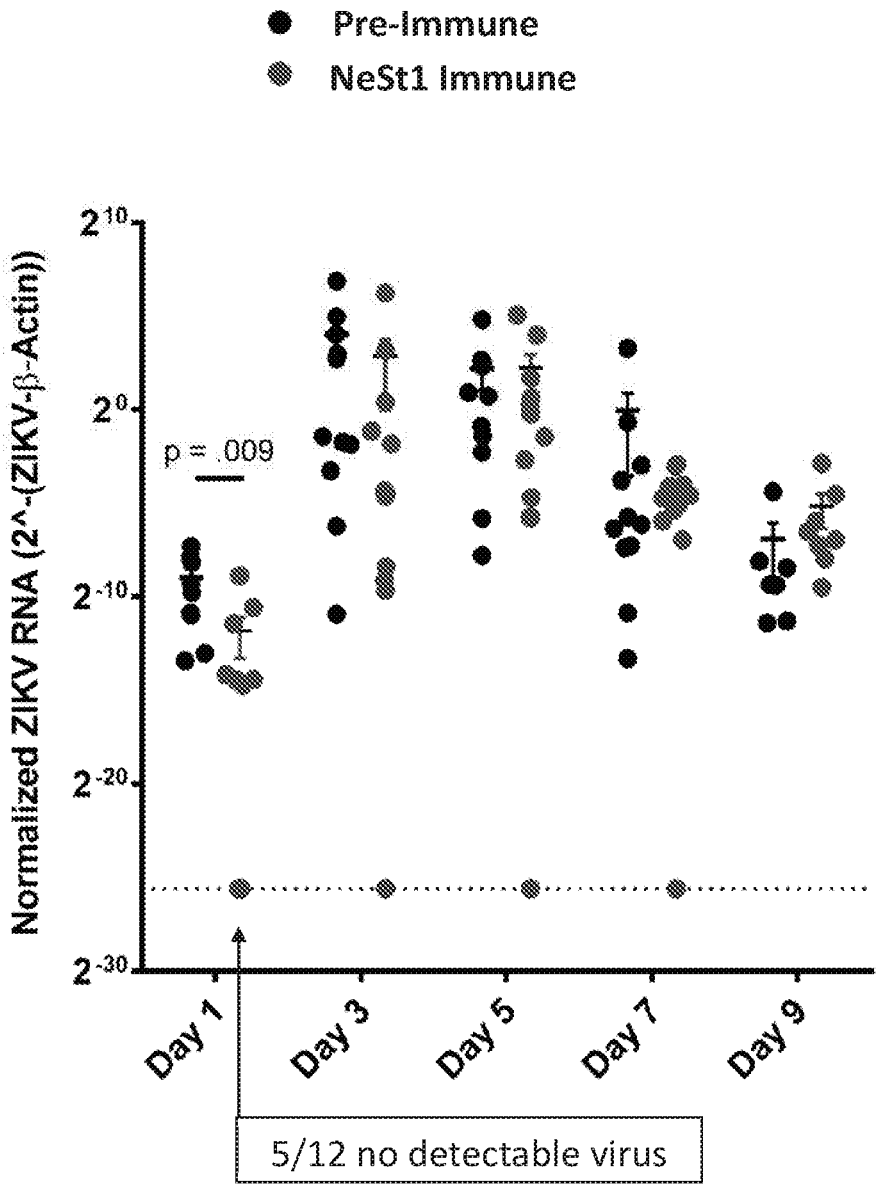
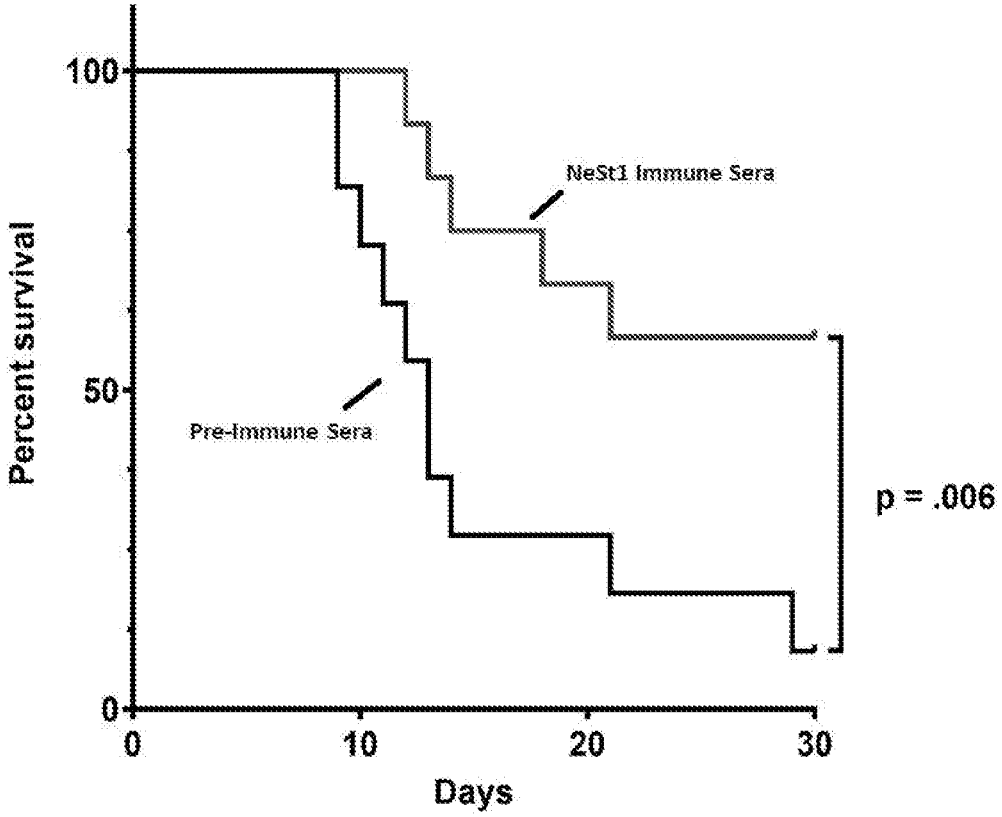

Pre-Immune
NeSt1 Immune
Normalized ZIKV RNA (2^-(ZIKV-β-Actin))
2^10
2^0
2^-10
2^-20
2^-30
p = .009
Day 1
Day 3
Day 5
Day 7
Day 9
5/12 no detectable virus

FIG. 26


100
50
0
Percent survival
0
10
20
30
Days
NeSt1 Immune Sera
Pre-Immune Sera
p = .006

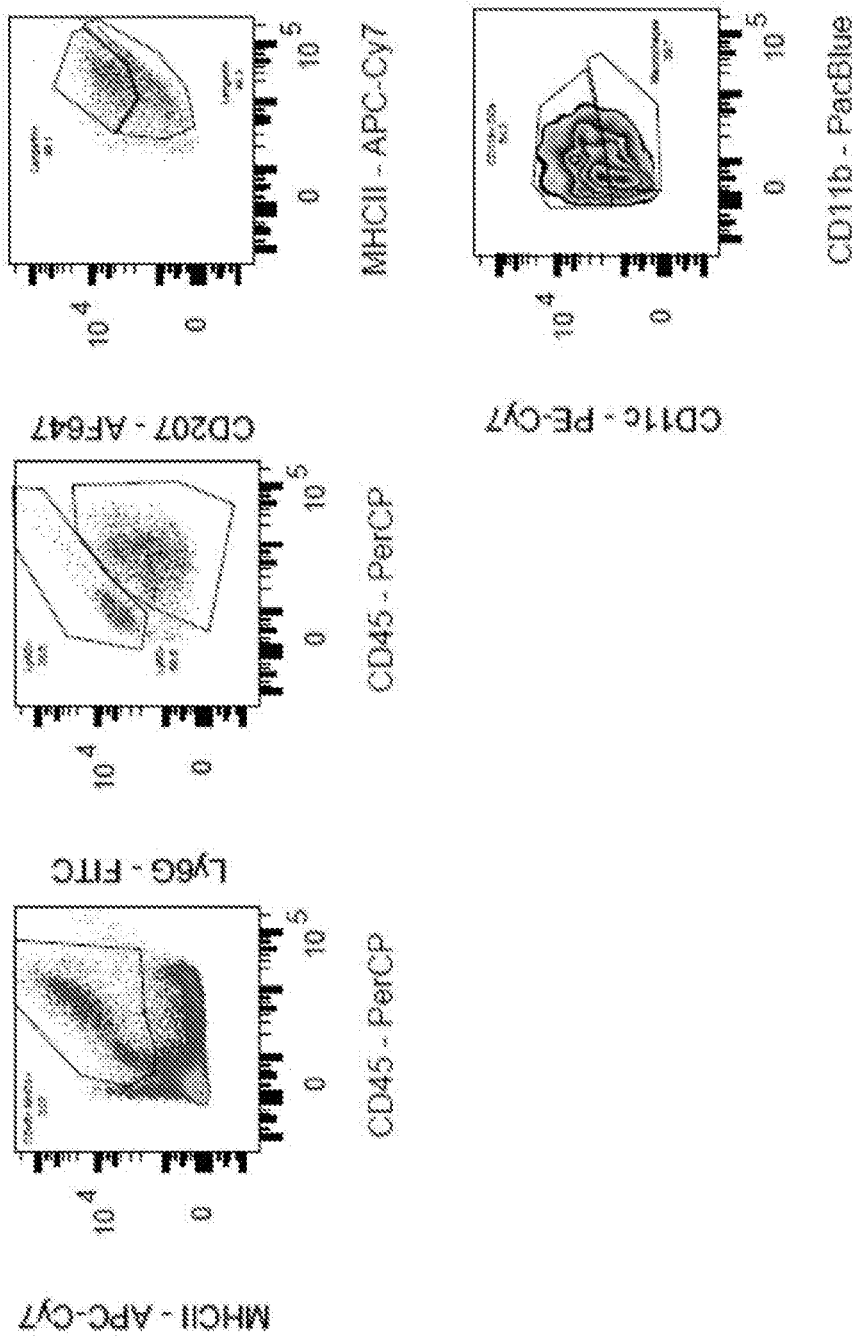

MHCII - APC-Cy7
CD11c - PE-Cy7
CD11b - PacBlue
CD207 - AF647
CD45 - PerCP
Ly6G - FITC
CD45 - PerCP
MHCII - APC-Cy7

FIG. 27

FIG. 28

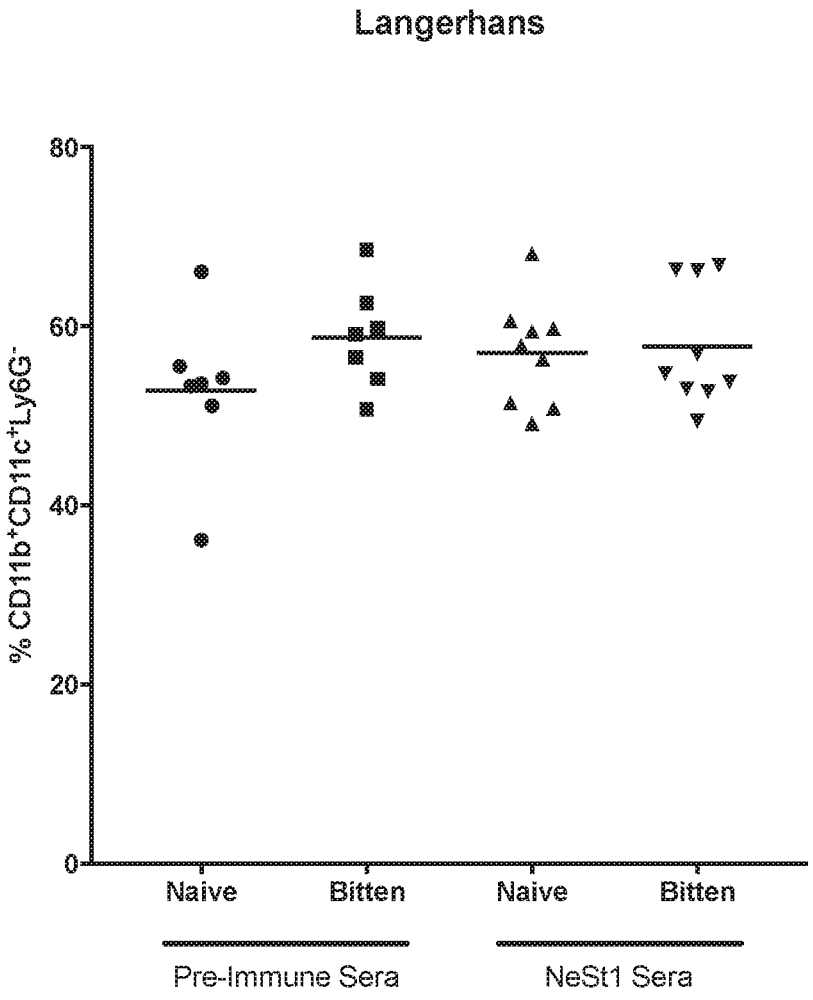

Langerhans
% CD11b+CD11c+Ly6G-
80
60
40
20
0
Naive
Bitten
Naive
Bitten
Pre-Immune Sera
NeSt1 Sera

FIG. 29

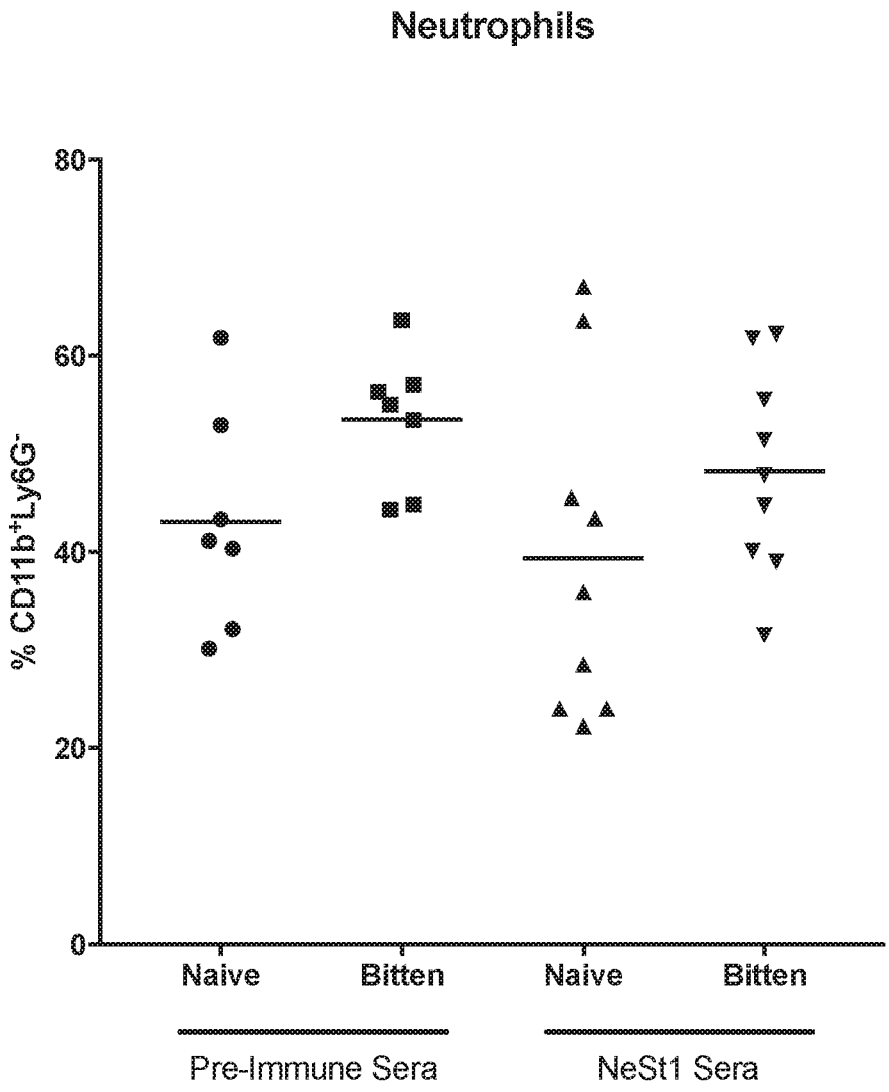

Neutrophils
% CD11b+Ly6G-
80
60
40
20
0
Naive
Bitten
Naive
Bitten
Pre-Immune Sera
NeSt1 Sera

FIG. 30

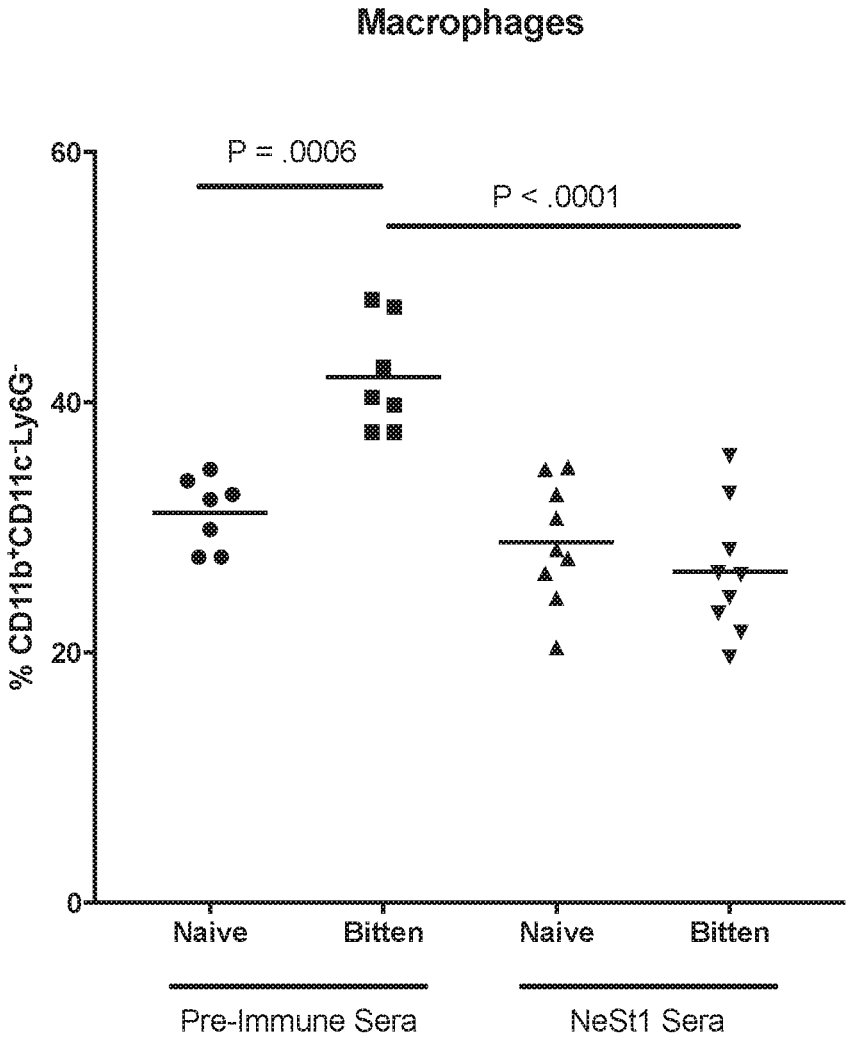

Macrophages
P = .0006
P < .0001
% CD11b+CD11c-Ly6G-
60
40
20
0
Naive
Bitten
Naive
Bitten
Pre-Immune Sera
NeSt1 Sera

FIG. 31

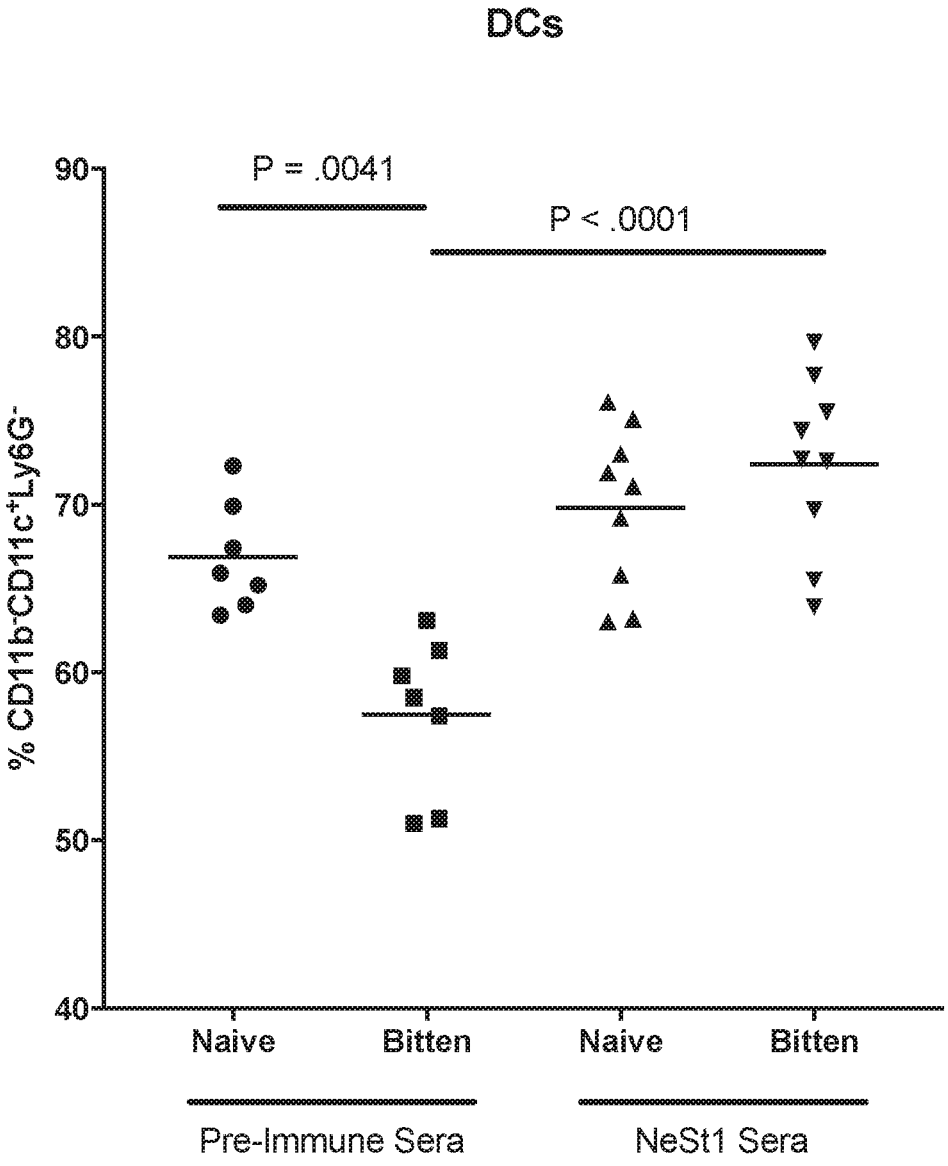

DCs
P = .0041
P < .0001
90
80
70
60
50
40
% CD11b+CD11c+Ly6G-
Naive
Bitten
Naive
Bitten
Pre-Immune Sera
NeSt1 Sera

FIG. 32A

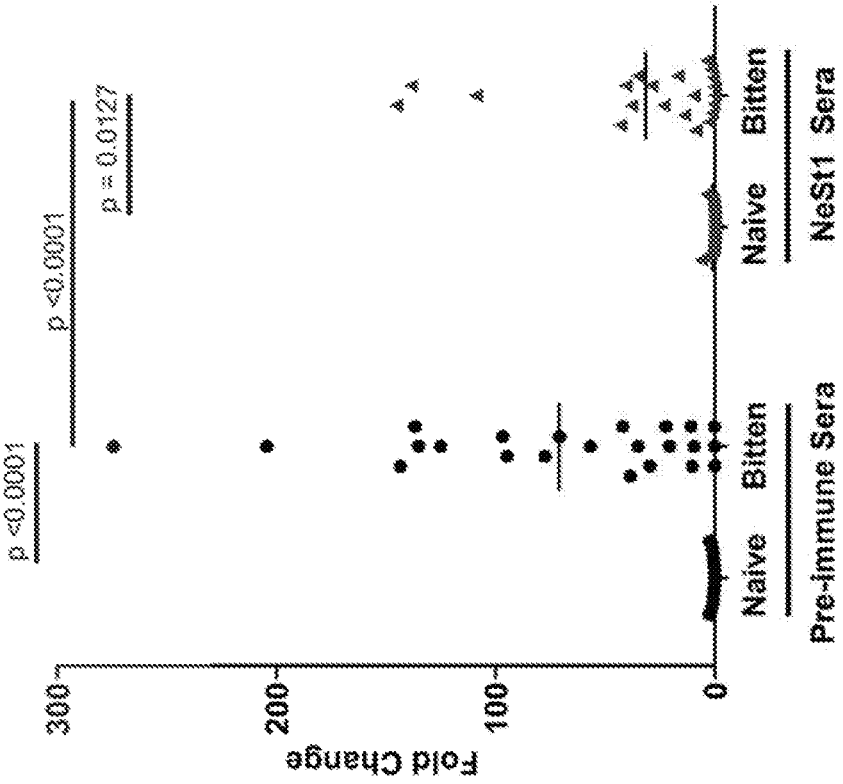
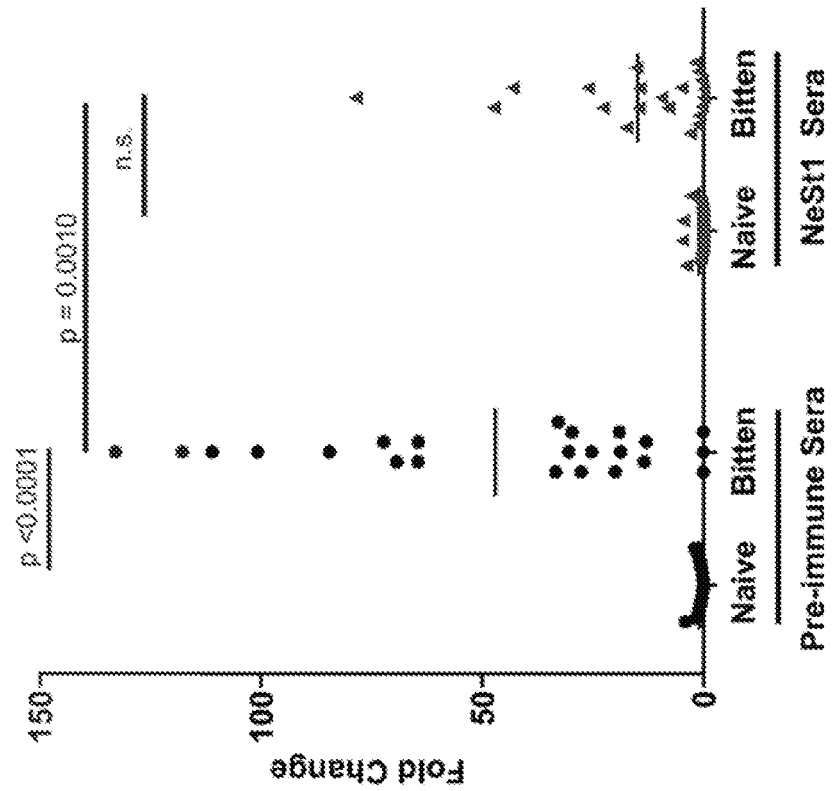


FIG. 32B



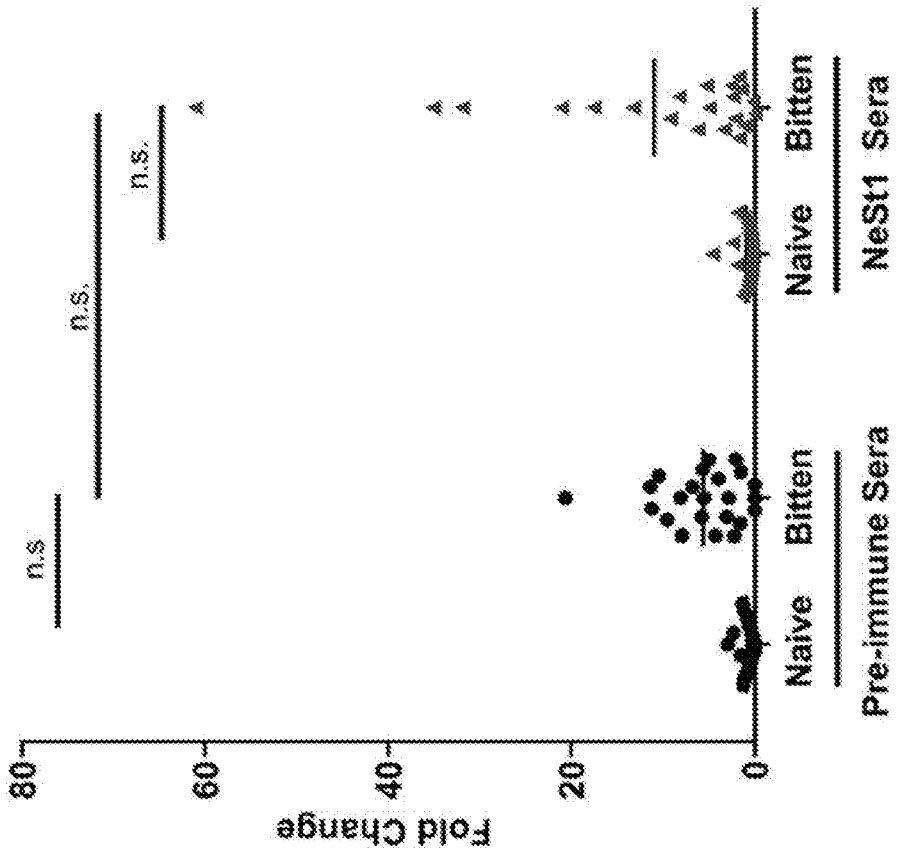

CCL2
Fold Change
80
60
40
20
0
n.s
n.s.
n.s.
Naive
Bitten
Pre-immune Sera
Naive
Bitten
NeSt1 Sera

FIG. 32C

TREATMENTS AGAINST MOSQUITO-BORNE VIRUSES BASED ON MOSQUITO SALIVARY GLAND PROTEINS

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 62/727,906, filed Sep. 6, 2018, which application is herein incorporated by reference in its entirety, and U.S. Provisional Application No. 62/735,597, filed Sep. 24, 2018, which application is herein incorporated by reference in its entirety.

STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH

[0002] This invention was made with government support under AI089992, AI127865, and AI145779 awarded by National Institutes of Health. The government has certain rights in the invention.

TECHNICAL FIELD OF THE INVENTION

[0003] The present invention is directed to compositions comprising mosquito (e.g., *Aedes aegypti*) salivary polypeptides and related methods for preventing and/or treating mosquito-borne viral infections such as infections caused by flaviviruses and alphaviruses.

BACKGROUND

[0004] Zika virus (ZIKV) is a member of the flavivirus family along with West Nile virus and Dengue virus. ZIKV was first isolated in 1947 from a sentinel monkey in the Zika forest of Uganda (1, 2). The first case of ZIKV infection in humans was reported in Nigeria in 1954 (3). For half a century, serologic evidence suggests that the virus circulated in Africa and Southeast Asia (4-11). Most recently, a large epidemic in the Americas, affecting well over a million people, has caused significant concern over this virus's potential to spread worldwide (12-14). Historically, Zika virus has manifested as a relatively mild self-limiting illness like dengue virus, with fever, rash and headache, and up to 80% of infected individuals remaining asymptomatic (9, 15, 16). However, these new epidemics have come with significantly more severe symptoms including Guillain-Barre syndrome (GBS) and birth defects (17-19). Zika virus can infect testes and is detected in semen, leading to sexual transmission (20-23). This has led to warnings to pregnant women to be mindful of insect repellant use and to limit travel to epidemic areas. Overall, this seeming increase in disease severity and rapid spread has led to increasing alarm across the globe.

[0005] The major mosquito vector for Zika virus is the *Aedes* species (*Ae. aegypti* and *Ae. albopictus*), which most likely originated in Africa and is now endemic in tropical and subtropical locations (31). This presents a significant public health risk that should be addressed. Although there are many efforts to develop Zika virus specific vaccines, there is currently no available commercial vaccine.

[0006] West Nile virus (WNV) is a single-stranded positive-sense RNA virus in the genus Flavivirus, which normally circulates in a bird-mosquito transmission cycle and is a common human mosquito-borne flaviviral infection in North America and other regions in the world (53-55). WNV can also infect horses, and other non-avian vertebrate hosts (56). Despite substantial efforts, effective FDA-approved preventive or therapeutic measures are not yet available (53,56,57).

[0007] *Culex* mosquito spp., now endemic in tropical and subtropical regions as well as more temperate areas, are the major vectors for WNV worldwide (57). However, the virus also has been isolated from *Aedes aegypti* mosquitoes, which is present in tropical and subtropical locations as well (58,59) and are a potential threat for transmission of WNV to humans (60). Although the vector competence of WNV in *Ae. aegypti* is lower than that of *Culex* spp., multiple factors can affect vector distribution, including climate change, and this may influence the vectorial capacity of *Aedes* mosquitoes for WNV in the future (61,62). Moreover, in laboratory studies, *Ae. aegypti* readily feed on mice and a well-annotated whole genome sequence is available (63).

[0008] When mosquitoes take a blood meal, they inoculate saliva into the skin (64). Mosquito saliva contains molecules which modulate various host responses, including coagulation, platelet aggregation, thrombin activation, vasodilation, and other mammalian host pathways (65,66).

[0009] Mosquitoes inject numerous salivary proteins into the skin of a host during blood feeding, and these molecules are capable of modulating various host responses (65,66). Indeed, mosquito saliva enhances transmission and pathogenicity of specific arboviruses (31,75). Although mosquito saliva can increase arboviral infectivity, only a limited number of specific salivary proteins have been characterized that influence these processes. The biogenic amine-binding D7 protein partially inhibits dengue infection, while saliva serine protease CLIPA3 enhances dissemination of dengue virus into the mammalian host (25,67). In addition, salivary factor LTRIN from *A. aegypti* facilitates the transmission of Zika virus by inhibiting NFκB signaling during infection (68). Despite these efforts, much remains to be discovered about how specific salivary factors facilitate mosquito-borne virus infection, and whether targeting these proteins can prevent or delay infection.

[0010] Components of saliva enhance the pathogenicity and transmission of arboviruses including WNV, dengue, Zika, and Semliki Forest viruses, suggesting that certain salivary proteins are important for influencing flavivirus infectivity during transmission from vector to host (25,31, 32,67,68). The expression of AgBR1 in the salivary glands is up-regulated after blood feeding and AgBR1 belongs to a family of proteins that have lost chitinolytic activity (41,70), however the function of this protein in the vertebrate host remains unclear. To determine whether this effect extends beyond Zika virus to another flavivirus, the influence of AgBR1 antibodies against *Ae. aegypti*-borne WNV infection in mice was examined.

[0011] Saliva from arthropod vectors, such as ticks, sand flies and mosquitoes, is capable of enhancing transmission and pathogenicity of important human pathogens such as arboviruses and *Leishmania* (24-31). A variety of salivary proteins have been discovered. See, e.g., Int. Pat. Appl. Pub. WO 2011/1104684 and (24-26), incorporated by reference herein in its entirety.

SUMMARY OF THE INVENTION

[0012] As specified in the Background Section, there is a great need in the art to develop effective vaccines and treatments for mosquito-borne viruses such as, e.g., flavivi-

ruses and alphaviruses. The present invention addresses this and other needs by providing compositions and methods disclosed herein.

[0013] In one aspect, the invention provides a composition comprising one or more polypeptides, wherein said one or more polypeptides are selected from the group consisting of LOC5573204 bacteria-responsive protein 1 (AgBR1), LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

[0014] In another aspect, the invention provides a composition comprising a nucleic acid molecule encoding one or more polypeptides, wherein said one or more polypeptides are selected from the group consisting of LOC5573204 (AgBR1), LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

[0015] In a further aspect, the invention provides a composition comprising an antibody which recognizes a polypeptide, wherein said polypeptide is selected from the group consisting of LOC5573204 (AgBR1), LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

[0016] In yet another aspect, the invention provides a composition comprising a molecule which inhibits a function of a mosquito salivary polypeptide or inhibits the interaction between a mosquito salivary polypeptide and a host cell or inhibits the interaction between a mosquito salivary polypeptide and a mosquito-borne infectious agent, wherein said mosquito salivary polypeptide is selected from the group consisting of LOC5573204 (AgBR1), LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof. In one embodiment, the mosquito-borne infectious agent is a mosquito-borne virus (e.g., a flavivirus [such as, e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, or yellow fever virus], or an alphavirus [such as, e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus]).

[0017] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5573204 bacteria-responsive protein 1 (AgBR1) or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide comprises the sequence SEQ ID NO: 1. In one specific embodiment, the polypeptide consists of the sequence SEQ ID NO: 1. In one specific embodiment, the polypeptide is a fragment of LOC5573204 (e.g., the polypeptide fragment of LOC5573204 comprising the sequence selected from SEQ ID NOS: 6-13).

[0018] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5578630 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5578630 comprises the sequence SEQ ID NO: 2. In one specific embodiment, the polypeptide LOC5578630 consists of the sequence SEQ ID NO: 2. In one specific embodiment, the polypeptide is a fragment of LOC5578630 (e.g., the polypeptide fragment of LOC5578630 comprising the sequence selected from SEQ ID NOS: 14-21).

[0019] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5578631 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5578631 comprises the sequence SEQ ID NO: 3. In one specific embodiment, the polypeptide LOC5578631 consists of the sequence SEQ ID NO: 3. In one specific embodiment, the polypeptide is a fragment of LOC5578631 (e.g., the polypeptide fragment of LOC5578631 comprising the sequence selected from SEQ ID NOS: 22-29).

[0020] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5567956 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5567956 comprises the sequence SEQ ID NO: 4. In one specific embodiment, the polypeptide LOC5567956 consists of the sequence SEQ ID NO: 4. In one specific embodiment, the polypeptide is a fragment of LOC5567956 (e.g., the polypeptide fragment of LOC5567956 comprising the sequence selected from SEQ ID NOS: 30-36).

[0021] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5580038 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5580038 comprises the sequence SEQ ID NO: 5. In one specific embodiment, the polypeptide LOC5580038 consists of the sequence SEQ ID NO: 5. In one specific embodiment, the polypeptide is a fragment of LOC5580038 (e.g., the polypeptide fragment of LOC5580038 comprising the sequence selected from SEQ ID NOS: 37-42).

[0022] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5566287 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5566287 comprises the sequence SEQ ID NO: 43. In one specific embodiment, the polypeptide LOC5566287 consists of the sequence SEQ ID NO: 43. In one specific embodiment, the polypeptide is a fragment of LOC5566287 (e.g., the polypeptide fragment of LOC5566287 comprising the sequence selected from SEQ ID NOS: 47-59).

[0023] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5567958 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC5567958 comprises the sequence SEQ ID NO: 44. In one specific embodiment, the polypeptide LOC5567958 consists of the sequence SEQ ID NO: 44. In one specific embodiment, the polypeptide is a fragment of LOC5567958 (e.g., the polypeptide fragment of LOC5567958 comprising the sequence selected from SEQ ID NOS: 60-70).

[0024] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC5568702 or a fragment, derivatives or variant thereof. In one specific embodiment, the polypeptide LOC5568702 comprises the sequence SEQ ID NO: 45. In one specific embodiment, the polypeptide LOC5568702 consists of the sequence SEQ ID NO: 45. In one specific embodiment, the polypeptide is a fragment of LOC5568702 (e.g., the polypeptide fragment of LOC5568702 comprising the sequence selected from SEQ ID NOS: 71-85).

[0025] In one embodiment of any of the above compositions of the invention, the polypeptide is LOC110675548 or a fragment, derivative or variant thereof. In one specific embodiment, the polypeptide LOC110675548 comprises the

sequence SEQ ID NO: 46. In one specific embodiment, the polypeptide LOC110675548 consists of the sequence SEQ ID NO: 44. In one specific embodiment, the polypeptide is a fragment of LOC110675548 (e.g., the polypeptide fragment of LOC110675548 comprising the sequence selected from SEQ ID NOS: 86-99).

[0026] In one embodiment of any of the above compositions of the invention, the composition further comprises a carrier or excipient.

[0027] In one embodiment of any of the above compositions of the invention, the composition further comprises an adjuvant.

[0028] In one embodiment of any of the above compositions of the invention, the composition comprises at least two different polypeptides.

[0029] In another aspect, the invention provides a method of preventing or treating a disease in a subject in need thereof, wherein the disease is associated with a mosquito-borne infectious agent, said method comprising administering to said subject an effective amount of any of the compositions of the invention. In one embodiment, the mosquito is *Aedes aegypti*. In one embodiment, the mosquito-borne infectious agent is a mosquito-borne virus (e.g., a flavivirus [such as, e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, or yellow fever virus], or an alphavirus [such as, e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus]). In one embodiment, the subject is human.

[0030] These and other aspects of the present invention will be apparent to those of ordinary skill in the art in the following description, drawings and claims.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] FIGS. **1**A-**1**B show the reactivity if serum of mice bitten by *A. aegypti* mosquitoes against mosquito salivary gland extract (SGE). FIG. **1**A and FIG. **1**B show that ELISA (A) and Western blot (B) analysis of SGE were performed by probing with naïve mouse serum and serum from mice bitten by mosquitoes.

[0032] FIGS. **2**A-**2**B show the reactivity if serum of human bitten by *A. aegypti* mosquitoes against mosquito salivary gland extract (SGE). FIGS. **2**A and **2**B show that ELISA (A) and Western blot (B) analysis of SGE were performed by probing with naïve human serum and serum from human bitten by mosquitoes.

[0033] FIGS. **3**A-**3**C show a yeast surface display (YSD) approach to identify mosquito antigenic proteins in mice bitten by *Aedes aegypti*. EBY-100 yeast cells, transformed with an *Ae. aegypti* salivary gland cDNA library, were induced overnight before magnetic sorting. In FIG. **3**A, after each magnetic sort, binding of transformed yeast cells using IgG from mice bitten by mosquitoes (red) and IgG derived from normal mouse serum (blue) was analyzed using flow cytometry (FACS). In FIG. **3**B, the percentages of IgG-binding yeast cells were determined by FACS analysis as shown. In FIG. **3**C, antigenic *A. aegypti* salivary proteins were identified by a YSD library using serum from mice bitten by *A. aegypti*.

[0034] FIGS. **4**A-**4**C show a yeast surface display (YSD) approach to identify mosquito antigenic proteins in humans bitten by *Aedes aegypti*. EBY-100 yeast cells, transformed with an *Ae. aegypti* salivary gland cDNA library, were induced overnight before magnetic sorting. In FIG. **4**A, after each magnetic sort, binding of transformed yeast cells using IgG from humans bitten by mosquitoes (red) and IgG derived from normal human serum (blue) was analyzed using flow cytometry (FACS). In FIG. **4**B, the percentages of IgG-binding yeast cells were determined by FACS analysis as shown. In FIG. **4**C, antigenic *A. aegypti* salivary proteins were identified by a YSD library using serum from human bitten by *A. aegypti*.

[0035] FIGS. **5**A-**5**D show purification of nine identified proteins and specificity of rabbit serum against them. Identified proteins produced in *Drosophila* S2 cells and purified using the TALON resin. FIG. **5**A is an SDS-PAGE gel stained with Coomassie Brilliant Blue, of recombinant proteins SP (LOC5578630), NeSt1 (LOC5578631), D7Bclu (LOC5567956), AILP (LOC5580038), AgBR1 (LOC5573204), FibRP (LOC5566287), AnLP (LOC110675548), Aada2 (LOC5567958) and Lipase (LOC5568702) (0.25 μg protein). FIG. **5**B is an immunoblot showing that anti-His antibody is able to recognize proteins. In FIG. **5**C, recombinant AgBR1 (0.25 μg protein) was run on SDS-PAGE and stained with Coomassie Brilliant Blue. FIG. **5**D shows detection of AgBR1 protein using an anti-His antibody. Data are representative of two independent experiments.

[0036] FIGS. **6**A-**6**I show titration curves for the sera of mice exposed to each of the antigenic proteins listed in FIGS. **2** and **3**, i.e. SP, SSP, D7Bclu, AILP, AgBR1, FibRP, Aada2, Lipase, and AnLP by using ELISA. As a control, a titration curve for naïve serum is also shown in FIG. **6**J.

[0037] FIGS. **7**A-**7**E show that a mixture of antiserum against each antigenic protein protects mice from mosquito-borne Zika virus infection. FIG. **7**A shows an experimental murine model of Zika virus transmission. A mouse is treated with an antibody (e.g., to a mosquito salivary protein) the day before exposure to the Zika virus by a bite from an infected *Ae. aegypti* mosquito. Viremia and survival are checked at days 1, 3, 5, 7, and 9. FIG. **7**B shows that the Zika virus level in salivary glands was the same in the CTL and Ab-mix groups by using real-time PCR (RT-PCR). Control group of mice (CTL) were treated with naïve rabbit serum, and the Ab-mix groups of mice (Ab-mix) were treated with the mixture of antiserum against SP, SSP, D7Bclu, AILP, AgBR1, FibRP, Aada2, Lipase, and AnLP. Error bars represent mean±SEM. Each data point represents one aliquot of tested salivary gland extract. FIGS. **7**C-**7**E show that antibody treatment suppressed Zika virus replication in mouse blood. Viremia and survival were checked on days 1, 3, 5, 7, and 9. Viremia was lower, and survival was greater, in mice treated with the antibody mixture. Antibody treatment suppressed Zika virus replication in the blood.

[0038] FIGS. **8**A-**8**B show no effect of the mixture of antisera against needle-injected Zika virus infection. Mice were administrated with the mixture of antisera one day before subcutaneous Zika virus injection. In FIG. **8**A, blood from mice was collected every other day for 9 days, and analyzed for Zika virus infection by qRT-PCR. Zika virus RNA levels were normalized to mouse β actin RNA levels. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using Wilcoxon-Mann-Whitney test. In FIG. **8**B, mice were monitored daily for survival after Zika virus infection. Survival was assessed using a Gehan-Wilcoxon test.

[0039] FIG. **9** shows the effect of AgBR1 in vitro, and that recombinant AgBR1 stimulates IL-6 but not TNF-α or IL-1β expression levels in vitro. Splenocytes were isolated from

mice and treated with AgBR1 (5 μg/ml), D7Bclu (5 μg/ml) or BSA (5 μg/ml). Cells were harvested 6 hours or 24 hours after treatment, and the expression levels of 116, Tnfa and Il1b were examined by qRT-PCR. Data were derived from two independent experiments and were analyzed by two-way ANOVA. n=5 or 6 biologically independent samples pooled from two separate experiments. Data are presented as mean±s.e.m.

[0040] FIGS. **10**A-**10**C show the effect of AgBR1 in vivo, with AgBR1 enhancing Zika virus replication and diseases. In FIG. **10**A, AgBR1 protein (5.1 μM, 10 μg in 40 μl) was co-inoculated with Zika virus, and blood was collected every other day for 9 days from mice. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using the Wilcoxon-Mann-Whitney test. (Zika virus: n=12, Zika virus+AgBR1: n=11 pooled from two separate experiments.) In FIG. **10**B, injected mice were monitored for survival after infection. Survival and median survival time (MST) was assessed using the Gehan-Wilcoxon test. Survival data shown are pooled from two independent experiments (Zika virus: n=12, Zika virus+AgBR1: n=11). FIG. **10**C is shows that the concentration of AgBR1 in mosquito saliva can be estimated to be between 1.6-8.2 μM.

[0041] FIGS. **11**A-**11**D show that AgBR1 antiserum protects mice from mosquito-borne Zika virus infection. FIG. **11**A shows workflow of passive immunization and mosquito-borne Zika virus infection. FIG. **11**B shows Zika virus RNA levels in the salivary glands at 10 days after intrathoracic injection. n=34 (Control) or 38 (AgBR1 antiserum) biologically independent samples pooled from five separate experiments. Data represent mean±s.e.m. FIG. **11**C shows Zika virus RNA levels in blood in mice. Data represent mean±s.e.m. Each data point represents one mouse. Normalized viral RNA levels were analyzed using two-sided Wilcoxon-Mann-Whitney test. n=17 (Control) or 19 (AgBR1 antiserum) biologically independent samples pooled from five separate experiments. In FIG. **11**D, survival and median survival time (MST) were assessed using the Gehan-Wilcoxon test. n=17 (Control) or 19 (AgBR1 antiserum) biologically independent samples pooled from five separate experiments. FIG. **11**E shows that the partial protective effect of AgBR1 antibodies was specific for mosquito-borne, and not needle-injected, Zika virus infection in mice.

[0042] FIGS. **12**A-**12**B show no effect of AgBR1 antiserum against needle-injected Zika virus infection. Mice were administrated with AgBR1 antiserum one day before subcutaneous Zika virus injection. In FIG. **12**A, blood from mice was collected every other day for 9 days and analyzed for Zika virus infection by qRT-PCR. Zika virus RNA levels were normalized to mouse β actin RNA levels. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using Wilcoxon-Mann-Whitney test. In FIG. **12**B, mice were monitored daily for survival after Zika virus infection. Survival was assessed using a Gehan-Wilcoxon test.

[0043] FIGS. **13**A-**13**D show the protective effects of different antibodies on mice infected with Zika virus. Mice were administrated with antiserum against SP or D7Bclu one day before Zika virus-infected mosquito feeding. Immunized mice were monitored for survival for 35 days after infected mosquito-feeding. Blood was collected every other day for 9 days from mice fed on by Zika virus-infected mosquitoes and analyzed for Zika virus infection by qRT-PCR. Zika virus RNA levels were normalized to mouse β-actin RNA levels. Mice immunized with naïve serum served as controls. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using Wilcoxon-Mann-Whitney test. In FIGS. **13**B and **13**D, mice were monitored for survival for 35 days after infected mosquito-feeding. Data shown are pooled from at least two independent experiments. Survival was assessed by a Gehan-Wilcoxon test. The results show that antisera against abundant proteins recognized in the yeast display assay were not protective against mosquito-borne Zika virus infection.

[0044] FIGS. **14**A-**14**H show the suppression of neutrophil recruitment at the mosquito bite site in mice administered AgBR1 antiserum. Mice were inoculated with AgBR1 antiserum or control serum prior to Zika virus-infected mosquito feeding. Twenty-four hours post feeding, the bitten ears together with control contralateral non-bitten ears were harvested for tissue sectioning. FIG. **14**A shows hematoxylin and eosin staining of the ears of mice 24 hours post-feeding. Scale bar, 200 μm (left panels) and 50 μm (right panels). Data are representative of two independent experiments with similar results. FIG. **14**B shows the histological findings were scored in terms of inflammation, neutrophil infiltration, mononuclear cell infiltration and edema. In FIG. **14**C, the total histology scores of the bite sites were compared between the AgBR1 antiserum and control group. Data are presented as means±SEM. Statistical analysis was performed using two-sided Wilcoxon-Mann-Whitney test. n=5 (Control) or 6 (AgBR1 antiserum) biologically independent samples pooled from two separate experiments. FIG. **14**D shows Imaging Mass Cytometry (IMC) labeling of ears of mice 24 hours post Zika virus-infected mosquito feeding. Sections of the ear skins were labeled with antibodies against CD3 (170Er), CD11b (149Sm), MHCII (174Yb), Ly6G (141Pr) or DNA (193Ir). Scale bar, 100 μm. In FIGS. **14**E and **14**F, both bitten and resting ears were harvested and enzymatically digested to obtain a single-cell suspension. The population of $CD45^+CD11b^+Ly6G^+$ (neutrophils) was analyzed using flow cytometry. Data are representative of two independent experiments with similar results. FIG. **14**F shows the percent of $CD45^+CD11b^+Ly6G^+$ (neutrophils) cells in $CD45^+$ leukocyte cells at 24 h after Zika virus-infected mosquito feeding. Each dot represents one mouse. Significance was calculated using a two-way ANOVA test for multiple comparisons. Data are presented as mean±s.e.m. Each dot represents one mouse (n=7; resting skin of mice treated with control serum, n=9; bitten skin of mice treated with control serum n=11; resting skin of mice treated with AgBR1 antiserum, n=11 biologically independent samples pooled from two separate experiments; bitten skin of mice treated with AgBR1 antiserum). The data in FIGS. **14**G-**14**I show that neither the D7Bclu nor SP antisera altered the viremia or protected mice from lethal mosquito-borne Zika virus infection.

[0045] FIGS. **15**A-**15**D show the host responses in mice treated with AgBR1 antiserum at the mosquito bite site. At 24 hours post feeding, the sites bitten by Zika virus-infected mosquitoes were collected, and total RNA was extracted for RNA-seq. In FIG. **15**A, the top panel shows 536 genes (54.4%) within 986 differentially expressed genes ($P<0.05$) were upregulated at the bitten sites of mice administered control serum. The bottom left panel shows that among these

536 genes, 78 genes were significantly upregulated at the bitten site of mice administered control serum compared with mice injected with AgBR1 antiserum. The bottom right panel shows that among the 536 genes, 272 genes were differentially upregulated in bitten sites of mice administered AgBR1 antiserum compared with the resting sites of mice inoculated with control serum. In FIG. **15**B, GSEA of inflammatory responses (Hallmark) and cytokine-cytokine receptor interaction (KEGG) pathway enriched at bite sites of mice compared with resting sites in control mice. In FIG. **15**C, the top panel is a Venn diagram depicting the overlap of genes differentially expressed across the conditions. The bottom panel is a heat map of hierarchical clustering performed on 18 upregulated genes across the conditions (Fold change >1.5, P<0.05). In FIGS. **15**A-**15**C, the parameters are as follows: Control-resting skin: n=2, Control-bitten skin: n=2, AgBR1 antiserum-bitten skin: n=2 biologically independent samples. Normalized read counts were statistically modeled using Partek Flow's Gene Specific Analysis (GSA) approach. FIG. **15**D shows a QRT-PCR based analysis of Il1b and Il6 expression, which is normalized to mouse β actin RNA levels. Each dot represents one bitten or control site. Data are presented as mean±s.e.m. Significance was determined by two-way ANOVA test. (Control-resting skin: n=13, Control-bitten skin: n=13, AgBR1 antiserum-resting skin: n=13, AgBR1 antiserum-bitten skin: n=13 biologically independent samples pooled from two separate experiments.)

[0046] FIG. **15**E shows that the direct inoculation of AgBR1 into the skin significantly induces Il1b and Il6 expression.

[0047] FIGS. **16**A-**16**C show the effect of active immunization with AgBR1 on mosquito-borne Zika infection in mice. Active immunization with AgBR1 reduces mosquito-borne Zika infection in mice. In FIG. **16**A, AG129 mice were immunized with AgBR1 or OVA in Freund's adjuvant. Two weeks after final boost, the sera from immunized mice were examined for specific antibodies with ELISA. Sera from AgBR1-immunized mice recognized AgBR1 (right panel), but not ovalbumin, OVA (left panel). In FIG. **16**B, blood was collected every other day for 9 days from immunized mice fed on by Zika virus-infected mosquitoes and analyzed for Zika virus infection by qRT-PCR. Zika virus RNA levels in mice were normalized to mouse β actin RNA levels. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were compared using Wilcoxon-Mann-Whitney test. In FIG. **16**C, mice were monitored for survival for 30 days after infected mosquito feeding. (Left panel) Survival and median survival time (MST) were assessed by a Gehan-Wilcoxon test (n=18/group).

[0048] FIGS. **17**A-**17**D show the protective effects of antibodies against mosquito salivary proteins on mice infected with West Nile virus. Anti-AgBR1 antiserum protected mice against West Nile virus transmission. Mice were administrated with anti-AgBR1 serum one day before WNV-infected mosquito feeding. Immunized mice were monitored for survival.

[0049] FIG. **17**A shows a schematic of the experiment, whose results are shown in FIGS. **17**B-**17**D. In these experiments, mice were administrated AgBR1 antiserum one day before WNV-infected mosquito feeding, and immunized mice were monitored for survival for 10 days after infected mosquito-feeding. FIG. **17**B shows the results of an experiment in which the virus levels in blood of mice fed by an infected mosquito was assayed. In this experiment, blood was collected every other day for 7 days from mice fed on by WNV-infected mosquitoes and analyzed by qRT-PCR. WNV RNA levels were normalized to mouse β actin RNA levels. Mice immunized with naïve serum served as controls. In FIG. **17**B, the error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using one-tailed Wilcoxon-Mann-Whitney test (n=13/each group biologically independent samples pooled from three separate experiments). FIG. **17**C shows the weight of mice fed by an infected mosquito in an experiment in which mice were monitored daily after WNV infection. Error bars represent mean±SEM. Weight at each time point were compared using one-tailed Wilcoxon-Mann-Whitney test (n=13/each group biologically independent samples pooled from three separate experiments). FIG. **17**D shows the results of an experiment in which survival was assessed by a Gehan-Wilcoxon test (n=13/each group biologically independent samples pooled from three separate experiments).

[0050] FIGS. **17**E and **17**F show that AgBR1 antiserum modulates host responses at the WNV-infected mosquito bite site. The expression levels of several cytokines were analyzed by qRT-PCR at (a) 6 hours (FIG. **17**E) or 24 hours (FIG. **17**F) after bites of infected mosquitoes, which is normalized to mouse β actin RNA levels. Error bars represent mean±SEM. Each dot represents one bitten or control site. Significance was determined by two-way ANOVA test (6 hours; n=19/control group, n=15/AgBR1 antiserum group, 24 hours; n=15/control group, n=17/AgBR1 antiserum group biologically independent samples pooled from two separate experiments). FIGS. **17**G-**17**I show the results of identical passive immunization experiments using SP antiserum. SP antiserum did not alter viremia, weight loss or survival time after lethal mosquito-borne WNV infection. FIG. **17**J is an immunoblot of *Ae. aegypti* and *Culex pipiens* salivary glands probed with rabbit AgBR1 antiserum, the immunoblot showing that AgBR1 antiserum also specifically recognizes a protein in *Culex pipiens* salivary glands.

[0051] FIGS. **18**A-**18**C show the effects of double-stranded RNAs (dsRNA) against AgBR1 on the levels of AgBR1 and Zika virus in mice. Mosquitoes treated with 200 ng AgBR1- or GFP-dsRNA were used to isolate total RNA at day 13 post dsRNA injection. In FIG. **18**A, mRNA levels were determined by qRT-PCR and normalized to mosquito Rp49 RNA levels. In FIG. **18**B, AgBR1-dsRNA- or GFP-dsRNA-treated mosquitoes were collected 13 days after gene silencing. The SGE was run by SDS-PAGE and probed with rabbit AgBR1 antisera. In FIG. **18**C, silencing AgBR1 does not alter ZIKV infection at day 10 after virus injection. Viral burden was examined at day 10 after infection by qRT-PCR and normalized to mosquito Rp49 RNA. The results shown are pooled from three independent experiments. Significance was calculated using the non-parametric Mann-Whitney test.

The primer sequences of dsRNA against AgBR1 are:

(SEQ ID NO: 126)
F-taatacgactcactatagggGATGGACAGATGTCTCTTCGTG;

(SEQ ID NO: 127)
R-taatacgactcactatagggCCAAATCCAATCCATCGAAA.

The primer sequences of dsRNA against GFP are:

(SEQ ID NO: 128)
F-TAATACGACTCACTATAGGGGTGAGCAAGGGCGAGGAG;

(SEQ ID NO: 129)
R-TAATACGACTCACTATAGGGCATGATATAGACGTTGTGGCTGTT.

In FIG. **18**D, a partial knock-down of AgBR1 impacts neutrophil recruitment in the skin. The percent of $CD45^+$ $CD11b^+Ly6G^+$ (neutrophils) cells in $CD45^+$ leukocyte cells at 24 h after dsRNA-treated and Zika virus-infected mosquito feeding. Each dot represents one mouse. Significance was calculated using a two-way ANOVA test for multiple comparisons.

[0052] FIG. **19** shows IL1β ex vivo expression in purified neutrophils from bone marrow of naïve mice after treatment with antigenic proteins. NeSt1 protein activates neutrophils to express IL1β ex vivo. N=8-16 technical replicates from 4 mice for each protein.

[0053] FIG. **20** shows CXCL2 ex vivo expression in purified neutrophils from bone marrow of naïve mice after treatment with antigenic proteins. NeSt1 protein activates neutrophils to express CXCL2 ex vivo. N=8-16 technical replicates from 4 mice for each protein.

[0054] FIG. **21** shows CCL2 ex vivo expression in purified neutrophils from bone marrow of naïve mice after treatment with antigenic proteins. NeSt1 protein activates neutrophils to express CCL2 ex vivo. N=8-16 technical replicates from 4 mice for each protein.

[0055] FIG. **22** shows in vitro expression of IL1β in RAW macrophage cells after treatment with antigenic proteins. NeSt1 protein does not activate RAW macrophage cells to express IL1β. N=8 technical replicates and 2 biological replicates.

[0056] FIG. **23** shows in vitro expression of CXCL2 in RAW macrophage cells after treatment with antigenic proteins. NeSt1 protein does not activate RAW macrophage cells to express CXCL2. N=8 technical replicates and 2 biological replicates.

[0057] FIG. **24** shows similar Zika virus levels by qRT-PCR in mosquitoes fed on naïve AG129 mice and similar numbers (~4) of infected mosquitoes fed on each mouse. Mosquito ZIKV burden is similar in insects fed on mice passively immunized with pre-immune sera and NeSt1 antisera.

[0058] FIG. **25** shows lower Zika virus level by qRT-PCR in AG129 treated with rabbit sera against mosquito protein NeSt1 (LOC5578631) at day 1 after feeding by ZIKV infected mosquitoes. Zika virus infected mosquitoes were allowed to feed on naïve AG129 mice and mice were bled every other day for 9 days. Viremia was measured by isolating RNA from serum and analyzing by qRT-PCR. N=12 mice/group in 3 independent experiments. Significance calculated by one-way ANOVA with post hoc Tukey test for multiple comparisons. Passive immunization against NeSt1 protein protects against early replication of ZIKV.

[0059] FIG. **26** shows serum against NeSt1 (LOC5578631) protects mice from severe Zika virus pathogenesis. Mice treated with NeSt1 antiserum and naïve rabbit serum were fed on by Zika virus infected mosquito and tracked for severe morbidity daily. N=12 mice/group in 3 independent experiments. Significance was calculated using log-rank test. Passive immunization against NeSt1 protein protects against pathogenesis of ZIKV.

[0060] FIG. **27** shows flow gating for experiments in FIGS. **28-31** in which mice treated with naïve rabbit serum or NeSt1 antiserum before feeding uninfected mosquitoes on ears and then isolating cells and analyzing by flow cytometry. $MHCII^+CD45^+$ cells were gated, $Ly6G^+$ (neutrophils) were gated from this population. From $MHCII^+CD45^+$ $Ly6G^-$ cells, $CD207^+$ (langerhan cells) were gated. From $MHCII^+CD45^+Ly6G^-$ $CD207^-$ cells, $CD11c^+$ (dendritic cells) and $CD11c^-$ (macrophages) were gated.

[0061] FIG. **28** shows similar numbers of $MHCII^+CD45^+$ $Ly6G^-$ $CD207^+$ Langerhan cells in naïve and bitten ears in mice treated with naïve or NeSt1 antiserum. No significant differences between groups. N=8/group in two independent experiments. Passive immunization against NeSt1 does not affect the percentage of Langerhan cells at the bite site.

[0062] FIG. **29** shows more $MHCII^+CD45^+Ly6G^+$ neutrophils in bitten compared to naïve ears in mice treated with naïve or NeSt1 antiserum. No significant differences between groups. N=8/group in two independent experiments. Passive immunization against NeSt1 does not affect the infiltration or expansion of neutrophils at the local bite site.

[0063] FIG. **30** shows higher percentage of $MHCII^+$ $CD45^+Ly6G^-CD207^-CD11c^-$ macrophages in bitten compared to naïve ears in mice treated with naïve but not NeSt1 antiserum. Significance calculated with one-way ANOVA with post hoc Tukey test for multiple comparisons. N=8/group in two independent experiments. Passive immunization against NeSt1 prevents the infiltration or expansion of macrophages at the local bite site.

[0064] FIG. **31** shows lower percentage of $MHCII^+CD45^+$ $Ly6G^-$ $CD207^-CD11c^+$ dendritic cells in bitten compared to naïve ears in mice treated with naïve but not NeSt1 antiserum. Significance calculated with one-way ANOVA with post hoc Tukey test for multiple comparisons. N=8/group in two independent experiments. Passive immunization against NeSt1 decreases the percentage of dendritic cells at the local bite site.

[0065] FIGS. **32**A-**32**C show that blocking NeSt1 reduces induction of IL-1β and CXCL2 expression in vivo. Five-week-old C57BL/6 mice were passively immunized with preimmune rabbit sera or rabbit sera against NeSt1 protein. After 24 h, mosquitoes were allowed to bite the right ear (bitten), and the left ear was left alone (naive). cDNA was generated, and qPCR was used to measure IL-1β (FIG. **32**A), CXCL2 (FIG. **32**B), or CCL2 (FIG. **32**C) expression. The data were normalized to mouse β-actin with the $\Delta\Delta C_T$ method and are presented as percentages of the average $\Delta\Delta C_T$ value of naive ear tissue (n=8 to 16 technical replicates from four mice in at least two independent biological replicates for each protein). Error bars represent the SEM. Significance was calculated by two-way ANOVA with a post hoc Tukey test for multiple comparisons. FIG. **32**A shows serum against NeSt1 (LOC5578631) significantly reduces IL1β expression at site of blood feeding by *Aedes aegypti* mosquito. FIG. **32**B shows serum against NeSt1 (LOC5578631) significantly reduces CXCL2 expression at site of blood feeding by *Aedes aegypti* mosquito. FIG. **32**C shows serum against NeSt1 (LOC5578631) does not significantly reduce CCL2 expression at site of blood feeding by *Aedes aegypti* mosquito.

DETAILED DESCRIPTION OF THE INVENTION

[0066] The present invention is based on an unexpected discovery by the present inventors that passive or active immunization against certain *Aedes aegypti* mosquito salivary gland proteins prevents and/or treats infection by flaviviruses such as Zika virus and West Nile virus.

[0067] As the global disease burden attributable to Zika virus continues to increase, new and creative strategies for vaccine design against this and other mosquito-borne viruses are needed. Although there are many efforts to develop Zika virus specific vaccines, there is currently no available commercial vaccine. The compositions and methods described herein utilize a new paradigm to develop a next-generation vaccine against Zika virus and other mosquito-borne viruses so as to address this important public health need. Human vaccines against infectious diseases are currently based upon components of specific pathogens, but the approach described herein targets arthropod vector proteins that affect pathogen transmission. The benefits of this novel approach include the possibility of developing vaccines that are effective for multiple viruses carried by the same arthropod vector and the shifting of selective evolutionary pressure away from the virus.

[0068] Without wishing to be bound by theory, it is hypothesized that salivary gland proteins from the mosquito vector, *Ae. aegypti*, are capable of enhancing virus infection of the mammalian host, and that viral transmission can be interrupted by mounting a robust immune response toward one or more of these proteins. The salivary gland is the last organ in the mosquito vector that viruses are in contact with before being inoculated into a host. Mosquito saliva is important for successful blood feeding.

[0069] The passive and active immunization approaches based on mosquito salivary gland proteins disclosed herein can be used alone or in conjunction with more conventional vaccines targeting viral components to increase their efficacy.

[0070] As disclosed in the Examples section, below, a yeast display screening conducted by the present inventors identified several *Ae. aegypti* antigenic salivary proteins, i.e., LOC5573204, LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, and LOC110675548 (numbering according to the LOC nomenclature used in vectorbase and the NCBI database for the *Aedes aegypti* Liverpool strain reference genome sequence from the *Aedes aegypti* Genome Working Group, see https://www.vectorbase.org/). One of these antigenic proteins, LOC5573204 bacteria-responsive protein 1 (AgBR1), shows particular promise as a candidate for a vaccine development. Described herein is a study of the protective effects of blocking the mosquito AgBR1 protein or the mosquito NeSt1 protein in preventing severe mosquito-borne Zika virus infection in mice. Mammals such as mice and humans may be actively immunized against the AgBR1 and/or NeSt1 protein.

Definitions

[0071] It must also be noted that, as used in the specification and the appended claims, the singular forms "a," "an" and "the" include plural references unless the context clearly dictates otherwise. For example, reference to a component is intended also to include composition of a plurality of components. References to a composition containing "a" constituent is intended to include other constituents in addition to the one named. In other words, the terms "a," "an," and "the" do not denote a limitation of quantity, but rather denote the presence of "at least one" of the referenced item.

[0072] Ranges may be expressed herein as from "about" or "approximately" or "substantially" one particular value and/or to "about" or "approximately" or "substantially" another particular value. When such a range is expressed, other exemplary embodiments include from the one particular value and/or to the other particular value. Further, the term "about" means within an acceptable error range for the particular value as determined by one of ordinary skill in the art, which will depend in part on how the value is measured or determined, i.e., the limitations of the measurement system. For example, "about" can mean within an acceptable standard deviation, per the practice in the art. Alternatively, "about" can mean a range of up to ±20%, preferably up to ±10%, more preferably up to ±5%, and more preferably still up to ±1% of a given value. Alternatively, particularly with respect to biological systems or processes, the term can mean within an order of magnitude, preferably within 2-fold, of a value. Where particular values are described in the application and claims, unless otherwise stated, the term "about" is implicit and in this context means within an acceptable error range for the particular value.

[0073] The dimensions and values disclosed herein are not to be understood as being strictly limited to the exact numerical values recited. Instead, unless otherwise specified, each such dimension is intended to mean both the recited value and a functionally equivalent range surrounding that value. For example, a dimension disclosed as "50 mm" is intended to mean "about 50 mm."

[0074] It is also to be understood that the mention of one or more method steps does not preclude the presence of additional method steps or intervening method steps between those steps expressly identified. Similarly, it is also to be understood that the mention of one or more components in a composition does not preclude the presence of additional components than those expressly identified.

[0075] The materials described hereinafter as making up the various elements of the present invention are intended to be illustrative and not restrictive. Many suitable materials that would perform the same or a similar function as the materials described herein are intended to be embraced within the scope of the invention. Such other materials not described herein can include, but are not limited to, materials that are developed after the time of the development of the invention, for example. Any dimensions listed in the various drawings are for illustrative purposes only and are not intended to be limiting. Other dimensions and proportions are contemplated and intended to be included within the scope of the invention.

[0076] As used herein, the term "subject" or "patient" refers to mammals and includes, without limitation, human and veterinary animals as well as experimental animal models. In a preferred embodiment, the subject is human.

[0077] The terms "treat" or "treatment" of a state, disorder or condition include: (1) preventing or delaying the appearance of at least one clinical or sub-clinical symptom of the state, disorder or condition developing in a subject that may be afflicted with or predisposed to the state, disorder or condition but does not yet experience or display clinical or

subclinical symptoms of the state, disorder or condition; or (2) inhibiting the state, disorder or condition, i.e., arresting, reducing or delaying the development of the disease or a relapse thereof (in case of maintenance treatment) or at least one clinical or sub-clinical symptom thereof; or (3) relieving the disease, i.e., causing regression of the state, disorder or condition or at least one of its clinical or sub-clinical symptoms. The benefit to a subject to be treated is either statistically significant or at least perceptible to the patient or to the physician.

[0078] As used herein, the term "prevent" encompasses any activity which reduces the burden of mortality or morbidity from disease. Prevention can occur at primary, secondary and tertiary prevention levels. While primary prevention avoids the development of a disease, secondary and tertiary levels of prevention encompass activities aimed at preventing the progression of a disease and the emergence of symptoms as well as reducing the negative impact of an already established disease by restoring function and reducing disease-related complications.

[0079] The term "therapeutic" as used herein means a treatment and/or prophylaxis. A therapeutic effect is obtained by suppression, diminution, remission, or eradication of a disease state.

[0080] As used herein the term "therapeutically effective" applied to dose or amount refers to that quantity of a compound or pharmaceutical composition that when administered to a subject for treating (e.g., preventing or ameliorating) a state, disorder or condition, is sufficient to effect such treatment. The "therapeutically effective amount" will vary depending on the compound administered as well as the disease and its severity and the age, weight, physical condition and responsiveness of the mammal to be treated.

[0081] The phrase "pharmaceutically acceptable", as used in connection with compositions of the invention, refers to molecular entities and other ingredients of such compositions that are physiologically tolerable and do not typically produce untoward reactions when administered to a mammal (e.g., a human). Preferably, as used herein, the term "pharmaceutically acceptable" means approved by a regulatory agency of the Federal or a state government or listed in the U.S. Pharmacopeia or other generally recognized pharmacopeia for use in mammals, and more particularly in humans.

[0082] The terms "pharmaceutical carrier" or "pharmaceutically acceptable carrier" refer to a diluent, adjuvant, excipient, or vehicle with which the compound is administered. Such pharmaceutical carriers can be sterile liquids, such as water and oils, including those of petroleum, animal, vegetable or synthetic origin, such as peanut oil, soybean oil, mineral oil, sesame oil and the like. Water or aqueous solution saline solutions and aqueous dextrose and glycerol solutions are preferably employed as carriers, particularly for injectable solutions. Alternatively, the pharmaceutical carrier can be a solid dosage form carrier, including but not limited to one or more of a binder (for compressed pills), a glidant, an encapsulating agent, a flavorant, and a colorant. Suitable pharmaceutical carriers are described in "Remington's Pharmaceutical Sciences" by E. W. Martin.

[0083] The terms "derivative" and "analog" are used interchangeably and refer to a related modified form of a polypeptide, wherein at least one amino acid substitution, deletion, addition, or chemical modification has been made. The terms "functional derivative" and "functional analog" mean that such derivative/analog/variant retains substantially the same biological activity as the unmodified form, in vivo and/or in vitro. A term "variant" refers to polypeptide derivatives/analogs, wherein (i) one or more of the amino acid residues are substituted with a conserved or non-conserved amino acid residue (preferably a conserved amino acid residue) and such substituted amino acid residue may or may not be one encoded by the genetic code, (ii) one in which there are one or more modified amino acid residues, e.g., residues that are modified by the attachment of substituent groups, (iii) one in which the polypeptide is an alternative splice variant of the polypeptide of the present invention, (iv) fragments of the polypeptides and/or (v) one in which the polypeptide is fused with another polypeptide, such as a leader or secretory sequence or a sequence which is employed for purification (for example, His-tag) or for detection (for example, Sv5 epitope tag). The fragments include polypeptides generated via proteolytic cleavage (including multi-site proteolysis) of an original sequence. Variants may be post-translationally, or chemically modified. Such variants are deemed to be within the scope of those skilled in the art from the teaching herein.

[0084] The term "antibody," as used herein, refers to an immunoglobulin molecule which specifically binds with an antigen. An antibody can be an intact immunoglobulin derived from a natural source or from a recombinant source. Such antibody can comprise an immunoreactive portion of an intact immunoglobulin. The antibody may exist in a variety of forms including, for example, polyclonal antibodies, monoclonal antibodies, Fv, Fab and F(ab)2, as well as single chain antibodies and humanized antibodies (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, N.Y.; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426).

[0085] The term "antigen" or "Ag" as used herein is defined as a molecule that provokes an immune response. This immune response may involve either antibody production, or the activation of specific immunologically-competent cells, or both. Any macromolecule, including virtually all proteins or peptides, can serve as an antigen. Furthermore, antigens can be derived from recombinant or genomic DNA. Any DNA which comprises a nucleotide sequences or a partial nucleotide sequence encoding a protein that elicits an immune response therefore encodes an "antigen" as that term is used herein. Furthermore, an antigen need not be encoded solely by a full-length nucleotide sequence of a gene. Partial nucleotide sequences of more than one gene may be used, for example these nucleotide sequences may be arranged in various combinations to elicit a desired immune response. Moreover, an antigen need not be encoded by a "gene" at all. An antigen can be generated synthesized or can be derived from a biological sample.

[0086] "Expression vector" refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., lentiviruses, ret-

roviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[0087] The terms "sequence identity" and "percent identity" are used interchangeably herein. For the purpose of this invention, it is defined here that in order to determine the percent identity of two amino acid sequences or two nucleic acid sequences, the sequences are aligned for optimal comparison purposes (e.g., gaps can be introduced in the sequence of a first amino acid or nucleic acid for optimal alignment with a second amino or nucleic acid sequence). The amino acid or nucleotide residues at corresponding amino acid or nucleotide positions are then compared. When a position in the first sequence is occupied by the same amino acid or nucleotide residue as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences (i.e., % identity=number of identical positions/total number of positions (i.e., overlapping positions)×100). Preferably, the two sequences are the same length.

[0088] Several different computer programs are available to determine the degree of identity between two sequences. For instance, a comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In a preferred embodiment, the percent identity between two amino acid or nucleic acid sequences is determined using the Needleman and Wunsch (J. Mol. Biol. (48): 444-453 (1970)) algorithm which has been incorporated into the GAP program in the Accelrys GCG software package (available at www.accelrys.com/products/gcg), using either a Blosum 62 matrix or a PAM250 matrix, and a gap weight of 16, 14, 12, 10, 8, 6, or 4 and a length weight of 1, 2, 3, 4, 5, or 6. These different parameters will yield slightly different results but the overall percentage identity of two sequences is not significantly altered when using different algorithms.

[0089] A sequence comparison may be carried out over the entire lengths of the two sequences being compared or over fragments of the two sequences. Typically, the comparison will be carried out over the full length of the two sequences being compared. However, sequence identity may be carried out over a region of, for example, twenty, fifty, one hundred or more contiguous amino acid residues.

[0090] Sequence identity can be readily calculated by known methods, including but not limited to, those described in Computational Molecular Biology, Lesk, A. N., ed., Oxford University Press, New York (1988), Biocomputing: Informatics and Genome Projects, Smith, D. W., ed., Academic Press, New York (1993); Computer Analysis of Sequence Data, Part I, Griffin, A. M., and Griffin, H. G., eds., Humana Press, New Jersey (1994); Sequence Analysis in Molecular Biology, von Heinge, G., Academic Press (1987); Sequence Analysis Primer, Gribskov, M. and Devereux, J., eds., M. Stockton Press, New York (1991); and Carillo, H., and Lipman, D., SIAM J. Applied Math., 48: 1073 (1988), the teachings of which are incorporated herein by reference. Preferred methods to determine the sequence identity are designed to give the largest match between the sequences tested. Methods to determine sequence identity are codified in publicly available computer programs which determine sequence identity between given sequences. Examples of such programs include, but are not limited to, the GCG program package (Devereux, J., et al., Nucleic Acids Research, 12(1):387 (1984)), BLASTP, BLASTN and FASTA (Altschul, S. F. et al., J. Molec. Biol., 215:403-410 (1990). The BLASTX program is publicly available from NCBI and other sources (BLAST Manual, Altschul, S. et al., NCVI NLM NIH Bethesda, Md. 20894, Altschul, S. F. et al., J. Molec. Biol., 215:403-410 (1990), the teachings of which are incorporated herein by reference). These programs optimally align sequences using default gap weights in order to produce the highest level of sequence identity between the given and reference sequences.

[0091] As used herein, the term "immune response" includes T-cell mediated and/or B-cell mediated immune responses. Exemplary immune responses include T cell responses, e.g., cytokine production and cellular cytotoxicity, and B cell responses, e.g., antibody production. In addition, the term "immune response" includes immune responses that are indirectly affected by T cell activation, e.g., antibody production (humoral responses) and activation of cytokine responsive cells, e.g., macrophages. Immune cells involved in the immune response include lymphocytes, such as B cells and T cells (CD4+, CD8+, Th1 and Th2 cells); antigen presenting cells (e.g., professional antigen presenting cells such as dendritic cells, macrophages, B lymphocytes, Langerhans cells, and non-professional antigen presenting cells such as keratinocytes, endothelial cells, astrocytes, fibroblasts, oligodendrocytes); natural killer cells; myeloid cells, such as macrophages, eosinophils, mast cells, basophils, and granulocytes.

[0092] "Isolated" means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not "isolated," but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is "isolated." An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

[0093] Throughout this disclosure, various aspects of the invention can be presented in a range format. The description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range.

[0094] In accordance with the present invention there may be employed conventional molecular biology, microbiology, and recombinant DNA techniques within the skill of the art. Such techniques are explained fully in the literature. See, e.g., Sambrook, Fritsch & Maniatis, *Molecular Cloning: A Laboratory Manual*, Second Edition (1989) Cold Spring Harbor Laboratory Press, Cold Spring Harbor, N.Y. (herein "Sambrook et al., 1989"); *DNA Cloning: A Practical Approach*, Volumes I and II (D. N. Glover ed. 1985); *Oligonucleotide Synthesis* (M. J. Gait ed. 1984); *Nucleic Acid Hybridization* (B. D. Hames & S. J. Higgins eds. (1985); *Transcription and Translation* (B. D. Hames & S. J. Higgins, eds. (1984); *Animal Cell Culture* (R. I. Freshney, ed. (1986); *Immobilized Cells and Enzymes* (IRL Press, (1986); B. Perbal, *A Practical Guide To Molecular Cloning*

(1984); F. M. Ausubel et al. (eds.), *Current Protocols in Molecular Biology*, John Wiley & Sons, Inc. (1994); among others.

[0095] The invention provides an immunological composition comprising a polypeptide or combination of polypeptides derived from at least one mosquito salivary protein associated with a mosquito-borne virus such as, e.g., a flavivirus (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) or an alphavirus (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus), useful in eliciting an immune response. The compositions comprising one or more polypeptide of the invention not only are useful as agents for immunoprotection but are also useful as agents for treatment of an ongoing disease or disorder associated with infection by mosquito-borne viruses such as, e.g., flaviviruses (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) and alphaviruses (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus) in a subject.

Compositions of the Invention

[0096] In one aspect, the present invention provides a polypeptide or a combination of polypeptides, or a polynucleotide or a combination of polynucleotides encoding such polypeptides, wherein such polypeptides comprise or are derived from a mosquito salivary protein and are useful in inducing an immune response which prevents and/or treats an infection by a mosquito-borne virus such as, e.g., a flavivirus (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) or an alphavirus (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus).

[0097] In one embodiment, the invention provides a vaccine composition comprising at least one polypeptide selected from the group consisting of LOC5573204 (AgBR1), LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof. In some embodiments, such fragments, derivatives or variants are capable of inducing an immune response which prevents and/or treats an infection by a mosquito-borne virus such as, e.g., a flavivirus (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) or an alphavirus (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus). In some embodiments, polypeptide comprises a sequence of any one of SEQ ID NOS: 100-125, or a sequence of a contiguous 10 amino acid portion of any one of SEQ ID NOS: 100-125. In some embodiments, the polypeptide LOC5573204 comprises the sequence SEQ ID NO: 1. In some embodiments, the polypeptide LOC5578630 comprises the sequence SEQ ID NO: 2. In some embodiments, the polypeptide LOC5578631 comprises the sequence SEQ ID NO: 3. In some embodiments, the polypeptide LOC5567956 comprises the sequence SEQ ID NO: 4. In some embodiments, the polypeptide LOC5580038 comprises the sequence SEQ ID NO: 5. In some embodiments, the polypeptide LOC5566287 comprises the sequence SEQ ID NO: 43. In some embodiments, the polypeptide LOC5567958 comprises the sequence SEQ ID NO: 44. In some embodiments, the polypeptide LOC5568702 comprises the sequence SEQ ID NO: 45. In some embodiments, the polypeptide LOC110675548 comprises the sequence SEQ ID NO: 46. In some embodiments, the polypeptide LOC5573204 consists of the sequence SEQ ID NO: 1. In some embodiments, the polypeptide LOC5578630 consists of the sequence SEQ ID NO: 2. In some embodiments, the polypeptide LOC5578631 consists of the sequence SEQ ID NO: 3. In some embodiments, the polypeptide LOC5567956 consists of the sequence SEQ ID NO: 4. In some embodiments, the polypeptide LOC5580038 consists of the sequence SEQ ID NO: 5. In some embodiments, the polypeptide LOC5566287 consists of the sequence SEQ ID NO: 43. In some embodiments, the polypeptide LOC5567958 consists of the sequence SEQ ID NO: 44. In some embodiments, the polypeptide LOC5568702 consists of the sequence SEQ ID NO: 45. In some embodiments, the polypeptide LOC110675548 consists of the sequence SEQ ID NO: 46. In some embodiments, the fragments of LOC5573204 comprise the sequence of any one of SEQ ID NOS: 6-13. In some embodiments, the fragments of LOC5578630 comprise the sequence of any one of SEQ ID NOS: 14-21. In some embodiments, the fragments of LOC5578631 comprise the sequence of any one of SEQ ID NOS: 22-29. In some embodiments, the fragments of LOC5567956 comprise the sequence of any one of SEQ ID NOS: 30-36. In some embodiments, the fragments of LOC5580038 comprise the sequence of any one of SEQ ID NOS: 37-42. In some embodiments, the fragments of LOC5566287 comprise the sequence of any one of SEQ ID NOS: 47-59. In some embodiments, the fragments of LOC5567958 comprise the sequence of any one of SEQ ID NOS: 60-70. In some embodiments, the fragments of LOC5568702 comprise the sequence of any one of SEQ ID NOS: 71-85. In some embodiments, the fragments of LOC110675548 comprise the sequence of any one of SEQ ID NOS: 86-99. In some embodiments, the polypeptides of the invention have at least 90% amino acid sequence identity to any of the above sequences, e.g., at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% amino acid sequence identity.

[0098] In one embodiment, the vaccine compositions of the invention also comprise one or more carriers and/or excipients. In one embodiment, the vaccine compositions of the invention also comprise one or more adjuvant. In one embodiment, the vaccine compositions of the invention also comprise one or more additional immunogenic polypeptides (e.g., an immunogenic polypeptide derived from the target virus such as, e.g., antigens from viral envelope or capsid).

[0099] Polypeptides of the present invention can be prepared using well known techniques. For example, the polypeptides can be prepared synthetically, using either recombinant DNA technology or chemical synthesis. Polypeptides of the present invention may be synthesized individually, or as longer polypeptides composed of two or more polypeptides. The polypeptides of the present invention can be isolated, i.e., substantially free of other naturally occurring host cell proteins and fragments thereof.

[0100] The polypeptides of the present invention may contain modifications, such as glycosylation, aglycosylation, side chain oxidation, or phosphorylation; so long as the modifications do not destroy the immunologic activity of the polypeptides. Other modifications include incorporation of D-amino acids or other amino acid mimetics that can be used, for example, to increase the serum half-life of the polypeptides.

[0101] The polypeptides of the invention can be modified whereby the amino acid is substituted for a different amino acid in which the properties of the amino acid side-chain are conserved (a process known as conservative amino acid substitution). Examples of properties of amino acid side chains are hydrophobic amino acids (A, I, L, M, F, P, W, Y, V), hydrophilic amino acids (R, D, N, C, E, Q, G, H, K, S, T), and side chains having the following functional groups or characteristics in common: an aliphatic side-chain (G, A, V, L, I, P); a hydroxyl group containing side-chain (S, T, Y); a sulfur atom containing side-chain (C, M); a carboxylic acid and amide containing side-chain (D, N, E, Q); a base containing side-chain (R, K, H); and an aromatic containing side-chain (H, F, Y, W). Note that the parenthetic letters indicate the one-letter codes of amino acids. As used herein, X stands for any amino acid.

[0102] The polypeptides of the invention can be prepared as a combination, which includes two or more of polypeptides of the invention, for use as a vaccine for the reduction, prevention, or treatment of a mosquito-borne virus infection (e.g., an infection by a flavivirus [such as, e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus] or an infection by an alphavirus [e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus]). The polypeptides may be in a cocktail or may be conjugated to each other using standard techniques. For example, the polypeptides can be expressed as a single polypeptide sequence. The polypeptides in the combination may be the same or different.

[0103] The present invention should also be construed to encompass "analogs," "mutants," "derivatives," and "variants" of the polypeptides of the invention (or of the DNA encoding the same) which analogs, mutants, derivatives and variants are polypeptides which are altered in one or more amino acids (or, when referring to the nucleotide sequence encoding the same, are altered in one or more base pairs) such that the resulting polypeptide (or DNA) is not identical to the sequences recited herein, but has the same biological property as the polypeptides disclosed herein.

[0104] The nucleic acid sequences include both the DNA sequence that is transcribed into RNA and the RNA sequence that is translated into a polypeptide. According to other embodiments, the polynucleotides of the invention are inferred from the amino acid sequence of the polypeptides of the invention. As is known in the art several alternative polynucleotides are possible due to redundant codons, while retaining the biological activity of the translated polypeptides.

[0105] It is to be understood explicitly that the scope of the present invention encompasses homologs, analogs, variants, fragments, derivatives and salts, including shorter and longer polypeptides and polynucleotides, as well as polypeptide and polynucleotide analogs with one or more amino acid or nucleic acid substitutions, as well as amino acid or nucleic acid derivatives, non-natural amino or nucleic acids and synthetic amino or nucleic acids as are known in the art, with the stipulation that these modifications must preserve the immunologic activity of the original molecule. Specifically, any active fragments of the active polypeptides as well as extensions, conjugates and mixtures are included and are disclosed herein according to the principles of the present invention.

[0106] In one embodiment, the compositions of the invention comprise a nucleic acid sequence encoding one or more of the above polypeptides, derivatives, variants or fragments. Such nucleic acid sequence can be included in a vector, e.g., an expression vector.

[0107] The nucleic acids of the invention may encompass an RNA or a DNA sequence encoding a polypeptide of the invention, and any modified forms thereof, including chemical modifications of the DNA or RNA which render the nucleotide sequence more stable when it is cell free or when it is associated with a cell. Chemical modifications of nucleotides may also be used to enhance the efficiency with which a nucleotide sequence is taken up by a cell or the efficiency with which it is expressed in a cell. Any and all combinations of modifications of the nucleotide sequences are contemplated in the present invention.

[0108] Further, any number of procedures may be used for the generation of mutant, derivative or variant forms of a protein of the invention using recombinant DNA methodology well known in the art such as, for example, that described in Sambrook et al. (2012, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York), and in Ausubel et al. (1997, Current Protocols in Molecular Biology, John Wiley & Sons, New York). Procedures for the introduction of amino acid changes in a polypeptide or polypeptide by altering the DNA sequence encoding the polypeptide are well known in the art and are also described in these, and other, treatises.

[0109] The nucleic acids encoding the polypeptide or combinations of polypeptides of the invention of the invention can be incorporated into suitable vectors, including but not limited to, plasmids and recombinant viral vectors (e.g., retroviral vectors, lentiviral vectors, adenoviral vectors, adeno-associated virus (AAV) vectors, herpes virus vectors). Such vectors are well known in the art and are therefore not described in detail herein.

[0110] In one embodiment, the invention includes a nucleic acid sequence encoding one or more polypeptides of the invention operably linked to a nucleic acid comprising a promoter/regulatory sequence such that the nucleic acid is preferably capable of directing expression of the protein encoded by the nucleic acid. Thus, the invention encompasses expression vectors and methods for the introduction of exogenous DNA into cells with concomitant expression of the exogenous DNA in the cells such as those described, for example, in Sambrook et al. (2012, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, New York), and in Ausubel et al. (1997, Current Protocols in Molecular Biology, John Wiley & Sons, New York). The incorporation of a desired polynucleotide into a vector and the choice of vectors is well-known in the art as described in, for example, Sambrook et al. (2012), and in Ausubel et al. (1997).

[0111] Numerous expression vector systems exist that comprise at least a part or all of the compositions discussed above. Prokaryote- and/or eukaryote-vector based systems can be employed for use with the present invention to produce polynucleotides, or their cognate polypeptides. Many such systems are commercially and widely available.

[0112] Further, the expression vector may be provided to a cell in the form of a viral vector. Viral vector technology is well known in the art and is described, for example, in Sambrook et al. (2012), and in Ausubel et al. (1997), and in other virology and molecular biology manuals. Viruses,

which are useful as vectors include, but are not limited to, retroviruses, adenoviruses, adeno-associated viruses, herpes viruses, and lentiviruses. In general, a suitable vector contains an origin of replication functional in at least one organism, a promoter sequence, convenient restriction endonuclease sites, and one or more selectable markers. (See, e.g., WO 01/96584; WO 01/29058; and U.S. Pat. No. 6,326,193.)

[0113] For expression of the desired nucleotide sequences of the invention, at least one module in each promoter functions to position the start site for RNA synthesis. The best-known example of this is the TATA box, but in some promoters lacking a TATA box, such as the promoter for the mammalian terminal deoxynucleotidyl transferase gene and the promoter for the SV40 genes, a discrete element overlying the start site itself helps to fix the place of initiation.

[0114] Additional promoter elements, i.e., enhancers, regulate the frequency of transcriptional initiation. Typically, these are located in the region 30-110 bp upstream of the start site, although a number of promoters have recently been shown to contain functional elements downstream of the start site as well. The spacing between promoter elements frequently is flexible, so that promoter function is preserved when elements are inverted or moved relative to one another. In the thymidine kinase (tk) promoter, the spacing between promoter elements can be increased to 50 bp apart before activity begins to decline. Depending on the promoter, it appears that individual elements can function either co-operatively or independently to activate transcription.

[0115] A promoter may be one naturally associated with a gene or polynucleotide sequence, as may be obtained by isolating the 5' non-coding sequences located upstream of the coding segment and/or exon. Such a promoter can be referred to as "endogenous." Similarly, an enhancer may be one naturally associated with a polynucleotide sequence, located either downstream or upstream of that sequence. Alternatively, certain advantages will be gained by positioning the coding polynucleotide segment under the control of a recombinant or heterologous promoter, which refers to a promoter that is not normally associated with a polynucleotide sequence in its natural environment. A recombinant or heterologous enhancer refers also to an enhancer not normally associated with a polynucleotide sequence in its natural environment. Such promoters or enhancers may include promoters or enhancers of other genes, and promoters or enhancers isolated from any other prokaryotic, viral, or eukaryotic cell, and promoters or enhancers not "naturally occurring," i.e., containing different elements of different transcriptional regulatory regions, and/or mutations that alter expression. In addition to producing nucleic acid sequences of promoters and enhancers synthetically, sequences may be produced using recombinant cloning and/or nucleic acid amplification technology, including PCR, in connection with the compositions disclosed herein (U.S. Pat. Nos. 4,683,202, 5,928,906). Furthermore, it is contemplated the control sequences that direct transcription and/or expression of sequences within non-nuclear organelles such as mitochondria, chloroplasts, and the like, can be employed as well.

[0116] A promoter and/or enhancer may be employed that effectively directs the expression of the DNA segment in the cell type, organelle, and organism chosen for expression. The promoters employed may be constitutive, tissue-specific, inducible, and/or useful under the appropriate conditions to direct high-level expression of the introduced DNA segment, such as is advantageous in the large-scale production of recombinant proteins and/or polypeptides. The promoter may be heterologous or endogenous.

[0117] One example of a constitutive promoter sequence is the immediate early cytomegalovirus (CMV) promoter sequence. This promoter sequence is a strong constitutive promoter sequence capable of driving high levels of expression of any polynucleotide sequence operatively linked thereto. However, other constitutive promoter sequences may also be used, including, but not limited to the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV), human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, Moloney virus promoter, the avian leukemia virus promoter, Epstein-Barr virus immediate early promoter, Rous sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the hemoglobin promoter, and the muscle creatine promoter. Further, the invention should not be limited to the use of constitutive promoters. Inducible promoters are also contemplated as part of the invention. The use of an inducible promoter in the invention provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionine promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter. Further, the invention includes the use of a tissue-specific promoter, where the promoter is active only in a desired tissue. Tissue-specific promoters are well known in the art and include, but are not limited to, the HER-2 promoter and the PSA associated promoter sequences.

[0118] The expression vector to be introduced into a cell can also contain either a selectable marker gene or a reporter gene or both to facilitate identification and selection of expressing cells from the population of cells sought to be transfected or infected through viral vectors. Such introduction of the expression vector may facilitate assessing the expression of the nucleotide sequences encoding the polypeptide or combinations of polypeptides of the invention. In other embodiments, the selectable marker may be carried on a separate piece of DNA and used in a co-transfection procedure. Both selectable markers and reporter genes may be flanked with appropriate regulatory sequences to enable expression in the host cells. Useful selectable markers are known in the art and include, for example, antibiotic-resistance genes, such as neo and the like.

[0119] Reporter genes are used for identifying potentially transfected cells and for evaluating the functionality of regulatory sequences. Reporter genes that encode for easily assayable proteins are well known in the art. In general, a reporter gene is a gene that is not present in or expressed by the recipient organism or tissue and that encodes a protein whose expression is manifested by some easily detectable property, e.g., enzymatic activity. Expression of the reporter gene is assayed at a suitable time after the DNA has been introduced into the recipient cells.

[0120] Suitable reporter genes may include genes encoding luciferase, beta-galactosidase, chloramphenicol acetyl transferase, secreted alkaline phosphatase, or the green fluorescent protein gene (see, e.g., Ui-Tei et al., 2000 FEBS

Lett. 479:79-82). Suitable expression systems are well known and may be prepared using well known techniques or obtained commercially. Internal deletion constructs may be generated using unique internal restriction sites or by partial digestion of non-unique restriction sites. Constructs may then be transfected into cells that display high levels of siRNA polynucleotide and/or polypeptide expression. In general, the construct with the minimal 5' flanking region showing the highest level of expression of reporter gene is identified as the promoter. Such promoter regions may be linked to a reporter gene and used to evaluate agents for the ability to modulate promoter-driven transcription.

[0121] In some embodiments, the expression vector is modified to increase the expression of the desired polypeptide. For example, the vector can undergo codon optimization to improve expression in a given mammal. For example, the vector can be codon-optimized for human expression. In another embodiment, the expression vector comprises an effective secretory leader. An exemplary leader is an IgE leader sequence. In another embodiment, the expression vector comprises a Kozak element to initiate translation. In another embodiment, the nucleic acid is removed of cis-acting sequence motifs/RNA secondary structures that would impede translation. Such modifications, and others, are known in the art for use in DNA vaccines (Kutzler et al, 2008, Nat. Rev. Gen. 9: 776-788; PCT App. No. PCT/US2007/000886; PCT App. No.; PCT/US2004/018962).

[0122] In various embodiments, the vaccine compositions of the invention are effective to induce an immune response to the antigen in a subject (e.g., a human). In some embodiments, said immune response is effective to prevent and/or treat mosquito-borne viral infections such as infections caused by flaviviruses (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, and yellow fever virus) and alphaviruses (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, and Semliki Forest virus).

[0123] In some embodiments, the vaccine composition comprises an additional immunostimulatory agent or nucleic acids encoding such an agent. Immunostimulatory agents include but are not limited to an additional antigen, an immunomodulator, an antigen presenting cell or an adjuvant. Non-limiting examples of suitable adjuvants include alum and such, cholera toxin, salmonella toxin, but are not limited thereto. In other embodiments, one or more of the additional agent(s) is covalently bonded to the antigen or an immunostimulatory agent, in any combination. In certain embodiments, the vaccine composition is conjugated to or comprises HLA anchor motif amino acids.

[0124] In one embodiment, the vaccine composition is administered in combination with an adjuvant. Non-limiting examples of suitable adjuvants include cholera toxin, salmonella toxin, alum and such, but are not limited thereto. In another embodiment, the vaccine is administered in the absence of an adjuvant.

[0125] In a non-limiting example, a nucleic encoding an antigen can also be formulated with an adjuvant. The various compositions described herein may further comprise additional components. For example, one or more vaccine components may be comprised in a lipid or liposome or nanoparticle.

[0126] Vaccine compositions of the present invention, and its various components, may be prepared and/or administered by any method disclosed herein or as would be known to one of ordinary skill in the art, in light of the present disclosure.

[0127] In one embodiment, the polypeptide vaccine of the invention includes, but is not limited to at least one polypeptide, or a fragment thereof, optionally mixed with adjuvant substances. In some embodiments, the polypeptide is introduced together with an antigen presenting cell (APC). The most common cells used for the latter type of vaccine are bone marrow and peripheral blood derived dendritic cells, as these cells express costimulatory molecules that help activation of T cells. WO 00/06723 discloses a cellular vaccine composition which includes an APC presenting tumor associated antigen polypeptides. Presenting the polypeptide can be effected by loading the APC with a polynucleotide (e.g., DNA, RNA) encoding the polypeptide or loading the APC with the polypeptide itself.

[0128] Vaccine compositions may further comprise a pharmaceutically acceptable carrier, diluent or excipient to form a pharmaceutical formulation, or unit dosage form. The total active ingredients (e.g., polypeptides and inhibitors) in such formulations include from 0.1 to 99.9% by weight of the formulation. The active ingredients (e.g., polypeptides and inhibitors) for administration may be present as a powder or as granules; as a solution, a suspension or an emulsion.

[0129] Pharmaceutical formulations containing the compositions of the invention can be prepared by procedures known in the art using well known and readily available ingredients. The compositions of the invention can also be formulated as solutions appropriate for parenteral administration, for instance by intramuscular, subcutaneous or intravenous routes.

[0130] Thus, the composition may be formulated for parenteral administration (e.g., by injection, for example, bolus injection or continuous infusion) and may be presented in unit dose form in ampules, pre-filled syringes, small volume infusion containers or in multi-dose containers with an added preservative. The active ingredients may take such forms as suspensions, solutions, or emulsions in oily or aqueous vehicles, and may contain formulatory agents such as suspending, stabilizing and/or dispersing agents. Alternatively, the active ingredients may be in powder form, obtained by aseptic isolation of sterile solid or by lyophilization from solution, for constitution with a suitable vehicle, e.g., sterile, pyrogen-free water, before use.

[0131] In general, water, suitable oil, saline, aqueous dextrose (glucose), and related sugar solutions and glycols such as propylene glycol or polyethylene glycols are suitable carriers for parenteral solutions. Solutions for parenteral administration contain the active ingredient, suitable stabilizing agents and, if necessary, buffer substances. Antioxidizing agents such as sodium bisulfate, sodium sulfite or ascorbic acid, either alone or combined, are suitable stabilizing agents. Also used are citric acid and its salts and sodium ethylenediaminetetraacetic acid (EDTA). In addition, parenteral solutions can contain preservatives such as benzalkonium chloride, methyl- or propyl-paraben and chlorobutanol. Suitable pharmaceutical carriers are described in Remington's Pharmaceutical Sciences, a standard reference text in this field.

[0132] Passive Immunization Compositions of the Invention

[0133] The present invention also encompasses various compositions comprising antibodies which interact with the

polypeptides of the invention (preferably specifically and selectively). Such antibody-containing compositions can be used for passive immunization against mosquito-borne viral infections such as infections caused by flaviviruses (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) and alphaviruses (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus). An antibody can be an intact immunoglobulin derived from a natural source or from a recombinant source. Such antibody can comprise an immunoreactive portion of an intact immunoglobulin. The antibody may exist in a variety of forms including, for example, polyclonal antibodies, monoclonal antibodies, Fv, Fab and F(ab)2, as well as single chain antibodies and humanized antibodies (Harlow et al., 1999, In: Using Antibodies: A Laboratory Manual, Cold Spring Harbor Laboratory Press, NY; Harlow et al., 1989, In: Antibodies: A Laboratory Manual, Cold Spring Harbor, N.Y.; Houston et al., 1988, Proc. Natl. Acad. Sci. USA 85:5879-5883; Bird et al., 1988, Science 242:423-426).

[0134] Inhibitor Compositions of the Invention

[0135] The invention also includes inhibitor compositions and methods for inhibiting a function of one or more of the mosquito salivary polypeptides disclosed herein or an interaction between the mosquito salivary polypeptides disclosed herein and host cells or proteins or between the mosquito salivary polypeptides disclosed herein and a mosquito-borne virus. The inhibitor compositions of the invention include, but are not limited to, a chemical compound, a protein, a peptide, a peptidomimetic, an antibody, a ribozyme, a small molecule chemical compound, a glycan, an antisense nucleic acid molecule (e.g., siRNA, miRNA, etc.), or combinations thereof. In some embodiments, the inhibitor compositions bind to the mosquito salivary polypeptide. In other embodiments, the inhibitor compositions bind to the host cell or virus.

[0136] Genetically Modified Mosquitos of the Invention

[0137] The invention also includes mosquitoes that have been genetically modified (e.g., using CRISPR-Cas9 technology) to alter or eliminate one or more of the mosquito salivary polypeptides disclosed herein.

[0138] Methods of the Invention

[0139] The compositions of the invention comprising mosquito salivary polypeptides of the invention or nucleotides encoding such polypeptides can be used as immunostimulatory agents to prevent and/or treat a mosquito-borne viral infection such as, e.g., an infection by a flavivirus (e.g., Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, yellow fever virus) or an alphavirus (e.g., Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, Semliki Forest virus) in a subject (e.g., human or veterinary animal) and associated disease or disorder. In one embodiment, the composition of the invention comprises a AgBR1 polypeptide, or a variant thereof.

[0140] The present invention also encompasses a method of inducing anti-mosquito-borne virus (e.g., anti-flavivirus or anti-alphavirus) immunity using the compositions described herein.

[0141] In another embodiment, the methods of the invention comprise administering to the subject a bacterium or virus comprising a nucleic acid sequence encoding at least one mosquito salivary protein. In another embodiment, the methods of the invention comprise administering to the subject a bacterium or virus expressing at least a portion of at least one mosquito salivary protein. In another embodiment, the methods of the invention comprise administering to the subject a bacterium or virus comprising at least a portion of at least one mosquito salivary protein.

[0142] Effectiveness of the resulting immune response can be determined for detecting the induction of cytotoxic T lymphocytes (CTL) which are well known in the art. A method for evaluating the inducing action of CTL using dendritic cells (DCs) as APC is well known in the art. DC is a representative APC having the strongest CTL inducing action among APCs. In this method, the polypeptide or combination of polypeptides is initially contacted with DC and then this DC is contacted with T cells. Detection of T cells having cytotoxic effects against the cells of interest after the contact with DC shows that the polypeptide or combination of polypeptides has an activity of inducing the cytotoxic T cells. Furthermore, the induced immune response can be also examined by measuring IFN-gamma produced and released by CTL in the presence of antigen-presenting cells that carry immobilized polypeptide or combination of polypeptides by visualizing using anti-IFN-gamma antibodies, such as an ELISPOT assay.

[0143] Apart from DC, peripheral blood mononuclear cells (PBMCs) may also be used as the APC. The induction of CTL is reported to be enhanced by culturing PBMC in the presence of GM-CSF and IL-4. Similarly, CTL has been shown to be induced by culturing PBMC in the presence of keyhole limpet hemocyanin (KLH) and IL-7.

[0144] Generally, when using a polypeptide for cellular immunotherapy, efficiency of the CTL-induction can be increased by combining a plurality of polypeptides having different structures and contacting them with DC. Therefore, when stimulating DC with protein fragments, it is advantageous in certain embodiments to use a mixture of multiple types of fragments.

[0145] The induction of immunity by the compositions of the invention can be further confirmed by observing the induction of antibody production.

[0146] Thus, the invention provides a method for treating or preventing an infection by a mosquito-borne virus such as, e.g., a flavivirus (such as but not limited to, Zika virus, West Nile virus, Dengue virus, tick-borne encephalitis virus, and yellow fever virus) or an alphavirus (such as but not limited to, Chikungunya virus (CHIKV), Ross River virus, O'nyong'nyong virus, and Semliki Forest virus). The therapeutic compounds or compositions of the invention may be administered prophylactically or therapeutically to subjects suffering from, at risk of developing, or susceptible to developing an infection by a mosquito-borne virus such as, e.g., a flavivirus or an alphavirus. Such subjects may be identified using standard clinical methods. In the context of the present invention, prophylactic administration occurs prior to the manifestation of overt clinical symptoms of a disease, such that a disease or disorder is prevented or alternatively delayed in its progression.

[0147] The polypeptide or combination of polypeptides of the invention having immunological activity, or a polynucleotide or vector encoding such a polypeptide or combination of polypeptides, may optionally be combined with an adjuvant. An adjuvant refers to a compound that enhances the immune response against the polypeptide or combination of polypeptides when administered together (or successively) with the polypeptide having immunological activity. Non-limiting examples of suitable adjuvants include cholera

toxin, salmonella toxin, alum and such, but are not limited thereto. Furthermore, a vaccine of this invention may be combined appropriately with a pharmaceutically acceptable carrier. Examples of such carriers are sterilized water, physiological saline, phosphate buffer, culture fluid and such. Furthermore, the vaccine may contain as necessary, stabilizers, suspensions, preservatives, surfactants and such. The vaccine is administered systemically or locally. Vaccine administration may be performed by single administration or boosted by multiple administrations.

[0148] Administration of the compositions of the invention can comprise, for example, intramuscular, intravenous, peritoneal, subcutaneous, intradermal, as well as topical administration.

[0149] The actual dose and schedule can vary depending on whether the compositions are administered in combination with other pharmaceutical compositions, or depending on inter-individual differences in pharmacokinetics, drug disposition, and metabolism. Similarly, amounts can vary in in vitro applications depending on the particular cell line utilized (e.g., based on the number of vector receptors present on the cell surface, or the ability of the particular vector employed for gene transfer to replicate in that cell line). Furthermore, the amount of vector to be added per cell will likely vary with the length and stability of the therapeutic gene inserted in the vector, as well as also the nature of the sequence, and is particularly a parameter which needs to be determined empirically, and can be altered due to factors not inherent to the methods of the present invention (for instance, the cost associated with synthesis). One skilled in the art can easily make any necessary adjustments in accordance with the exigencies of the particular situation.

[0150] These methods described herein are by no means all-inclusive, and further methods to suit the specific application will be apparent to the ordinary skilled artisan. Moreover, the effective amount of the compositions can be further approximated through analogy to compounds known to exert the desired effect.

[0151] Administration of the therapeutic composition in accordance with the present invention may be continuous or intermittent, depending, for example, upon the recipient's physiological condition, whether the purpose of the administration is therapeutic or prophylactic, and other factors known to skilled practitioners. The administration of the compositions of the invention may be essentially continuous over a preselected period of time or may be in a series of spaced doses. Both local and systemic administration is contemplated. The amount administered will vary depending on various factors including, but not limited to, the composition chosen, the particular disease, the weight, the physical condition, and the age of the subject, and whether prevention or treatment is to be achieved. Such factors can be readily determined by the clinician employing animal models or other test systems which are well known to the art.

[0152] Compositions of the invention can be administered singly or in any combination. Further, infection inhibitors (e.g., immunogenic compositions comprising viral antigens or nucleic acids encoding such viral antigens) and active compounds can be administered singly or in any combination in a temporal sense, in that they may be administered concurrently, or before, and/or after each other.

[0153] The present disclosure is not limited to treatment of a disease or disorder that is caused by a flavivirus or an alphavirus but can be useful for treating other mosquito-borne diseases.

EXAMPLES

[0154] The present invention is also described and demonstrated by way of the following examples. However, the use of these and other examples anywhere in the specification is illustrative only and in no way limits the scope and meaning of the invention or of any exemplified term. Likewise, the invention is not limited to any particular preferred embodiments described here. Indeed, many modifications and variations of the invention may be apparent to those skilled in the art upon reading this specification, and such variations can be made without departing from the invention in spirit or in scope. The invention is therefore to be limited only by the terms of the appended claims along with the full scope of equivalents to which those claims are entitled.

Materials and Methods for Examples 1-7

[0155] All experiments were performed in accordance with guidelines from the Guide for the Care and Use of Laboratory Animals of the NIH. The animal experimental protocols were approved by the Institutional Animal Care and Use Committee (IACUC) at the Yale University School of Medicine (Assurance number A3230-01). All infection experiments were performed in a biosafety level 2 animal facility, according to Yale University regulations. Every effort was made to minimize murine pain and distress. Mice were anesthetized with ketamine/xylazine for mosquito infection experiments and euthanized as suggested by the Yale IACUC.

Viruses and Cell Lines

[0156] Vero cells (ATCC) were maintained in DMEM containing 10% FBS and antibiotics at 37° C. with 5% CO_2. *Aedes albopictus* C6/36 cells were grown in DMEM supplemented with 10% FBS, 1% tryptose phosphate, and antibiotics at 30° C. with 5% CO_2. *Drosophila* S2 cells (ATCC) were passaged in Schneider's *Drosophila* media with 10% FBS at 28° C. A Mexican strain of Zika virus (Accession number KX446950), MEX2-81, was propagated in C6/36 insect cells.

Mosquitoes and Animals

[0157] *A. aegypti* (Ho Chi Minh strain, obtained from the J. Powell laboratory at Yale) mosquitoes were maintained on 10% sucrose feeders inside a 12"×12"×12" metal mesh cage (BioQuip #1450B) at 28° C. and ~80% humidity. Egg masses were generated via blood meal feeding on naïve mice. All mosquitoes were housed in a warm chamber in a space approved for BSL2 and ACL3 research. Four to six-week old gender mixed Ifnαr $1^{-/-}$Ifnγr$^{-/-}$ mice (AG129-SV129 background) were used in the Zika virus infection studies (30). Mice were randomly chosen for experimental groups. For isolating splenocytes, 5-week old male C57BL/6 mice were purchased from the Jackson Laboratory. All mice were kept in a pathogen-free facility at Yale University.

Yeast Display Screening

[0158] To prepare RNA for library construction, salivary glands from about 300 *A. aegypti* mosquitoes, which had previously fed on mice once, were harvested. RNA was purified with the RNeasy Mini Kit (QIAGEN) and the purity of collected RNA was validated by gel electrophoresis confirm the presence of 18S and 28S rRNA. The cDNAs were synthesized by a modified SMART™ cDNA synthesis kit according to protocols by Bio S&T Inc. (Quebec, Canada). After generating double strand cDNAs by primer extension and cDNA normalization, cDNAs were directionally cloned into the yeast expression vector pYD1 (Invitrogen, CA) to generate a salivary gland expression library (Invitrogen, CA). Digestion of plasmids purified from 10 clones of the pYD1-salivary gland library showed an average insert size of 1.2 kb and 100% of the clones contained inserts. The total number of primary clones was over 1 million. Plasmid DNA was purified from the library using the QIAGEN Plasmid Midi Kit (QIAGEN, CA, USA). Growth of transformed yeast cells and induction of recombinant protein production was done as previously described (12,50). Briefly, fresh *Saccharomyces cerevisiae* EBY100 cells (Invitrogen, CA) with 2 μg of plasmid DNA were electroporated and subsequently grown in SDCAA medium (2% dextrose, 0.67% yeast nitrogen base, 0.5% bacto amino acids, 30 mM $NaHPO_4$, 62 mM NaH_2PO_4) overnight at 30° C. with shaking at 200 rpm.

[0159] The induction of surface protein expression was performed as described previously (12,50). In brief, transformed yeast cells were grown for 2.4 hours at 30° C. in SGCAA medium (2% galactose, 0.67% yeast nitrogen base, 0.5% bacto amino acids, 30 mM $NaHPO_4$, 62 mM NaH_2PO_4). After induction with galactose, selection was performed by MACS separation (Miltenyi Biotec, Auburn, Calif.). Induced yeast cells were incubated with purified IgG derived from mice repeatedly bitten by *A. aegypti*. For MACS separation, an LS column (Miltenyi Biotec Cat #130-042-401) was placed onto the magnet and stand assembly. After washing the column, induced yeast cells were applied to the column. After passing through the column, bound yeast cells were eluted by removing the column from the magnet and adding SDCAA medium to the column. Then, eluted yeast cells were propagated for additional rounds of sorting. After 4 rounds of magnetic sorting, plasmids were recovered using a Zymoprep™ II Yeast Plasmid Miniprep kit (Zymo Research), transformed into *E. coli* DH5α-competent cells (Invitrogen, CA), and sequenced.

Purification of Recombinant Proteins and Antiserum Preparation

[0160] AgBR1 (LOC5573204), SP (LOC5578630) and D7Bclu (LOC5567956) were cloned in-frame into the pMT-Bip-V5-His tag vector (Invitrogen, CA) and recombinant proteins expressed and purified using the *Drosophila* Expression System (Invitrogen, CA) as described earlier (50). AgBR1, SP and D7Bclu were purified from the supernatant by TALON Metal Affinity Resin (Clontech, CA) and eluted with 150 mM imidazole. The eluted samples were filtered through a 0.22-μm filter and concentrated with a 10-kDa concentrator (Sigma-Aldrich, MO) by centrifugation at 4° C., washed and dialyzed against PBS. Recombinant protein purities were assessed by SDS-PAGE and quantified using the BCA protein estimation kit (Thermo Scientific. IL). The PCR primer sequences for cloning are listed in Table 3.

[0161] To generate rabbit sera against recombinant proteins, rabbits were immunized subcutaneously with 80-150 μg of recombinant proteins in complete Freund's adjuvant and boosted twice at every two weeks with 80-150 μg of recombinant proteins in incomplete Freund's adjuvant. Rabbits were euthanized and sera were obtained by cardiac puncture two weeks after the final boost. Reactivity to recombinant proteins was examined by immunoblot and ELISA.

Enzyme-Linked Immunosorbent Assay (ELISA)

[0162] Recombinant AgBR1, SP, D7Bclu, OVA, or salivary gland extracts in PBS (0.1 μg/50 μl/well) were coated on 96 well plates overnight at 4° C. After being blocked with 2% non-fat milk for one hour at room temperature, the plates were then incubated with serum samples serially diluted in PBS for one hour at room temperature. After being washed with PBS plus 0.05% Tween-20 (PBS-T) (Sigma) three times, the plates were incubated with HRP-conjugated secondary antibodies. Enzyme activity was detected by incubation with 100 μl of 3,3',5,5'-Tetramethylbenzidine solution (KPL, USA) for 15 minutes at room temperature in the dark. The reaction was stopped by the addition of 1M H_2SO_4. The optical density (OD) at 450 nm was measured with a microplate reader.

Immunoblot

[0163] Recombinant proteins, BSA or salivary gland extracts were separated by SDS-PAGE using 4-20% Mini-Protean TGX gels (Bio-Rad) at 200 V for 25 min. Proteins were transferred onto a PVDF membrane for 60 min at 4 V. Blots were blocked in 1% non-fat milk in water for 60 min. Primary antibodies were diluted in 0.05% PBS-T and incubated with the blots for 1 h at room temperature or 4° C. overnight. HRP-conjugated secondary antibodies were diluted in PBS-T and incubated for 1 h at room temperature. After washing by PBS-T, the immunoblots were imaged with a LI-COR Odyssey imaging system.

Splenocyte Stimulation with Recombinant AgBR1

[0164] Splenocytes were isolated from C57BL/6 mice. Briefly, the spleens were minced in RPMI 1640 (Sigma-Aldrich) and forced gently through a 70 μm cell-strainer nylon mesh using a sterile syringe plunger and centrifuged at 400 g for 5 min. After washing once using cold PBS, spleen cells were incubated in 2 ml 0.83% NH_4Cl for 5 min, then placed in 20 ml PBS, centrifuged at 400 g for five minutes and then resuspended in RPMI 1640. The total number of cells was calculated using a hemocytometer. Isolated splenocytes were stimulated with 5 μg/ml recombinant AgBR1 or BSA and cultured with serum-free RPMI medium for 6 hours and 24 hours. Total RNA was extracted by the RNeasy Mini Kit (QIAGEN) according to the instructions. The cDNA was generated with iScript cDNA Synthesis Kit (Bio-rad) according to manufacturer's protocol. Gene expression was examined by quantitative RT-PCR (qRT-PCR) using IQ™ SYBR Green Supermix. Target gene mRNA levels were normalized to mouse β actin RNA levels according to the $2^{-\Delta\Delta Ct}$ calculations. The qRT-PCR primer sequences are listed in Table 3.

Co-Inoculation of Zika Virus with AgBR1

[0165] AG129 mice were inoculated via subcutaneous (footpad) with 3 PFU of Zika virus along with 10 μg AgBR1 (total volume; 40 μl). Survivals were monitored everyday post-infection. Mice exhibiting neurologic disease such as paralysis or weight loss of over 20% of body weight were euthanized. The weight loss is very rapid and usually begins three days before death, coinciding with neurological symptoms. Total RNA from murine blood was extracted in TRIzol Reagent and qRT-PCR was performed to examine Zika virus levels as previously described (23).

Passive or Active Immunization Studies

[0166] Zika virus injection was performed as described in Uraki et al. (33). Briefly, Zika virus-filled needles were carefully inserted into the thorax of each mosquito and 69 nl of virus (100 PFU) was injected using a Nanoject II auto-nanoliter injector (Drummond). Infected mosquitoes were placed back in paper cups with mesh lids and maintained in triple containment for 10 days in a warm chamber. Mosquitoes were knocked-down on ice and salivary glands were dissected to examine the virus levels after mosquito feeding. RNA from salivary glands was purified with the RNeasy Mini Kit (QIAGEN), and cDNA was generated with iScript cDNA Synthesis Kit (Bio-rad) according to manufacturer's protocol. Gene expression was examined by quantitative RT-PCR (qRT-PCR) using IQ™ SYBR Green Supermix. Viral RNA levels were normalized to mosquito Rp49 RNA levels according to the $2^{-\Delta\Delta Ct}$ calculations.

[0167] For passive rabbit antiserum transfer experiments, mice were injected intraperitoneally with 150 μl per animal of antiserum against specific mosquito proteins or naive rabbit serum one day before challenge. On the same day, two infected mosquitoes were randomly aliquoted into individual cups with mesh covers. On the following day, mice were anesthetized with ketamine-xylazine and fed on by two Zika virus-infected mosquitoes. For active immunization, mice were immunized subcutaneously with 10 μg of AgBR1 or ovalbumin in complete Freund's adjuvant and boosted twice every 2 weeks with the same amount of AgBR1 or ovalbumin in incomplete Freund's adjuvant. Two weeks after the final immunization, mice were anesthetized with ketamine-xylazine and fed on by two Zika virus infected mosquitoes. The blood of fed mice was collected at 1, 3, 5, 7 and 9 days post infection. Survivals were monitored every day. Mice exhibiting weight loss of >20% of initial body weight or neurologic disease were euthanized. The weight loss is very rapid and usually begins three days before death, coinciding with neurological symptoms. Viremia levels were examined at 1, 3, 5, 7, 9 days post infection (dpi) as described above.

Needle Inoculation of Zika Virus after Passive Immunization

[0168] Mice were injected intraperitoneally with control serum or AgBR1 antiserum one day before challenge. On the following day, mice were inoculated via subcutaneous footpad injection with 0.3 PFU of Zika virus. Survivals were monitored everyday post-infection. Mice exhibiting weight loss of >20% of initial body weight or neurologic disease were euthanized. The weight loss is very rapid and usually begins three days before death, coinciding with neurological symptoms. Viremia levels were examined at 1, 3, 5, 7, 9 dpi as described above.

Gene Silencing

[0169] RNA interference of genes expressed in the mosquito SGs was performed. Double stranded (ds) RNA targeting either a 400 bp region of the AgBR1 gene or an irrelevant green fluorescent protein (GFP) gene were transcribed using gene-specific primers designed with a T7 promoter and the MEGAScript RNAi kit (Thermo Fisher Scientific, Ambion). The primers for generating dsRNA are listed in Table 3. For silencing the AgBR1 gene, adult female *A. aegypti* mosquitoes were kept on ice and then transferred to a cold tray to receive a dsRNA injection. Two hundred ng of dsRNA in PBS were microinjected into the thorax of each mosquito using a Nanoject II Auto-Nanoliter Injector (Drummond). At day 3 post dsRNA injection, mosquitoes were knocked-down on ice and injected with Zika virus described above. At day 10 post virus injection, salivary glands were dissected to examine the AgBR1 expression levels by qRT-PCR and AgBR1 protein production by immunoblot.

Analysis of Local Immune Responses after Bites of Zika Virus Infected Mosquitoes or Intradermal Injection

[0170] For the analysis of local immune responses after bites of Zika virus infected mosquitoes, AG129 mice were allowed to be fed on the left ear by Zika virus-infected *A. aegypti* mosquitoes.

[0171] For the analysis of local immune responses after intradermal injection, AgBR1 was intradermally injected into the left ear. Briefly, the ear of an individual mouse was gently immobilized over a 14 ml Falcon tube covered with double stick tape. Five hundred nanoliters containing 0.5 μg/μl were injected intradermally into the dorsal ear using glass micropipettes with a 80 μm diameter beveled opening made as described elsewhere (33) and a Nanoject II Auto-Nanoliter Injector (Drummond).

[0172] One day later, mice were euthanized, and the locations bitten by mosquitoes or intradermally-injected locations and naïve skins were punched using a Disposable Biopsy Punch. Total RNA was extracted by the RNeasy Fibrous Tissue Mini Kit (QIAGEN) according to the manufacturer's instructions.

[0173] For qRT-PCR, the cDNA generation and analysis of gene expression was conducted as described above. Gene expression was queried using IQ™ SYBR Green Supermix. Target gene mRNA levels were normalized to mouse β actin RNA levels according to the $2^{-\Delta\Delta Ct}$ calculations. The qRT-PCR primer sequences are listed in Table 3.

[0174] For RNA-seq library preparation and sequencing, barcoded libraries were generated by standard Truseq mRNA library protocol (Illumina) and sequenced with a 2×75 bp paired-end protocol on the HiSeq 4000 Sequencing System (Illumina).

[0175] All the analysis of RNA-seq data was performed using Partek flow (v7.0). RNA-seq data were trimmed and mapped to a mm10 genome reference using STAR (2.5.0e). The aligned reads were quantified to ENSEMBL transcripts release 91 using the Partek' E/M algorithm and the subsequent steps were performed on gene-level annotation followed by total count normalization. The gene-level data were normalized by dividing the gene counts by total number of reads followed by addition of a small offset (0.001). Differential expression was assessed by fitting the Partek's log-normal model with shrinkage (comparable in performance to limma-trend). Genes having geometric mean below value of 1.0 were filtered out from the analysis.

Hierarchal clustering was performed on the genes, which were differentially expressed across the conditions (P value <0.05, fold change >1.5 for each comparison). Gene set enrichment analysis (GSEA) was performed on normalized gene expression counts of RNA-seq data as described previously (34). Gene sets with an estimated false discovery rate (FDR) of <0.05 were considered significant according to the GSEA guidelines.

Histopathology

[0176] Ear skins of the bite site and non-bite site on the contralateral ear were harvested by punch biopsy, fixed in 4% paraformaldehyde/PBS, paraffin embedded, and processed for hematoxylin and eosin staining. The histological findings were scored for the severity and character of the inflammatory response using a blinded grading scale that was previously described (51), with minor modifications. Responses were graded as follows: 0, no response; 1, minimal response; 2, mild response; 3, moderate response; and 4, marked response. The responses were evaluated and graded on the histological sites with the most prominent responses in each specimen. The total histology score was calculated as the sum of scores, including inflammation, neutrophils, mononuclear cells and edema. The slides were blinded, randomized, and reread to determine the histology score by the same dermatopathologist throughout all studies.

Imaging Mass Cytometry (IMC)

[0177] IMC was performed on slides dewaxed in xylene for 20 minutes according to previously described studies (52). After hydration in sequential concentrations of ethanol (100%, 95%, 80%, 70%) for 5 min, slides were incubated with antigen retrieval solution at 90-95° C. for 20 min. Slides were then cooled to room temperature and washed with ddH_2O and PBS (lacking Ca^{++} or Mg^{++}) for 5 min. After blocking with 3% BSA in PBS for 45 min, slides were labeled with metal-conjugated antibodies against CD3 (170Er-Polyclonal, C-Terminal), CD11b (149Sm-EPR1344), MHCII (174Yb-M5/114.15.2) and Ly6G (141Pr-1A8) diluted in PBS with 0.5% BSA at 4° C. overnight. After being washed with 0.1% Triton-X in PBS and then PBS, slides were labeled with intercalator-Ir (1:2,000 dilution) in PBS (lacking Ca^{++} or Mg^{++}) for 30 minutes at room temperature. After being washed again with ddH_2O for 5 min, the slides were dried. Tissues were laser ablated using a 200 Hz Hyperion™ Imaging System (Fluidigm Corp., South San Francisco, Calif. and the aerosol containing the ion cloud was directly transported to a Helios Mass Cytometer (Fluidigm). Images of labeled slides were obtained using the MCD viewer 1.0 (www.fluidigm.com/software).

Analysis of Immune Cells in Mice Following Zika Virus-Infected Mosquito Bites or Intradermal Injection.

[0178] For the analysis of immune cells following Zika virus-infected mosquito bites, AG129 mice were allowed to be fed by Zika virus-infected *A. aegypti* mosquitoes on the ear. For the analysis of immune cells following AgBR1 injection, AG129 mice were intradermally injected with AgBR1 in the ear as described above. After 24 hours, mice were sacrificed and both the bitten or injected and naive ears were cut off at the base and split into dorsal and ventral halves. Ears were incubated for 1.5 hours in 2 mg/ml of Dispase II (Sigma) in DMEM media with 10% FBS, and then cut into small pieces. Small pieces were then digested for 1.5 hours in 5 mg/ml of collagenase (Gibco) in media. Digested samples were then individually passed through 70 μM filters to obtain single-cell suspensions.

[0179] After washing once with PBS containing 2% FBS (FACS buffer), cells were stained using the LIVE/DEAD™ Fixable Violet Dead Cell Stain Kit (Thermo Fisher) and then incubated with fluorochrome-conjugated monoclonal antibodies against CD45 (PerCP—BD Pharmingen; Clone 30-F11), MHCII (APC-Cy7—Biolegend; Clone M4/114.15.2), CD11b (PE—Biolegend; Clone M1/70), CD11c (PE-Cy7—BD Pharmingen; Clone HL3), and Ly6G (FITC—Tonbo; Clone RB6-8C5) for 30 minutes at room temperature, washed twice with FACS buffer. Samples were run on a BD LSRII flow cytometer and analyzed using FlowJo software.

Statistical Analysis

[0180] GraphPad Prism software was used to analyze all the data. Animals were randomly allocated into different groups. No statistical methods were used to predetermine sample size. Rp49 and mouse β actin normalized viral RNA levels were analyzed using the two-sided Wilcoxon-Mann-Whitney test. Host responses in vitro and in vivo were performed using a two-way ANOVA for multiple comparisons or using the two-sided Wilcoxon-Mann-Whitney or the two-sided Wilcoxon matched-pairs signed rank test for two sample comparisons, as indicated in the figure legends. Survival was assessed by a Gehan-Wilcoxon test. A p value of <0.05 was considered statistically significant.

Example 1: Identification and Characterization of Potential Target Salivary Gland Proteins

[0181] To breed mosquitos with Zika virus, eggs were hatched in a shallow dish with distilled water with 2 parts brewer's yeast (Bioserv #1710) and 3 parts desiccated liver powder (Bioserv #1320). After pupae emerged, mosquitoes were collected and placed in a small crystal dish with distilled water inside a 12"×12"×12" metal mesh cage (Bio-Quip #1450B). Adult mosquitoes were maintained on 10% sucrose feeders in walk-in incubator at 28° C. and ~80% humidity. Egg masses were generated via blood meal on naïve mice. For Zika virus injection experiments, mosquitoes were knocked-down on ice before transfer to a cold plate under a dissecting microscope. A pulled microcapillary needle was filled with ZIKV using a Nanoject II auto-nanoliter injector (Drummond). The Zika virus-filled needle was carefully inserted into the thorax of each mosquito and 69 nl of virus is injected. Infected mosquitoes were placed back in paper cups with mesh lids and maintained in triple containment for 10 days. All mosquitoes, clean and infected were housed in a warm chamber.

[0182] A murine model of the Zika virus was created as follows. *Ae. aegypti* mosquitoes intrathoracically injected with ZIKV were allowed to feed on AG129 mice which lack interferon α/β and γ receptors, so as to easily and efficiently transmit ZIKV to these mice (33). *Ae. aegypti* mosquitoes feed and engorge on AG129 mice.

[0183] Passive immunizations were performed by IP injections of antigen-specific IgG (total volume not exceeding 150 μl) in PBS one day prior to mosquito feeding. For active immunization of mice, 10 μg of antigen were administered subcutaneously in Freund's adjuvant at 2-3 sites in a

total volume not greater than 0.2 ml. A post-immunization sample (test bleed) was similarly drawn by retro-orbital bleeding 7 days after the final immunization to confirm reactivity to recombinant antigens by western blotting or ELISA.

[0184] AG129 mice are susceptible to very small amounts of Zika virus and develop viremia, leading to the death at 1-5 weeks (34). Therefore, this model is useful to access vaccine efficacy in the natural context of mosquito-bite infection to test vaccine efficacy on several strains of Zika virus, including pre-epidemic and post-epidemic strains.

[0185] Mosquito feeding generally resulted in minimal discomfort and injury to mice. Not more than 5 Zika virus-infected mosquitoes were placed on mice. Animals to be infected or immunized were restrained in an appropriate apparatus designed to limit the chances of injury and reduce the amount of distress of the animal during these procedures. Mice were observed daily for symptoms of Zika virus after mosquito feeding. If any animal showed 20% weight loss, scruffy fur or paralysis, it was euthanized.

[0186] Mice were anesthetized during the process of mosquito feeding with IP injection of Ketamine/Xylazine (100 mg/10 mg per kg body weight). Anesthetized mice were laid on top of mesh lids to allow mosquitoes to feed. The mice did not experience undue stress during the process of mosquito feeding. The application of feeding can be classified as minimal distress and did not affect the general health of the animals. Mosquitoes were fed for approximately 10-30 min. Mosquito carcasses after dissection were placed in 10% chlorine bleach solution for 20 minutes prior to autoclaving.

[0187] Antigenic proteins in mice that were bitten by *Ae. aegypti* were identified using a screen overcoming disadvantages inherent in SDS-PAGE and proteomics for detection of proteins of low-abundance and low-antigenicity. Yeast surface display screening was used because the method can identify uncommon proteins by iterative rounds of magnetic-activated cell sorting (50). An *Ae. aegypti* salivary gland yeast surface display library was generated by isolating RNA from salivary glands, reverse transcribing these transcripts to cDNA and cloning into the pYD1 vector before transformation into yeast cells. The protocol for enrichment of yeast clones expressing salivary gland proteins is adapted from a recent publication (12). An *A. aegypti* salivary gland yeast surface display library was generated and probed with IgG from mice repeatedly bitten by *A. aegypti* (FIGS. **1**A and **1**B) or humans bitten by *Ae. aegypti*. These mouse and human sera were highly reactive with an *Ae. aegypti* salivary gland extract, as demonstrated by ELISA and immunoblot (FIGS. **1**A, **1**B, **2**A and **2**B). Magnetic-activated cell sorting was used to enrich for yeast cells expressing salivary proteins recognized by mouse antibodies (FIGS. **3**A and **3**B) and human antibodies (FIGS. **4**A and **4**B) and after four rounds of sorting individual yeast clones were isolated, and the recombinant plasmids were recovered. Five clones, encoding unique mosquito genes were antigenic in mice (LOC5578630, LOC5578631 (NeSt1), LOC5567956, LOC5580038, LOC5573204 (AgBR1)) (FIG. **3**C) and four unique mosquito genes were antigenic in humans (LOC5566287, LOC5567958, LOC5568702, and LOC110675548) (FIG. **4**C) were identified using this method.

[0188] To examine the effect of these nine proteins on Zika infection, nucleic acid sequences encoding each of these proteins were cloned into the pMT *Drosophila* vector, expressed the recombinant proteins in *Drosophila* S2 cells, and purified using nickel affinity chromatography. The nine proteins were run on an SDS-PAGE gel, then stained with Coomassie Brilliant Blue (FIG. **5**A) and analyzed by Western blot with anti-His antibody (FIG. **5**B). To generate antibodies to use in passive immunization experiments and for the further analysis of these proteins, rabbit serum was generated against all identified antigenic proteins and validated by immunoblot using the recombinant proteins and mosquito salivary gland extract (FIG. **6**).

Example 2: Mixture of Antiserum Against Antigenic Mosquito Salivary Gland Proteins Protects Against Zika Virus Infection

[0189] Mice were passively immunized intraperitoneally with 150 μl of a mixture of all specific antisera, or control antiserum. One day later, the passively immunized mice were fed upon by Zika virus-infected mosquitoes with similar levels of virus in their salivary glands (FIG. **7**B). Blood was collected every other day for 9 days from mice fed on by Zika virus-infected mosquitoes and analyzed for Zika virus infection by qRT-PCR using primers described previously (40). The tested pooled antisera significantly reduced Zika virus levels over the course of infection (FIG. **7**C) and in mice on day 5 (FIG. **7**D), and conferred significant protection against pathogenesis, measured by survival, compared with the control group (FIG. **7**D). This mixture of antibodies against these antigenic proteins does not affect Zika virus replication (FIG. **8**A) or pathogenesis (FIG. **8**B) when mice are passively immunized and then infected using subcutaneous needle infection.

Example 3: Effect of AgBR1 Protein in Zika Virus Infection

[0190] To identify if any of these proteins is capable of inducing an immune response in cells, splenocytes were treated with antigenic mosquito salivary gland proteins. One protein, called AgBR1 is a Bacteria-responsive protein 1 which belongs to group V chitinase-like proteins (41). Next, it was examined whether AgBR1 stimulates inflammatory responses in vitro. Murine splenocytes stimulated with recombinant AgBR1 (see FIGS. **5**C and **5**D) produced in S2 cells (5 μg/ml) demonstrated significantly higher levels of Il6 expression compared with controls, with the data shown in FIG. **9**. As increased vascular permeability contributes to flavivirus pathogenicity (42) and IL-6 is associated with these processes (43), it was next examined whether AgBR1 influences Zika virus infection in vivo. Given previous studies demonstrating that approximately half of the protein in the salivary glands is discharged during a blood meal (44,45), the concentration of AgBR1 in mosquito saliva can be estimated to be between 1.6-8.2 μM (FIG. **10**C, Table 1). Therefore, AG129 mice were injected with Zika virus and AgBR1 (5.1 μM, 10 μg of AgBR1 in total volume 40 μl).

[0191] At day 3 post infection, significantly higher viremia levels were observed in the group of mice inoculated with Zika virus in conjunction with AgBR1, compared to those of mice challenged with Zika virus alone. When AgBR1 is co-inoculated along with Zika virus, higher levels of virus are detected in the blood by qRT-PCR at day 3 after subcutaneous injection (FIG. **10**A). In addition, AgBR1 protein significantly impaired the survival of Zika virus-

infected mice. Mice injected with a mixture of virus and AgBR1 also experienced significantly more pathogenesis as measured by survival (FIG. **10**B). AgBR1 protein significantly impaired the survival of Zika virus-infected mice (FIG. **10**B). These results demonstrate that AgBR1 can exacerbate Zika virus infection and disease in vivo.

[0192] To determine if passive immunization can protect mice from Zika virus infection, AG129 mice were injected with 150 uL of rabbit serum against AgBR1 before infection via mosquito bite. Mosquitoes with similar levels of viral infection (FIG. **11**A) were allowed to feed on mice, and then blood was collected from mice for 9 days. AgBR1 antiserum significantly reduced Zika virus levels on days 1, 3 and 9 after infection (FIG. **11**B). This also significantly protected mice from pathogenesis as measured by survival over 30 days (FIG. **11**C). This protection is not from a non-specific interaction as this antiserum failed to protect from needle infection with Zika virus (FIG. **12**). Antiserum against two other abundant antigenic salivary gland proteins is not protective against Zika virus infection (FIG. **13**).

[0193] Here, AG129 mice were used that lack both Type I and II IFN receptors but can elicit B-cell and T-cell responses (76,77). As type I interferon signaling can contribute to optimal antibody responses (78), it is possible that further efforts using alternative adjuvants, protein concentration or different animal models could enhance the effect of active immunization. Overall, these results indicate that immunization with AgBR1 partially influenced mosquito-transmitted Zika virus infection.

[0194] To determine whether the effects observed with AgBR1 extended to other proteins identified in the screen, two additional proteins were selected: D7Bclu and SP, whose expression has been identified as upregulated salivary gland proteins during flavivirus infection (67). D7Bclu and SP antisera were generated in a similar fashion to the AgBR1 antiserum and performed passive immunization experiments. Neither the D7Bclu nor SP antisera altered the viremia or protected mice from lethal mosquito-borne Zika virus infection, as shown in FIGS. **13**A-D.

[0195] To more fully understand the underlying mechanism of protection of immunization with AgBR1, assays were performed to determine whether AgBR1 antiserum influenced the early innate immune response at the bite site after exposure of mice to Zika virus-infected mosquitoes. A histological analysis of the bite site 24 hours post-feeding by Zika virus-infected mosquitoes showed prominent inflammatory cell infiltration mainly composed of neutrophils in the dermis of mice administered naïve serum (control), which was less apparent in mice administered AgBR1 antiserum. The data is shown in FIGS. **14**A and **14**B. Consistent with these findings, histology scores were significantly lower in mice administered AgBR1 antiserum compared with mice administered naïve serum, as shown in FIG. **14**C. Furthermore, imaging mass cytometry showed that infiltrating cells at the bite site of Zika virus-infected mosquito bites were mainly $Ly6G^+$ and $CD11b^+$ cells, supporting the observation made with hematoxylin and eosin staining that the infiltrating cells are predominantly composed of neutrophils, monocytes, and macrophages, with some minor populations of T cells or other immune cells (FIG. **14**D). In addition, the infiltration of $Ly6G^+$ cells and $CD11b^+$ cells is reduced in mice administered AgBR1 antiserum, in contrast to control animals (FIG. **14**D). The alteration of infiltrating cell populations in the skin of bitten mice administered AgBR1 antiserum indicates that the AgBR1 antiserum influenced the number of $CD45^+CD11b^+$ Ly6 G^+ neutrophils at the bite site. See FIGS. **14**E and **14**F. These results suggest that AgBR1 antiserum suppressed acute inflammation, and particularly the neutrophilic response, at the mosquito bite site.

[0196] Analysis by RNAseq also indicates an increase in inflammatory and cytokine response in the control serum group as compared to AgBR1 antiserum (FIG. **15**).

[0197] To further understand how AgBR1 may influence mosquito-borne Zika infection, RNA sequencing was performed on tissue collected at the bite site of mice 24 hours after Zika virus-infected mosquito feeding. 536 upregulated genes were found out of 986 differentially expressed genes between the bite site and resting site in control mice following Zika virus-infected mosquito feedings. See FIG. **15**A and Table 2. A variety of cytokine and chemokine genes, including neutrophil-attracting chemokines Cxcl1, proinflammatory cytokine Il1b, monocytic chemoattractive chemokines Ccl2 and Ccl6, were significantly upregulated at the bite site compared to the resting site. This result was consistent with a previous report describing a detrimental role for inflammatory neutrophils that express IL-1β in the induction of cutaneous inflammatory responses at the bite site (31,49). GSEA analysis also revealed that inflammatory responses and cytokine signaling, which are mediated by host immune cells, were highly enriched in bitten skin, supporting these histological findings (FIG. **15**B, Tables 4-7).

[0198] The impact of AgBR1 antiserum on inflammatory responses induced by Zika virus-infected mosquito bites was evaluated. By focusing on genes that were upregulated in the bite site, 18 genes were identified, including Il1b, Cxcl1 and Ccl2, which were attenuated in mice inoculated with AgBR1 antiserum (FIGS. **15**A and **15**C). The reduction of Il1b was also confirmed by qPCR (FIG. **15**D). In addition, Il6 expression levels were examined in each group because AgBR1 stimulates Il6 expression in vitro. Though Il6 was initially not included in the differential gene expression analysis due to the low expression in control skin, Il6 expression levels were nonetheless significantly suppressed in AgBR1 antiserum-treated mice compared with control mice, consistent with the in vitro data (FIG. **15**D). It was also found that the direct inoculation of AgBR1 into the skin significantly induces IL1b and Il6 expression (FIG. **15**E).

[0199] Arboviral infection triggers the recruitment of peripheral neutrophils and monocytes to the site of infection (31,46) and, previous studies showed that neutrophils are important targets of flaviviruses in vivo and that infiltration of neutrophils contribute to the initial flavivirus infection and dissemination (31,46-48). Here, it is shown that AgBR1 induces neutrophil recruitment at the bite site and blocking this effect suppresses the early host response. These data suggest that targeting AgBR1 blocks the early host responses caused by the bite of Zika virus-infected mosquitoes, leading to the suppression of viral dissemination and protection against lethal Zika virus infection.

Example 4: Examine the Efficacy of AgBR1 as a Vaccine Candidate

[0200] Standard immunization protocols approved by the Yale Animal Care and Use Committee are followed to immunize mice with rAgBR1. Briefly, four to six-week-old AG129 mice are actively immunized by subcutaneous injec-

tion of 10 μg of purified recombinant protein in Freund's adjuvant. Either one or two booster immunizations with 10 μg of recombinant protein in adjuvant are provided once every two weeks. Control animals are immunized with ovalbumin (InvivoGen, CA).

[0201] Five-10 μl samples of blood are collected by retro-orbital bleed two weeks after every booster immunization. Reactivity against both rAgBR1 and the native mosquito antigens in a salivary gland extract are assessed by ELISA (FIG. **16**A). Using data obtained from active immunization testing, a determination is made whether active immunization with rAgBR1 is likely to elicit sufficient concentrations of anti-AgBR1 specific antibodies for protection against Zika virus transmission. From the data regarding reactivity to native and recombinant protein, an assessment is made as to which immunization protocol is optimal for effective antibody production in mice. Immunization with recombinant proteins often fails to result in constant, high concentrations of antibodies. Mosquito bites may boost the existing immune response and therefore help maintain a high concentration of antibodies.

[0202] Wild-type mice are not susceptible to infection with Zika virus, and AG129 mice, which lack IFN receptor α and γ subunits, must be used in challenge experiments. However, AG129 mice are often immunocompromised and may fail to mount a sufficiently robust antibody response. In such case, wild-type mice are immunized and their interferon receptors are inactivated by passive immunization of IFNAR1-blocking mAb (MAR1-5A3) as described in Lazear et al. (39).

[0203] The protective effect of active immunization with AgBR1 antigen in preventing mosquito-borne Zika virus infection was assessed using a murine model. Two weeks after the final immunization with the optimal conditions, mice are fed on by either two Zika virus infected mosquitoes. Every other day until nine days after mosquito feeding (representing the time point when ZIKV is expected to have fully disseminated throughout the mice), transmission is assessed by taking 10-15 μl of blood from control and experimental animals by retro-orbital bleed and virus burden is assessed by RNA isolation and qRT-PCR as described previously (41). The cDNA template in each reaction is normalized to mouse β-actin. The significance of difference in virus level in mice and survival between the groups is assessed by a Gehan-Wilcoxon test, respectively. Mice immunized with AgBR1 protein have less virus at day 5 (FIG. **16**B) and are protected from Zika virus pathogenesis, as shown in FIG. **16**C.

[0204] Animals can be immunized with heat inactivated antigens or truncated recombinant antigens. Salivary antigens secreted into the host skin upon future *Ae. aegypti* mosquito bites (both infected and uninfected), have the potential advantage of boosting the anamnestic response in the host and are preferred vaccine candidates.

[0205] The passive immunization experiments were repeated using the same techniques in West Nile virus (WNV) infection and it was demonstrated that blocking AgBR1 can also enhance survival after WNV infection with mosquito bite, as shown in FIG. **17**.

Example 5: Effect of AgBR1 on Neutrophil Recruitment in the Skin

[0206] To examine whether suppression of AgBR1 gene and AgBR1 protein expression in the salivary glands alters the levels of $CD45^+CD11b^+Ly6G^+$ cells infiltration after mosquito bites. dsRNA against AgBR1 was injected intrathoracically into *Aedes aegypti* mosquitoes. Expression level of AgBR1 RNA after knockdown was measured using qRT-PCR (FIG. **18**A) and protein levels were measured using Western Blot using AgBR1 rabbit antiserum (FIG. **18**B). Mosquitoes were infected intrathoracically with Zika virus and after 10 days mosquitoes were collected, and RNA was isolated. Using Zika virus specific primers, viral levels in mosquito were measured, and the levels of Zika virus replication was not altered in the AgBR1 knockdown group (FIG. **18**C). The levels of $CD45^+CD11b^+Ly6G^+$ cells were significantly increased in mice bitten by control mosquitoes, but not in mice bitten by AgBR1 dsRNA-treated mosquitoes (FIG. **18**D). These results further demonstrate that AgBR1 plays a role in recruiting $CD45^+CD11b^+Ly6G^+$ cells to the Zika virus infected-mosquito bite site.

Example 6: Role of Antigenic Salivary Gland Proteins in Stimulation of Neutrophils

[0207] Mosquito saliva can stimulate local immune cells to express IL1ß, CCL2 and CXCL2 at the bite site to change the local immune environment, which leads to an increase of flavivirus-susceptible myeloid-lineage cells. To assess whether any of the antigenic proteins are capable of stimulating immune cells to express these molecules, each of the antigenic proteins were used to treat primary naïve neutrophils harvested from uninfected WT mice and RAW 264.7 macrophage cells. Most SG proteins showed no effect on primary neutrophils ex vivo, but one SG protein, LOC5578631, induced the expression of IL1ß (FIG. **19**), CXCL2 (FIG. **20**) and CCL2 (FIG. **21**). This protein fails to induce IL1ß (FIG. **22**) or CXCL2 (FIG. **23**) in the RAW macrophage cell line. These data suggest that the LOC5578631 protein is capable of activating neutrophils and thus LOC5578631 protein is called Neutrophil Stimulating Factor 1 (NeSt1).

Example 7: NeSt1 Enhances Zika Virus Infection In Vivo

[0208] To determine if passive immunization against NeSt1 can protect mice from Zika virus infection, AG129 mice were injected with 150 uL of rabbit serum against NeSt1 before infection via mosquito bite. Mosquitoes with similar levels of viral infection (FIG. **24**) were allowed to feed on mice, and then blood was collected from mice for 9 days. NeSt1 antiserum significantly reduced Zika virus levels on day 1 after infection (FIG. **25**), with no virus detected in 5 out of 12 animals in NeSt1 antiserum group. Passive immunization against NeSt1 also significantly protected mice from pathogenesis as measured by survival over 30 days, as shown in FIG. **26**.

[0209] In order to examine whether blocking the NeSt1 protein can change the immune microenvironment at the bite site, serum generated from rabbits inoculated against NeSt1 and pre-immune sera from the same animals were used to passive immunize WT mice before feeding naïve mosquitoes on the ear of these animals. Three hours elapsed to allow for infiltration or expansion of immune cells at the local bite site before harvesting the ears and examining the immune response by flow cytometry (FIG. **27**). No difference was detected in langerhans cell percentage in the ears of naïve and bitten mice or between NeSt1 antiserum treated

compared to naïve sera treated group (FIG. **28**). More neutrophils were seen after mosquito bite in both the naïve and NeSt1 antisera, but no differences were detected through the two groups (FIG. **29**). The percentage of macrophages in the bitten ear was increased in the control group (FIG. **30**) and the percentage of dendritic cells was decreased after mosquito bite in the control group (FIG. **31**). Mice treated with NeSt1 antisera did not experience this change in macrophage and dendritic cell percentage (FIGS. **30** and **31**) indicating that blocking NeSt1 was capable of preventing the infiltration of macrophages, which are susceptible to Zika virus infection, into the bite site.

[0210] To determine whether blocking NeSt1 at the bite site can affect the induction of pro-IL-1β, CXCL2, and/or CCL2 at the bite site, mice were first passively immunized against NeSt1. Mosquitoes were then allowed to feed on one of the ears (bitten), while leaving the other ear unbitten (naive). After 3 h, ear tissue at the bite site was removed and assayed for pro-IL-1β, CXCL2, and CCL2. Mice that had been passively immunized against NeSt1 were shown to express significantly lower levels of pro-IL-1β (FIG. **32**A) and CXCL2 (FIG. **32**B) after a mosquito bite. No significant differences in CCL2 expression levels were observed between the two groups (FIG. **32**C). These data suggest that NeSt1 is capable of inducing pro-IL-1β and CXCL2, two molecules that are capable of increasing the number of ZIKV-susceptible cells at the bite site.

Example 8: AgBR1 Antibodies Delays Lethal *Aedes aegypti*-Borne West Nile Virus Infection in Mice

[0211] To determine whether targeting AgBR1 altered pathogenesis during mosquito-borne WNV infection, immunized mice were passively immunized with AgBR1 antiserum before challenging them with WNV by mosquito bite. *Ae. aegypti* mosquitoes were used as a vector model, since the well-annotated whole genome sequence and easy maintenance make this species ideal for laboratory viral transmission studies (63,71).

Mosquitoes and Animals

[0212] *Ae. aegypti* (Orlando strain, collected from Orlando, Fla. in 1952) and *Cx. pipiens* mosquitoes were maintained on 10% sucrose feeders inside a 12"×12"×12" metal mesh cage (BioQuip #1450B) at 28° C. and ~80% humidity. Eggs were generated via blood meal feeding on an artificial membrane feeder with defibrinated sheep's blood (Hemostat Laboratories). All mosquitoes were housed in a warm chamber in a space approved for BSL3 and ACL3 research. Four-week-old male mice (Swiss Webster mice from Charles River) were used in the WNV infection studies. All mice were kept in a pathogen-free facility at the Connecticut Agricultural Experiment Station.

Mosquito Injection and Dissections

[0213] For WNV injection, WNV-filled needles were carefully inserted into the thorax of each mosquito and 69 nl of virus (3.4×10^3 PFU) was injected using a Nanoject II auto-nanoliter injector (Drummond). Infected mosquitoes were placed back in paper cups with mesh lids and maintained in triple containment for 7 days in a warm chamber. After feeding infected mosquitoes on naïve mice, they were knocked-down on ice and salivary glands were dissected to examine the virus levels.

Passive Immunization Studies

[0214] Mice were injected intraperitoneally with 150 μl per animal of AgBR1 or SP antiserum or naive rabbit serum one day before challenge. On the following day, mice were anesthetized with ketamine-xylazine and fed on by a single WNV-infected mosquito per mouse. The blood of fed mice was collected at 1, 3, 5 and 7 days post infection. Survivals and weights were monitored every day. Mice exhibiting weight loss of >20% of initial body weight or neurologic disease were euthanized. Viremia levels were examined at 1, 3, 5 and 7 days post infection by quantitative real time-PCR.

Analysis of Local Immune Responses after Bites of West Nile Virus Infected Mosquitoes

[0215] Mice were passively immunized with either AgBR1 or naive antiserum 24 hours prior to allowing infected *Ae. aegypti* mosquitoes to feed on the left ear. After 6 or 24 hours post feedings, mice were euthanized, and the locations bitten by mosquitoes and naïve locations on the opposite ear were punched using a Disposable Biopsy Punch. Total RNA was extracted by the RNeasy Fibrous Tissue Mini Kit (QIAGEN) according to the manufacturer's instructions. For quantitative RT-PCR, the cDNA was generated with iScript cDNA Synthesis Kit (Bio-rad) according to manufacturer's protocol. Gene expression was examined by qRT-PCR using IQ™ SYBR Green Supermix. Target gene mRNA levels were normalized to mouse β actin RNA levels according to the $2^{-\Delta\Delta Ct}$ calculations. The qRT-PCR primer sequences are available upon request.

Immunoblot

[0216] Three sets of salivary glands from *Ae. aegypti* and *Cx. pipiens* were placed in 20 μl Novex 2× Tris-Glycine SDS Sample Buffer, heated to 85° C. for 5 min, diluted 1:1 with water and the whole sample was loaded on a 16% Tris-glycine gel. AgBR1 and homologous proteins were examined with AgBR1 antiserum (1:1000 dilution), followed by incubation with HRP-conjugated secondary antibodies.

Statistical Analysis

[0217] GraphPad Prism software was used to analyze all the data. Mouse β actin-normalized viral RNA levels and body weights were analyzed using the Wilcoxon-Mann-Whitney test. Host responses in vivo was performed using a two-way ANOVA for multiple comparisons. Survival was assessed by a Gehan-Wilcoxon test. A p value of <0.05 was considered statistically significant.

[0218] To determine whether targeting AgBR1 altered pathogenesis during mosquito-borne WNV infection, mice were passively immunized with AgBR1 antiserum before challenging them with WNV by mosquito bite. *Ae. aegypti* mosquitoes were used as a vector model, since the well-annotated whole genome sequence and easy maintenance make this species ideal for laboratory viral transmission studies (63,71). Wild type Swiss Webster mice were administered AgBR1 or control antiserum and 24 hours later were bitten by WNV-infected *Ae. aegypti* mosquitoes (FIG. **17**A). Passive immunization with AgBR1 antiserum significantly reduced WNV RNA levels in the murine bloodstream at an early stage (3 days) of infection (FIG. **17**B). Components of

mosquito saliva can modulate local host responses and recruit several immune cells which can be target of virus replication (31,69,72), which may lead to virus dissemination at an earlier, rather than later, time point. Although a significant difference as not detected at Day 1, it may be due to the complex interplay of recruited immune cells at the bite site, which leads to shifting populations of WNV-susceptible cells over the first hours and days of infection. In addition, pretreatment with AgBR1 antiserum delayed virally-induced weight loss (FIG. **17**C) and prolonged median survival time of mice by 20% (FIG. **17**D). As the mosquito-borne WNV infection model used in this study (survival rate: 0%, median survival time: 7 days in control) is much more virulent than a mosquito-borne Zika infection model (survival rate: 30-45%, mean survival time: 12-25 days in control) (69), the 1.5-day delay of fatal outcome is noteworthy. Overall, these results indicate that blocking AgBR1 suppresses virus replication and/or dissemination at early time points and alters mosquito-borne WNV infection.

[0219] An experiment was then performed to determine whether the effects observed with AgBR1 were specific to this protein or if any antigenic *Ae. aegypti* salivary gland protein was capable of affecting WNV infection. An additional protein was selected: the putative 34 kDa family secreted salivary protein (SP). Sera from mice bitten by mosquitoes showed strong reactivity to the SP protein (69). SP has also been reported as a salivary gland protein that was upregulated during flavivirus infection (67).

[0220] Identical passive immunization experiments were performed using SP antiserum. SP antiserum did not alter viremia, weight loss or survival time after lethal mosquito-borne WNV infection. The results are shown in FIGS. **17**G-**17**I. In FIG. **17**G, the virus levels in blood of mice treated with SP antiserum, fed by an infected mosquito. Blood was collected every other day for 7 days from mice fed on by WNV-infected mosquitoes and analyzed by qRT-PCR. WNV RNA levels were normalized to mouse β actin RNA levels. Mice immunized with naïve serum served as controls. Error bars represent mean±SEM. Each data point represents one mouse. Normalized viral RNA levels were analyzed using one-tailed Wilcoxon-Mann-Whitney test. In FIG. **17**H, the weight of mice fed by an infected mosquito. Mice were monitored daily after WNV infection. Error bars represent mean±SEM. Weight at each time point were compared using one-tailed Wilcoxon-Mann-Whitney test. FIG. **17**I shows the results of survival assessment by a Gehan-Wilcoxon test (n=8/each group biologically independent samples pooled from two separate experiments).

[0221] An experiment was performed to determine whether AgBR1 antibodies alter the early host responses after feeding by mosquitoes infected with WNV. Proinflammatory genes including Il1b, Il6 and Tnfα, were significantly suppressed at the bite site in mice treated with AgBR1 antiserum at 6 hours post feeding (FIG. **17**E). In addition to these genes, the expression levels of Mmp9, which is previously reported to play an important role in WNV entry into the brain (73), and those of Nlrp3, which is a key molecule of NLRP3 inflammasome that drives IL-1β signaling and is involved in WNV control in the central nervous system (CNS) (74) were examined. As shown in FIG. **17**H, Mmp9 and Nlrp3 genes were significantly suppressed in AgBR1 antiserum-treated mice at 6 hours post feedings. Interestingly, no differences in the expression level of any of these genes was seen 24 hours after bites with WNV-infected mosquitoes (FIG. **17**F). The present study of WNV took advantage of immunocompetent wild type mice, as contrasted with the immuno-incompetent Ifnar$^{-/-}$ Ifngr$^{-/-}$ mice, such that it is possible that the difference of mouse models could cause the time lag of early host responses. Overall, these results demonstrated that AgBR1 antiserum suppresses the early local host responses after WNV-infected mosquito feedings, suggesting that the suppression of host responses by AgBR1 antibodies leads to the delay of viral dissemination and fatal outcome.

[0222] AgBR1 antiserum also specifically recognizes a protein in *Culex pipiens* salivary glands (FIG. **17**J). Since *Ae. aegypti* AgBR1 has high homology (amino acid identities=80%) with *Culex* spp. chitotriosidase-1 protein, which is predicted in silico to be secreted from the salivary gland, it is hypothesized that this *Culex* protein recognized by AgBR1 antiserum may have similar function during WNV infection.

[0223] In conclusion, this example demonstrates that passive immunization with AgBR1 antiserum delays lethal *Ae. aegypti*-borne WNV infection in mice, similar to that shown for Zika virus infection transmitted by the same mosquitoes. A strategy of targeting individual arthropod salivary factors such as AgBR1 might be broadly applicable to other mosquito-borne pathogens.

LIST OF SEQUENCES:

LOC5573204 (SEQ ID NO: 1; Genbank Accession No. ABF18180.1)

MWFFKVGALLFLAALVSANNATTGPKVLCYYDGQMSLREGLGKITVTDIE

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NLKVLLSVGGYKDLTEEKPFEKYLTLLESAGSRTAFVNSVYSTLKTYDFD

GLDLAWQFPQTKPKRIRGWTGKVWHGFKKLFTGDSVLDPKADEHREEFTA

LVRDLKNALVADNFILGLTVLPHVNESIFMDVPLLKDNLDYVNLASFDQQ

TPERNPKEGDYTAPIYEPSERVEGNNVDAEASYWQGTPAGKIVIGIPTYG

RGWKLVEKSGITGVPPIPADGPSIPGPHSGINGFYSWAEVCAKLPNPGNA

NLQGADQPLRKIGDPTRRFGAYAFRIPDENEEHGIWLSYEDPDTAGNKAA

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AMKAMMKTCKANLKEKNPGKIAVHYYKCLMNDSKVTNDFKEAFDYREVRS

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LOC5573204 Antigenic Peptide (SEQ ID NO: 7)
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LOC5573204 Antigenic Peptide (SEQ ID NO: 8)
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LOC5573204 Antigenic Peptide (SEQ ID NO: 9)
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CNLSGLPNVWMGGEPSNHERGVKGIFMVHTNSEAPFAKD

LOC110675548 (SEQ ID NO: 46; Uniprot Accession No. Q17NB9)
MILQFWVVTFSVLFAARADENHSILIKLNDLDHRFTQMFSQQFYRHTQQV

TDRVSALKISIDTNLLELDQQIQQALDGIQSNESSSSASATKPPGLTTIP

IGSEPRVPALYERERYGGDWLVVMHRYDGSVKFDRTWAEYRDGFGMVGQE

FWYGLERLHQLTKEKSYELMVEMEDFNGSLKYAWYDKFVVGPEEQRYALV

ELGTFNGTTDGDSLKPHKGSGFSTYDNDDFGCSNKYAKGGWWYYSGKCYG

SSLTGIWKNELAYSSIVWMKFSDVSNTPLKLVRMMIRPKN

LOC5566287 Antigenic Peptide (SEQ ID NO: 47)
LWIIIFAILCVAQA

LOC5566287 Antigenic Peptide (SEQ ID NO: 48)
FYSYVEAVSQVLADLE

LOC5566287 Antigenic Peptide (SEQ ID NO: 49)
GSVIPVSYE

LOC5566287 Antigenic Peptide (SEQ ID NO: 50)
ITQIKHRIKHLLQEKCNLCSAK

LOC5566287 Antigenic Peptide (SEQ ID NO: 51)
KKQVPLKF

LOC5566287 Antigenic Peptide (SEQ ID NO: 52)
YPLAKVG

LOC5566287 Antigenic Peptide (SEQ ID NO: 53)
RKSCFGASLTG

LOC5566287 Antigenic Peptide (SEQ ID NO: 54)
GWIVLMQ

LOC5566287 Antigenic Peptide (SEQ ID NO: 55)
LDQGYVTT

LOC5566287 Antigenic Peptide (SEQ ID NO: 56)
YAGYDAFAVG

LOC5566287 Antigenic Peptide (SEQ ID NO: 57)
TAYVDSF

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LOC5566287 Antigenic Peptide (SEQ ID NO: 58)
ISWVWFS

LOC5566287 Antigenic Peptide (SEQ ID NO: 59)
WLGLERI

LOC5567958 Antigenic Peptide (SEQ ID NO: 60)
PLLLAIVTTFSVVAST

LOC5567958 Antigenic Peptide (SEQ ID NO: 61)
WHYYKCLVESS

LOC5567958 Antigenic Peptide (SEQ ID NO: 62)
PVDSPATQCFGKCVLVRTG

LOC5567958 Antigenic Peptide (SEQ ID NO: 63)
CAAVFKAYDPVHKA

LOC5567958 Antigenic Peptide (SEQ ID NO: 64)
YREVRSQIYAFNLPKKQVYSKPAVQSQVM

LOC5567958 Antigenic Peptide (SEQ ID NO: 65)
KVEAYANAVQQLP

LOC5567958 Antigenic Peptide (SEQ ID NO: 66)
YDPVAQKFDASVIQEQFKAYPSL

LOC5567958 Antigenic Peptide (SEQ ID NO: 67)
QQLCKIRQYTVLDDA

LOC5567958 Antigenic Peptide (SEQ ID NO: 68)
LEKVLNDC

LOC5567958 Antigenic Peptide (SEQ ID NO: 69)
YFEFCENKYYPA

LOC5567958 Antigenic Peptide (SEQ ID NO: 70)
FKEHTDCVMKG

LOC5568702 Antigenic Peptide (SEQ ID NO: 71)
FPVLLITLSLAFEVHSS

LOC5568702 Antigenic Peptide (SEQ ID NO: 72)
VESVGLVTSQLIDTLVDASGVILDSIYVIGHSLGAHVAGIVGKH

LOC5568702 Antigenic Peptide (SEQ ID NO: 73)
QAGCGLDLFGICAHARSWIYFAE

LOC5568702 Antigenic Peptide (SEQ ID NO: 74)
LQLVRD

LOC5568702 Antigenic Peptide (SEQ ID NO: 75)
TQQLVNPNPYRVLNAH

LOC5568702 Antigenic Peptide (SEQ ID NO: 76)
TINYVMAR

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LOC5568702 Antigenic Peptide (SEQ ID NO: 77)
AQYVEMV

LOC5568702 Antigenic Peptide (SEQ ID NO: 78)
NTIVGLDPAGPLFSLNSS

LOC5568702 Antigenic Peptide (SEQ ID NO: 79)
KGIFMVH

LOC5568702 Antigenic Peptide (SEQ ID NO: 80)
CNLSGLPNV

LOC5568702 Antigenic Peptide (SEQ ID NO: 81)
DILIELRRSYLSVEDF

LOC5568702 Antigenic Peptide (SEQ ID NO: 82)
PTRFLIHG

LOC5568702 Antigenic Peptide (SEQ ID NO: 83)
SDIIFRLY

LOC5568702 Antigenic Peptide (SEQ ID NO: 84)
GIKCAMI

LOC5568702 Antigenic Peptide (SEQ ID NO: 85)
GARLLGTY

LOC110675548 Antigenic Peptide (SEQ ID NO: 86)
QFWVVTFSVLFAA

LOC110675548 Antigenic Peptide (SEQ ID NO: 87)
LAYSSIVWMKFSDVSNTPLKLVRM

LOC110675548 Antigenic Peptide (SEQ ID NO: 88)
DWLVVMHR

LOC110675548 Antigenic Peptide (SEQ ID NO: 89)
EPRVPALY

LOC110675548 Antigenic Peptide (SEQ ID NO: 90)
HSILIKLND

LOC110675548 Antigenic Peptide (SEQ ID NO: 91)
RYALVELG

LOC110675548 Antigenic Peptide (SEQ ID NO: 92)
TDRVSALKIS

LOC110675548 Antigenic Peptide (SEQ ID NO: 93)
SGKCYGSSLTG

LOC110675548 Antigenic Peptide (SEQ ID NO: 94)
SLKYAWYDKFVVGP

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LOC110675548 Antigenic Peptide (SEQ ID NO: 95)

LERLHQL

LOC110675548 Antigenic Peptide (SEQ ID NO: 96)

DTNLLELDQQIQQALDG

LOC110675548 Antigenic Peptide (SEQ ID NO: 97)

SQQFYRHTQQ

LOC110675548 Antigenic Peptide (SEQ ID NO: 98)

DGSVKF

LOC110675548 Antigenic Peptide (SEQ ID NO: 99)

PPGLTTIPIG

(*Aedes aegypti* Polypeptide) SEQ ID NO: 100

MAKAPAVGIDLGTTYSCVGVFQHGKVEIIANDQGNRTTPSYVAFTDTERL

IGDAAKNQVAMNPTNTIFDAKRLIGRKFDDPAIQADMKHWPFDVISVEGK

PKIQVEYKGETKNFFPEEISSMVLTKMKETAEAYLGKTVSNAVVTVPAYF

NDSQRQATKDAGTISGLNVLRIINEPTAAAIAYGLDKKTAGERNVLIFDL

GGGTFDVSILSIDDGIFEVKSTAGDTHLGGEDFDNRLVNHFAQEFKRKHK

KDLSTNKRALRRLRTACERAKRTLSSSTQASIEIDSLFEGTDFYTSITRA

RFEELNADLFRSTMEPVEKAIRDAKMDKASIHDIVLVGGSTRIPKVQKLL

QDFFNGKELNKSINPDEAVAYGAAVQAAILHGDKSEEVQDLLLLDVTPLS

LGIETAGGVMSVLIKRNTTIPTKQTQTFTTYSDNQPGVLIQVFEGERAMT

KDNNLLGKFELSGIPPAPRGVPQIEVTFDIDANGILNVTALEKSTNKENK

ITITNDKGRLSKEDIERMVNEAEKYRSEDEKQKETISAKNALESYCFNMK

ATMEDDKLKDKITDSDKTLIMDKCNDTIKWLDANQLAEKEEYEHRQKELE

SVCNPIITKLYQSAGGAPGGMPGFPGGAPGAGAGAAPGAGSGSGPTIEEV

D

(*Aedes aegypti* Polypeptide) SEQ ID NO: 101

MSVNRTISAHQAAKEHVLAVSRDFISQPRLTYKTVSGVNGPLVILDEVKF

PKFAEIVQLRLNDGTVRSGQVLEVSGSKAVVQVFEGTSGIDAKNTVCEFT

GDILRTPVSEDMLGRVFNGSGKPIDKGPPILAEDFLDIQGQPINPWSRIY

PEEMIQTGISAIDVMNSIARGQKIPIFSAAGLPHNEIAAQICRQAGLVKH

TGKSVLDEHEDNFAIVFAAMGVNMETARFFKQDFEENGSMENVCLFLNLA

NDPTIERIITPRLALTAAEFLAYQCEKHVLVILTDMSSYAEALREVSAAR

EEVPGRRGFPGYMYTDLATIYERAGRVEGRNGSITQIPILTMPNDDITHP

IPDLTGYITEGQIYVDRQLHNRQIYPPVNVLPSLSRLMKSAIGEGMTRKD

HSDVSNQLYACYAIGKDVQAMKAVVGEEALTPDDLLYLEFLTKFEKNFIS

QGNYENRTVFESLDIGWQLLRIFPKEMLKRIPASILAEFYPRDSRH

(*Aedes aegypti* Polypeptide) SEQ ID NO: 102

MPANIIMKILITSILILKLAIHVVPQHLISSGASAVESKPVSARPTYEDY

KRQRENFLQAEEYHFLGANVTLNENEQLVNKFLMRLKLEEMVKGFNDSYN

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FIPARHIFEVLDRFGQSKVFKVIQRLPKGGVLHAHDMALGSTDLIVNATY

RENLWQKGNFGVSHGPQFKFSKEKPGKEWSLVSEIRQWMTDKVYDAKVGE

IFSLYNADPLNAYKSLDDVWSKFQNLFGSLAPLITFAPVWRQYYHDSLKQ

FYDDHVQYLEFRGVLPDVYDLDGKIYSAEEIVQMYYEETEEFKSSHPEFI

GAKFIYAPGRFATDDEFLKIIDTAKRLHKKFPTFLAGFDLVGQEDPGRSL

LEFAPALLKLPASINFFFHAGETNWYGMKTDQNLIDAVLLGSKRIGHGFA

VLKHPKVLKEIKRRQICIEINPISNQVLKLVQDQRNHPAALLFSDNYPVV

VSSDDPSFWRSTPLSHDFYVAFTGIASAKQDLRLLKQLALNSIEYSAMNS

EEKTSAKEKWSQAWHDQISALATDIVAGSV

(*Aedes aegypti* polypeptide) SEQ ID NO: 103

MAGRPGYSEVIFLYVVSVAVIARATDNMPVNKDVSKLFPLTLIHINDLHA

RFEETNMKSNVCTQKDQCIAGIARVYQKIKDLLKEYESKNPIYLNAGDNF

QGTLWYNLLRWNVTADFIKKLKPAAMTLGNHEFDHTPKGLAPYLAELNKE

GIPTIVANLVMNNDPDLKSSKIPKSIKLTVGKRKIGIIGVLYDKTHEIAQ

TGKVTLSNAVEAVRREAAALKKDNIDIIVVLSHCSYEEDKKIAAEAGDDI

DVIVGAHSHSFLYSPDSKQPHDPKDKVEGPYPTLVESKNKRKIPIVQAKS

FGKYVGRLTLYFDEEGEVKNWEGYPVFIDHKVQQDPQILKDLVPWRAKVE

AIGSTVVGETMIELDRDSCRDQECTLGVLYADGFADQYTNDTFRPFAIIQ

AGNFRNPIKVGKITNGDIIEAAPFGSTADLIRLKGADIWDVAEHSFALDD

EGRTNCLQVSGLRIVIDISKPVRSRVKKIEVMDYTNPKSDKLKPLDKEAE

YYIVVPSYLADGKDGFSAMKRATARRTGPLDSDVFKNYVEKIKKVDNLKL

GRVIVCKGSKCT

(*Aedes aegypti* polypeptide) SEQ ID NO: 104

MIDQCACSHQLSAALSTEDMLRTSSIVFLTCCLTFLIEGSSFKLKIIHFN

DIHARFDEVTNSSSPCSGNGETCVAGIARLVTTIEKLRKQNENHLVLNAG

DVFQGTIWYTLLKWNVSQQFMNMVKADAMTLGNHEFDDSFPVLIPFLENT

KNVTPVVVSNLVFPKQLSRDVTKFRSLIKEDPLVLTVGGQSIGIIGVIFD

ETDKIGNSDPLKFKSSIETVRIAAKQLKSKGVNIIIVLSHCGVFDDKKIA

EQAGEDIDIIVGGHTHTLLYNGDPPSKHAALDKYPIVVETGNNHKVLIVQ

AFCHGHYVGNIDLTFDDEGEITAFEGQPIYQENRIEKNALVEARVRELRK

DVEVKSLVKVGESKLELSNDCRLKDCTFGSVLADAYVWHFRSRSNAPMIA

MIHPGNFRISLAAGAITRGQILTALPFNSNANRVTVLGSTIKKAIEFGTS

INPRRCSFNALQTAGIKIDVDYGKPVGNRTVILLKTGGKYKRLVESKKYD

ILVNSYVFKGGDGFDMFKHLAVKGRAPFDAELLEQYIVARKGIQKSGLLQ

SRMNVSHVEKALSEVKSCKQSR

(*Aedes aegypti* polypeptide) SEQ ID NO: 105

MCSTGFCLVFFLAQVVFQMNYSEQQTTVVMENGAISESEINVDIVMEQYI

LKFYTKRFVEGQNLVVAPLLTFRVFMSLYKAMDASAKFDLHSLLGIQQDT

SVEKMSEIEAFANKHTLPVDEKQISVETRLYYDKSIGNARSVLTAKSLKP

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IGTSFSDKRAFCEKVNSWIRNAPIKGTDNLVRDYDLNNETQAFVAGALSI

YWNTQLKSSTDQKGFQGENVKFLEGSISAGYAKLDNLKVEVVELISDKVD

GVKLWLIMPDRASSIKDFNDQLSVESIRQIENGLTAQKVDVSLALPMVTI

EYNSQEDAYVTEVFEVFSSLFTKPSVKLVDGKDDLYVIKNFLMKCILRFV

ESDASADSKAQSTGMLVKFDRPFVMMMLSKEGNVPILLANYFSPTDKLRA

LEAKERRLKAEANEHLDL

(*Aedes aegypti* polypeptide)

SEQ ID NO: 106

MNLWIIGFCSIYFACSVRSQFTSVPVSYDAQNDHNEFSWNAFKKVFTDYK

ENFVMSPYSLRRLFSCFQGVKLLTSASGTNLQQELSNVLKIVPNQQPSGQ

DHRPYVEQWVRYSSAKYLNRTAMAVAIGSEKVSTVYESIINNCVIYTGHL

QPSNAQRMGQVINDALKNITNNAVQSYLTDTDINPNWKFFAIDSWQFEGL

WKFKFQEEFSATCYFYASREKKGLTKFLYLEEMLKYGNFPEWNVQAVELP

YHDQSPLSCLLMMPLDGNYESLIHSMNQSRFKEVLSKLNEIKTTVRIPQF

GLQTTVPGRQLLESMGMKVPFNQGVFKVFEQGQDVALGEIVQKMEMSIAA

DGEKQAQSFVDKRQDKQFTAHQPFLFVVYDRNELVPILVGFYLKTPPEAA

MGLEDKQKCDDPPVGYQ

(*Aedes aegypti* polypeptide)

SEQ ID NO: 107

MNRQLWIIIFAILCVAQAEEDNPTTEKMEELGIATINNFTREFYSYVEAV

SQVLADLELTTTASITQIKHRIKHLLQEKCNLCSAKAEGPALDQGYVTTS

NGSVIPVSYEQTRFGGGWIVLMQRYDGTVRFNRSWAEYRDGFGMVGHEFW

LGLERIHQMTKDAEYELMIEMQDFEGNYKYAGYDAFAVGPEEERYPLAKV

GKFNKTAYVDSFGKHRGYGFSTYDNDDNGCSNQYGRGGWWYYRKSCFGAS

LTGIWQNKQDWKSISWVWFSTEKKQVPLKFARMMMRLKTAE

(*Aedes aegypti* polypeptide)

SEQ ID NO: 108

MILQFWFVTFSVLFAARADENHSILIKLNDLDHRFTQMFSQQFYRHTREV

TDRVSALKASIDTNLLELDQQIQQALDGIQSNESSSSTSATKSSGLTTIP

IGSEPRVPALYERERYGGDWLVVMHRYDGSVKFDRTWAEYRDGFGMVGQE

FWYGLERLHQLTKEKSYELMVEMEDFNGNLKYAWYDKFVVGPEEQRYALV

ELGTFNGTTDGDSLKPHKGSGFSTYDNDDFGCSNKYAKGGWWYYSGKCYG

SSLTGIWKNELAYSSIVWVKFSDVSNTPLKLVRMMIRPKN

(*Aedes aegypti* polypeptide)

SEQ ID NO: 109

MSPSNKILVLLLFPILLVSSHPIPAEDPAKQCNLSEDDLTKLKAAISGAS

SAKAANEDILPNTTLAACPMLKNFTEMLKTVATDMEVLKTQGVSNMEVQL

LRESFEEKLNDLAKNKDIFERQANQDTSKAEGEMVEKINKLQLEMAKLQE

EIEEQTKQMYVDMIEYIFERLKMNDTEAIDSYAQIVMKTKMHELIMKLKT

DRLVLWEMVKYVEGKKNKWVGRKVLNTILDQVNKLKLYKPEEVEIGKNSL

VVVWCWKFNSETVYGTTDEDQKSFHLAKLFFPKEKGCKECANVKSRTMCN

NDYPKVMVKAFG

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(*Aedes aegypti* polypeptide)

SEQ ID NO: 110

MKLPLLLAIVTTFSVVASTGPFDPEEMLFTFTRCMEDNLEDGPNRLPMLA

KWKEWINEPVDSPATQCFGKCVLVRTGLYDPVAQKFDASVIQEQFKAYPS

LGEKSKVEAYANAVQQLPSTNNDCAAVFKAYDPVHKAHKDTSKNLFHGNK

ELTKGLYEKLGKDIRQKKQSYFEFCENKYYPAGSDKRQQLCKIRQYTVLD

DALFKEHTDCVMKGIRYITKNNELDAEEVKRDFMQVNKDTKALEKVLNDC

KSKEPSNAGEKSWHYYKCLVESSVKDDFKEAFDYREVRSQIYAFNLPKKQ

VYSKPAVQSQVMEIDGKQCPQ

(*Aedes aegypti* polypeptide)

SEQ ID NO: 111

MHSPKSFLLLAVVFVALRVTAAPLWNAKNPEQLQYIAARCMEEWSPKAKD

PKAALKNWMEWKLQPSNEEATQCYTKCMLENIGYYEPGEKRLKGVRVMQQ

WETFNRYQSADRNKVHDLTDTFDFIKPLKSSSCSDVFNAYKDVHAKHLET

IKAILFCDGKSAEKYYKDKGKNVKQKGESIFVHCEEIHYPVGSPQRNELC

KVRKYELGTGKPFENLMECIFKGVRYFNDKNELNIDEIARDFTQVGKKPD

AVKAAMENCKSKTKETDPGKKAVEYYKCLLADSKVKKDFMEAFDYREIRS

KDYYAQITGKLKPYSASDVRKEVNDIDSNKCV

(*Aedes aegypti* polypeptide)

SEQ ID NO: 112

MKLKVYICQVIFSFLAVSVFCEENCNIPESELSKIDHVLRHMEKPIYSEE

QFASDNEECTNLLNGIHAQLRRLTQRYKLMNKGYVKVEEYQRMADDYEKQ

LKTLNDELVELQQHTSEKASATIAKLKEDIKKLDEEVGTLHEKLKGIKQD

FEKVKRDLCVTYLNSNQMSKAKAKLKEMASTYLIEIVQQQLNKSNANIMP

MLEFSAAIPDLDDMGEAYKEIYKFLEEQKRLEGEDSVLLEATVLKMNASL

KEGSNITDERRTQIEGLLKDLATKSTIVFSTWTKELKKINDAVVIKNALD

HMFVSQMKVFGALVGDTSDFGSIRNFVKLTVVCNNYYKVAAYKELIDRKI

GNALGTIMFDLLTLEVNEMKFDPHVPDEIPKLFEATLSSLPNSLTELRTC

LGKVQIYNKKTNKCVVATGNDFDVHKDKLGDFYRVVVADYGCTSFRLEAS

GDKASVRIVTPSGNPMSNVNLHLEGNSLHNYVATPKSNKPDRTPSSSDEW

ILDANYNNDTIKIESQFSDYKTKKTEVDHLLVRDINHLPHVLVARYGFMG

LKNSDAKDTIEWNLKCGS

(*Aedes aegypti* polypeptide)

SEQ ID NO: 113

METSLPITVVFLIVLITGAQTKPTQGSCTLTDEDISDIKSAVQKASKAAV

NDIVLDPTLIDKCPMLEKITASLKSVATEIVQMRDSAISTDQVDQLKQNF

EDQVNQIVKSRDIFEKQSGTQATKEHGEMLERMTALQVKVTELEQQIAKQ

TASMYEDMAELIFQRLQMNSTESVRSYTKHMMEEKLEELMNKLETNYRIY

LGALRFLNHMNDQELIGKVFDGILKRLGDMKADSDDVKENGRNLLVNLLC

WTVNNDFLGKKYKERQVDLYRMALKFYPKTYEKAANEADVRSRQFCEENF

PANLITWFAVSWNDRG

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(*Aedes aegypti* polypeptide)

SEQ ID NO: 114

MKYLLTFLMALSLVNLMLTRPTPEDDGGTSEEPQTQETTGSDEKNGASEE

PNADDASKPDDVEEKGDDDTAKKEDDGESKDGEGSEKSDKEKGEPKNDPR

ETYNKVIEQLDQIKVDNVEDGHERSELAADIQRYLRNPIVDVIGSAGDFS

KIAKCFKSMVGDAKKAIEEDVKGFKECTAKKDSNAYQCSQDRSTVQDKIA

KMSSKIASCVASNRS

(*Aedes albopictus* polypeptide)

SEQ ID NO: 115

MHSLKSSPLLAAVFLALHVTGAPFWNAKNPDELQSIAARCMDEWSPKAKD

PKAALKNWKEWRLQPSNDEATKCYTKCMLENIGFYEPAEKRLKGVRIMQQ

WETFSRYQSADREKVHDLTDTFNFIRPLKSSSCTDVFNAYKDVHARHLET

IKAILFCDGKSAEKYYKDKGKTSKQKKVLCTGS

(*Aedes albopictus* polypeptide)

SEQ ID NO: 116

MKTSLPIVVLLTAVISGVHPNPTPKSCTVSEEDLTTIRNAIQKASRASLD

DVNLDEDLIAKCPLLKTITASLKSVASEIATLKDTGISEEQVDELKQSYE

QQVNEIVKSRDIFEKQSGGDVMKEQGAMINRMTELQVQVAQLQQQIGEQT

SRMYDDMAELIFQRLAMNSTDSIRNYTAHMMEQKLHTLMTKLETNYRIFL

GALRYLDHLGDQPLIDKVFDGILKRLDEMSLETNKERENGKYVLVNLLCW

TVNNRFLTEKYRKKQLELFRIALKFYPKTGNKEANEADIRGRQFCDANFP

VNVITWFAVSRAAEGWGLRGTL

(*Aedes aegypti* polypeptide)

SEQ ID NO: 117

MSTLKKISDEDRESKFGYVFAVSGPVVTAERMSGSAMYELVRVGYYELVG

EIIRLEGDMATIQVYEETSGVTVGDPVLRTGKPLSVELGPGIMGSIFDGI

QRPLKDINELTSSIYIPKGVNIPCLSRTQSWGFNPLNVKVGSHITGGDLY

GLVHENTLVKHKLLVPPRAKGTVRYIAPPGNYTVDDIILETEFDGEINKW

SMLQVWPVRQPRPVTEKLPANHPLLTGQRVLDSLFPCVQGGTTAIPGAFG

CGKTVISQALSKYSNSDVIIYVGCGERGNEMSEVLRDFPELSVEIDGVTE

SIMKRTALVANTSNMPVAAREASIYTGITLSEYFRDMGYNVSMMADSTSR

WAEALREISGRLAEMPADSGYPAYLGARLASFYERAGRVKCLGNPEREGS

VSIVGAVSPPGGDFSDPVTSATLGIVQVFWGLDKKLAQRKHFPSINWLIS

YSKYMRALDDFYDKNFQEFVPLRTKVKEILQEEEDLSEIVQLVGKASLAE

TDKITLEVAKLLKDDFLQQNSYSAYDRFCPFYKTVGMLRNMIGFYDMARH

AVETTAQSENKITWNVIRDSMGNILYQLSSMKFKDPVKDGEAKIKADFDQ

LYEDLQQAFRNLED

(*Aedes albopictus* polypeptide)

SEQ ID NO: 118

MAGKPGIQLFVIFILLSSFAAVVWTTDNMPADKDVSKLFPLTLIHINDLH

ARFDETNMKSNACTAKDQCIAGIARVYQKIQDLLKEYKSKNAIYLNAGDN

FQGTLWYNLLRWQVTADFITKLKPTAMTLGNHEFDHTPKGLAPYLAELDK

AGIPTLVANLVMNDDPDLKSSKIQKSIKVTVGGKTIGIIGVLYDKTHEIA

QTGKVTLSNAVETVKREAAALKKDKVDIIVVLSHCSYDEDKKIAKEAGQD

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IDVIVGAHSHSFLYSKESNKPYDQKDKIEGPYPTIVESNNKRKIPIVQAK

SFGKYVGRLTLYFDNEGEVKHWEGYPEFIDNKVKQDPKILEALIPWRKKV

QEIGSTKVGETTIELDRDSCRDKECTLGVLYADAFADHYTNSSFRPFAII

QAGNFRNPIKVGKITNGDIIEAAPFGSTADLIRLKGDSLWAVAEHSFALD

DENRTNCLQVSGLRIVIDPSKKIGSRVVKIDVMDNRNPKSEDLKPLDKNA

EYFIALPSYLADGKDGFSAMKKATARWTGPLDSDVFKSYVEKIKKVDKLK

WGRVIVCKAGSPCT

(*Aedes albopictus* polypeptide)

SEQ ID NO: 119

MKWSVYIALLVFAFLTSPVFSEENCNIPESELSKIDDVLRHMEKPIYSED

HYTSNNEECTNLLNGIHAQLRRLTQRYKLMNKGYVKVEEYKRMAEDYENQ

LKTLNAELLELQEHTSDKANAAIAKLKEDIKKLDEDVDTLHNKLKGIKQD

FEKVKRDLCLTYLNSNQMSNAKAKVKEMASTYLIEIIQQRLNTKYANIIP

MLDFSTAIPDLDDRGEAYKEIYKFIETHERLDGEDAVLLEASLLKMNATL

KEGSNITDERRTEIEKMLKELAEKSAVVFKTWSTELKGIEDTIIKYALDH

LFVNQMKVFGGIVGDTFEFAPIRHLLKLLVVCNNYYKVAAYKELIDRKIG

NVLGTIMFDLTTLEANEMSFDLHVPDEIPKLFNATLGSLPNSLTQLLPCL

NKVHVYNAKTNMCIVAPEDRFDVQQEKLTDFHRVVLAKYGCTAFRLESSP

NKASVKFVKPSGNALSSINLQLENDQWHSHVGTPTANKPDRKPSSSDEWI

LDANYVNDTVKIQSEFNEYKASQAEVDHLLVMDVKYLPHVVVGRYGVRGL

KRSSAKDTIEWYLKCAS

(*Aedes albopictus* polypeptide)

SEQ ID NO: 120

MAFNGIALLITATIFIGSCYANYCDSSLCRQGPHVACNAPQQFGPACGNN

RKFVPMDSKLKTIILNTHNKLRAEIANGMHGFPQAARMPTLVWDDELAHI

ASFNARKCIFAHDKCRNTRQFKFSGQNLAITTFYGFNFQAGDRAENFTQE

WFNEHKDCPKSYVDAYPSSHRGPQIGHFTQLVNDRTWKVGCSMMHYITNG

KMINYYLVCNYTMTNMIGEPIYTKGRTGSKCETGQNPQFKGLCSPREKVK

SESYNG

(*Aedes albopictus* polypeptide)

SEQ ID NO: 121

MCSTGLCLVFFIAQAVFLMNYSEQQTTVVMENGAISEKETNVDEVMTQFI

MKFYTKRFVEGQNLVVAPLLIFRVFMSMYGEMDASAKFDLHSLVGIPQEA

SAEKMSEFEAFANKYALPVGVQRNLVETRLYYDKSIGKIRSSLEAKSLKP

FPTNFADKQTFCNEVNTWIRNTPINGTDDLVHDYYLNNETAAFVAGALSI

DWNMQLKTSSDVKAPEGENVKFLEGSISTRYAKLDNLKVEVVEMVTDNLS

GVKLWLIMPDEASSIKKFNDQLSIASIRQIEKGLTALQKEDVALTVPMVT

IEYNSQEDAYVTEVFEVFSSLFSKPAVKPWFRVSVKDDLYAVKNFLMKCI

LRFVGSDAPADSKGQSTEKAVSFNRPFVMMILSKESNVPILLANYFSPKD

KLRALEAKERHLRMKAKEHLDL

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(*Aedes albopictus* polypeptide)

SEQ ID NO: 122

MKILLAVVFVLNLTNLAVPQHLITSSPSLPESKPVGRRPTYEEYKQQRES

FLQTEDHHLLGANVTLTENEQLVNKFIMQMKLDEMEKGFNDSYNFIPARH

IFEVLDRFGQSKVFNVIRRLPKGGVLHAHDMALGSTDLIVNATYLENLWQ

KGNFGLNHGPEFKFSRERPGKEWSLVSEIRQWMTNEVYDAKVAEVFSLYN

ADPLNAYKSLDNVWSKFQNLFACLAPLITFAPVWRQYYHDSLKQFYDDHV

QYLEFRGVLPEVYDLDGKVYSAEEIVQLYYEETEQFKAKYPDFIGVKFIY

APGRYASDEEFQKLLDTTNRLHKKFPNFLAGFDLVGQEDPGRSLFEFAPA

LLKLPASINFFFHAGETNWYGMKTDQNLVDAVLLGTKRIGHGFAVLKHPK

VLKEIKRRQICIEINPISNQVLKLVQDQRNHPAALLFSDNYPVVVSSDDP

SFGRSTPLSHDFYVAFTGIASAKQDWRWLKQLALNSIEYSAMNSEEKTVA

KEKWNQAWDHQFSRLAVDFVAGKILENWIMKIV

(*Aedes aegypti* Polypeptide)

SEQ ID NO: 123

MQPRILHLTVLATIIGVALTANVPSTPGRKLNIPAFSNAGKTKGIEIWRI

ENFQPVAVPKAEYGKFYTGDSYLVLNTNEDKNKKKSYDVHFWLGLKTTQD

EAGSAAILTVQLDDLLGGGPVQHREVEGSESDLFLSYFKGGIRYLEGGVA

SGFKHVQTNAAHPKRLFHVKGAKNIRLRQVELAVSAMNKGDCFILDSDRD

VFVWVGPKANRVEKLKAINVANDIRDRDHNGRATVHIVDEFSTLSDQESF

FKSLGSGSPSTVPDQSTAKEDAAFEKADAARVELYKVTDSKAGKLAVEPI

TQKPLKQEMLKPDDAFILDTGSGLYVWIGKSATQQEKTQSLVKAQEFIKN

KKYPAWTPVERIVQNAETAPFKHFFQTWRDAGSTGSRLV

(Polypeptide)

SEQ ID NO: 124

MKSIVSITITVLAIICEGQATNYCDPSLCARGTPHIACNGLSTLSRTCGA

GSFEVALNRADQQLIVDLHNKLRSKVAMGQQKNSAGQRFQQACRMATLQW

DPELAHIAATNARRCVYGHDTCRNTASMKFAGQNIAIKYYYGMTFTNEQL

LTGFINSWFSEFKDATPQQIARYPANYRGPAIGHFTQIVSDRTSRIGCSM

VSYNKNGFINKLFVCNYGLTNIINQPVYVAGNVCSGCTTGCNKVFPGLCN

TAERVSNNP

(Polypeptide)

SEQ ID NO: 125

MKVYICQVIFSFLAVSVFCEENCNIPESELSKIDHVLRHMEKPIYSEEQF

ASDNEECTNLLNGIHAQLRRLTQRYKLMNKGYVKVEEYQRMADNYEKQLK

TLNDELVELQQHTSEKASATIAKLKEDIKKLDEEVGTLHEKLKGIKQDFE

KVKRDLCVTYLNSNQMSKAKAKLKEMASTYLIEIVQQQLNKSNANIMPML

EFSAAIPDLDDMGEAYKEIYKFLEEQKRLEGEDSVLLEATVLKMNASLKE

GSNITDERRTQIEGLLKDLATKSTIVFSTWTKELKKINDAVVIKNALDHM

FVSQMKVFGALVGDTSDFGSIRNFVKLTIVCNNYYKVAAYKELIDRKIGN

ALGTIMFDLLTLEVNEMKFDPHVPDEIPKLFEATLSSLPNSLTELRTCLG

KVQIYNKKTNKCVVATGNDFDVHKDKLGDFYRVVVADYGCTSFRLEASGD

-continued

KASVRIVTPSGNPMSNVNLHLEGNSLHNYVATPKSNKPDRTPSSSDEWIL

DANYNNDTIKIESQFSDYKTKKTEVDHLLVRDINHLPHVLVARYGFMGLK

NSDAKDTIEWNLKCGS

(Oligonucleotide)

SEQ ID NO: 126

TAATACGACTCACTATAGGGGATGGACAGATGTCTCTTCGTG

(Oligonucleotide)

SEQ ID NO: 127

TAATACGACTCACTATAGGGCCAAATCCAATCCATCGAAA

(Oligonucleotide)

SEQ ID NO: 128

TAATACGACTCACTATAGGGGTGAGCAAGGGCGAGGAG

(Oligonucleotide)

SEQ ID NO: 129

TAATACGACTCACTATAGGGCATGATATAGACGTTGTGGCTGTT

TABLE 1

Endogenous AgBR1 concentration of an *A. aegypti* salivary gland.

Salivary gland extract (SGE, µg)	Relative Band Intensity	Estimated AgBR1 (ng)	Concentration (µM)
4	0.0111	1.6	1.6-8.2

TABLE 2

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Gene ID	Total counts	P-value (Naive-control* Bites vs. Naive-control* No bites)	FDR step up (Naive-control* Bites vs. Naive-control* No bites)	Ratio (Naive) control* Bites vs. Naive-control* No bites)
Serpine1	9.20E+01	5.30E−06	2.67E−02	5.59E+00
Chil3	5.58E+01	1.79E−06	2.67E−02	2.01E+02
Ly6c1	5.53E+02	5.80E−04	9.70E−02	2.03E+00
Ccl9	1.82E+02	3.19E−05	7.01E−02	8.69E+00
Il1b	2.91E+01	3.58E−06	2.67E−02	2.41E+01
Msr1	5.87E+01	3.48E−05	7.01E−02	1.15E+01
Ccl2	8.25E+01	1.76E−05	5.31E−02	3.01E+01
Ly6a	1.45E+03	1.63E−04	9.70E−02	2.49E+00
Ifitm3	1.01E+03	4.38E−05	7.01E−02	3.15E+00
Hsd11b1	1.23E+02	4.85E−03	1.67E−01	1.77E+00
Cd53	1.35E+02	3.85E−05	7.01E−02	3.29E+00
Ccl7	1.04E+02	4.63E−05	7.01E−02	2.07E+01
Ccl8	3.03E+02	1.93E−04	9.70E−02	3.02E+00
Hp	1.59E+03	3.42E−02	3.01E−01	2.92E+00
Lilrb4a	7.02E+01	5.78E−05	7.28E−02	7.41E+00
Ms4a6d	8.59E+01	9.10E−05	8.61E−02	6.10E+00
Ccl6	3.16E+02	1.03E−02	2.09E−01	1.67E+00
Adm	8.62E+01	9.03E−03	2.03E−01	3.22E+00
Lyve1	2.09E+02	2.66E−03	1.46E−01	4.01E+00
Slfn2	7.26E+01	2.94E−04	9.70E−02	4.01E+00
Wfdc17	8.84E+01	2.27E−04	9.70E−02	4.79E+00
Akr1b8	9.98E+01	3.92E−04	9.70E−02	2.32E+00
Lrg1	1.82E+02	4.84E−02	3.35E−01	2.23E+00
Icam1	1.41E+02	8.49E−05	8.56E−02	2.78E+00
Cxcl14	3.03E+02	9.29E−04	1.13E−01	2.10E+00
Ifitm2	1.94E+03	6.61E−04	1.04E−01	1.87E+00
Ctsb	3.28E+03	5.24E−03	1.70E−01	1.58E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Upp1	1.37E+01	8.52E−04	1.09E−01	4.35E+00
Bst1	2.99E+01	5.09E−04	9.70E−02	3.15E+00
Timp1	1.49E+02	4.23E−04	9.70E−02	1.32E+01
Ccnd3	4.42E+02	1.81E−03	1.30E−01	1.77E+00
Csf1	2.94E+02	3.00E−03	1.48E−01	2.09E+00
Li1r4b	5.34E+01	6.39E−05	7.29E−02	5.52E+00
Ifi204	2.09E+01	2.16E−02	2.62E−01	2.96E+00
Ctla2a	1.39E+02	2.31E−03	1.40E−01	3.49E+00
Capn2	4.59E+02	1.98E−03	1.31E−01	1.72E+00
Tmsb10	3.60E+02	6.31E−04	1.03E−01	2.56E+00
C5ar1	1.41E+01	1.25E−03	1.20E−01	5.38E+00
Serpina3m	3.18E+01	6.71E−04	1.05E−01	6.61E+00
Ccr5	1.90E+01	4.71E−04	9.70E−02	1.09E+01
Gsta4	5.53E+01	1.03E−04	9.12E−02	4.54E+00
Ddr2	4.69E+02	9.25E−04	1.13E−01	2.70E+00
Ifi207	2.69E+01	1.74E−02	2.47E−01	2.14E+00
Cfb	1.58E+02	4.37E−02	3.26E−01	2.05E+00
AC160962.1	2.06E+01	3.06E−03	1.48E−01	4.65E+00
Gm6560	6.28E+02	2.07E−04	9.70E−02	1.92E+00
Fcgr2b	1.62E+02	1.59E−03	1.30E−01	2.79E+00
Ccr1	4.16E+01	1.68E−04	9.70E−02	7.47E+00
AB124611	1.28E+01	9.80E−04	1.14E−01	4.62E+00
Spp1	1.26E+02	8.04E−04	1.08E−01	6.08E+00
Hspa5	2.59E+03	4.64E−04	9.70E−02	1.79E+00
Trim46	1.01E+01	3.43E−02	3.01E−01	1.92E+00
Clec7a	2.60E+01	1.48E−04	9.70E−02	8.27E+00
Dok2	5.82E+01	4.70E−03	1.66E−01	3.96E+00
Srgn	1.02E+02	5.09E−04	9.70E−02	4.53E+00
Sprr1b	1.09E+02	2.63E−04	9.70E−02	2.37E+01
Calr	2.92E+03	3.18E−04	9.70E−02	2.12E+00
Clec5a	1.64E+01	1.58E−03	1.30E−01	3.67E+00
Ms4a4a	3.02E+01	7.70E−04	1.08E−01	5.15E+00
Pxdc1	9.46E+01	6.38E−03	1.82E−01	1.51E+00
Pdpn	7.96E+01	9.06E−03	2.03E−01	2.62E+00
Serpina3n	1.93E+03	4.84E−04	9.70E−02	6.74E+00
Ptafr	2.48E+01	4.85E−03	1.67E−01	2.74E+00
Mrc1	3.18E+02	3.42E−03	1.52E−01	3.22E+00
Tmem8	3.89E+01	1.07E−03	1.15E−01	4.00E+00
Plaur	4.55E+01	1.81E−03	1.30E−01	5.19E+00
Gm15922	2.45E+01	3.32E−03	1.50E−01	4.81E+00
Cd163	1.66E+02	6.23E−03	1.81E−01	2.30E+00
Samhd1	2.75E+02	2.34E−04	9.70E−02	2.42E+00
Lcp2	2.05E+01	4.09E−03	1.62E−01	2.68E+00
Ifnar2	1.29E+02	5.96E−03	1.80E−01	1.67E+00
Mfsd10	1.95E+02	3.35E−04	9.70E−02	1.64E+00
Ccr2	1.38E+02	1.95E−03	1.31E−01	6.36E+00
Tnfaip2	9.92E+01	6.50E−03	1.82E−01	1.56E+00
Cd68	1.53E+02	1.50E−02	2.34E−01	2.29E+00
Lbp	2.77E+02	9.22E−03	2.04E−01	2.45E+00
Lrrc25	2.93E+01	1.42E−03	1.29E−01	3.85E+00
Anxa3	4.44E+01	3.56E−02	3.05E−01	2.61E+00
Hdc	3.97E+01	1.79E−03	1.30E−01	3.52E+00
Lyz2	1.25E+03	1.18E−02	2.19E−01	2.37E+00
Cebpd	1.35E+02	1.29E−02	2.24E−01	1.96E+00
Clec4d	2.23E+01	1.87E−04	9.70E−02	2.17E+01
Tnfrsf1b	6.68E+01	2.67E−03	1.46E−01	3.77E+00
Manf	4.85E+02	1.55E−04	9.70E−02	1.86E+00
Hk3	1.48E+01	5.47E−03	1.72E−01	5.51E+00
Cyp7b1	3.90E+01	5.84E−04	9.70E−02	3.99E+00
Parm1	3.93E+01	2.22E−02	2.63E−01	1.96E+00
Msn	8.65E+02	4.35E−03	1.64E−01	1.90E+00
Plek	1.10E+02	7.40E−04	1.06E−01	3.14E+00
Tlr13	3.26E+01	6.50E−04	1.04E−01	4.59E+00
Sema3a	6.32E+01	2.90E−02	2.84E−01	2.07E+00
Slc27a3	3.50E+02	3.33E−04	9.70E−02	3.11E+00
Csf3r	2.63E+01	1.43E−04	9.70E−02	1.39E+01
Nek6	1.13E+02	1.20E−02	2.20E−01	1.54E+00
Tubb6	2.04E+02	9.10E−03	2.03E−01	2.76E+00
Capns1	1.15E+03	5.29E−03	1.71E−01	1.65E+00
Lyn	7.33E+01	3.21E−03	1.48E−01	2.74E+00
Krt16	8.15E+02	2.27E−04	9.70E−02	4.32E+01
Apbb1ip	7.21E+01	1.65E−02	2.41E−01	2.50E+00
Sirpb1c	2.98E+01	5.22E−04	9.70E−02	1.59E+01
Gm27029	1.25E+01	1.16E−02	2.18E−01	2.33E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Fcer1g	1.53E+02	2.65E−03	1.46E−01	3.38E+00
Ptx3	2.16E+01	1.81E−03	1.30E−01	5.03E+00
Cd14	6.62E+01	1.72E−03	1.30E−01	3.77E+00
Cd7	1.69E+01	4.83E−02	3.35E−01	2.41E+00
Mpeg1	1.56E+02	2.34E−03	1.40E−01	2.62E+00
Cpne2	1.51E+02	7.32E−04	1.05E−01	1.92E+00
Pdia4	4.10E+02	5.88E−03	1.79E−01	1.69E+00
Creld2	2.13E+02	2.69E−04	9.70E−02	1.86E+00
Atrip	1.59E+01	3.82E−02	3.15E−01	1.65E+00
C3ar1	5.14E+01	6.02E−03	1.80E−01	3.00E+00
Svep1	2.91E+02	4.85E−02	3.35E−01	2.98E+00
Gm3788	1.07E+01	1.85E−03	1.30E−01	3.38E+00
Rnasel	8.01E+01	3.56E−02	3.05E−01	1.70E+00
Thbs1	1.83E+03	4.43E−02	3.28E−01	1.59E+00
C1qb	3.71E+02	3.90E−02	3.15E−01	2.05E+00
Ftl1	2.68E+03	1.58E−02	2.38E−01	1.63E+00
Ptprc	1.11E+02	1.36E−02	2.27E−01	1.89E+00
Angptl4	7.60E+01	2.04E−02	2.58E−01	2.15E+00
Relt	2.52E+01	5.73E−03	1.77E−01	3.00E+00
Pdia6	9.19E+02	2.85E−03	1.48E−01	1.73E+00
Serpina3e-ps	1.36E+01	1.51E−03	1.30E−01	4.57E+00
Clec4n	4.65E+01	5.79E−04	9.70E−02	4.75E+00
Wisp2	2.20E+02	7.80E−03	1.91E−01	3.16E+00
Fgr	2.53E+01	2.47E−03	1.42E−01	3.83E+00
Layn	1.39E+01	1.86E−02	2.52E−01	2.54E+00
Pcdhb22	3.76E+01	1.25E−02	2.20E−01	2.10E+00
Adam8	1.38E+02	5.23E−05	7.20E−02	2.74E+00
Lgmn	8.96E+02	8.53E−03	1.98E−01	2.26E+00
March1	2.46E+01	4.18E−02	3.22E−01	1.53E+00
Clec4a2	5.48E+01	2.46E−03	1.42E−01	5.46E+00
Dab2	4.96E+02	1.77E−02	2.49E−01	2.56E+00
Lcp1	3.02E+02	2.04E−02	2.58E−01	2.15E+00
Cd300lb	1.58E+01	7.28E−03	1.85E−01	4.52E+00
Slco2a1	4.88E+02	3.11E−03	1.48E−01	1.54E+00
Slc11a1	1.75E+01	2.38E−02	2.67E−01	3.01E+00
Ceacam1	2.84E+01	3.88E−02	3.15E−01	2.64E+00
Emilin2	1.63E+02	2.20E−02	2.63E−01	3.08E+00
Dnajb11	4.71E+02	3.48E−04	9.70E−02	1.56E+00
Rnf141	3.86E+02	1.41E−03	1.29E−01	1.52E+00
N1rp3	9.65E+00	1.05E−03	1.15E−01	4.64E+00
Itgb2	9.96E+01	1.89E−02	2.53E−01	3.05E+00
Mcemp1	1.05E+01	1.40E−03	1.29E−01	5.17E+00
Tmem150a	4.66E+01	1.87E−02	2.53E−01	1.73E+00
Cyba	1.65E+02	2.91E−02	2.84E−01	2.16E+00
Itgal	1.54E+01	3.59E−03	1.55E−01	2.65E+00
Gm9844	8.95E+01	4.47E−03	1.64E−01	2.40E+00
Slc15a3	5.39E+01	1.67E−03	1.30E−01	1.84E+00
Pfn1	1.74E+03	5.76E−04	9.70E−02	1.63E+00
Fam49b	1.71E+02	3.62E−03	1.55E−01	1.86E+00
Ssbp4	1.49E+02	1.48E−02	2.34E−01	1.50E+00
Cyth4	7.95E+01	1.40E−02	2.28E−01	3.25E+00
Gda	2.89E+02	6.60E−03	1.82E−01	2.17E+00
Syk	8.97E+01	1.21E−02	2.20E−01	1.88E+00
Samsn1	1.35E+01	8.64E−03	1.99E−01	3.22E+00
Nqo1	1.33E+02	6.75E−05	7.29E−02	2.30E+00
Pik3r5	3.23E+01	1.47E−02	2.33E−01	2.30E+00
Tpsab1	2.10E+02	5.58E−03	1.74E−01	2.82E+00
Hsp90b1	2.00E+03	9.00E−03	2.03E−01	1.56E+00
Mgp	1.14E+03	3.24E−02	2.95E−01	2.61E+00
F630028O10Rik	1.25E+01	5.57E−04	9.70E−02	5.60E+00
AI662270	2.54E+01	2.21E−02	2.63E−01	2.76E+00
Cd200r1	1.63E+01	1.63E−02	2.41E−01	3.25E+00
Pf4	1.79E+02	1.43E−02	2.29E−01	3.06E+00
Fth1	6.18E+03	1.47E−02	2.33E−01	1.60E+00
Smim3	7.18E+01	3.50E−02	3.03E−01	1.68E+00
Sash3	2.15E+01	2.41E−02	2.67E−01	2.86E+00
Cd48	3.84E+01	4.03E−02	3.17E−01	1.93E+00
Mcoln2	2.57E+01	1.52E−02	2.35E−01	2.57E+00
Adgrg3	1.46E+01	2.66E−02	2.78E−01	2.84E+00
Coro1a	2.53E+02	2.16E−02	2.62E−01	2.72E+00
Pkm	4.24E+03	4.04E−03	1.62E−01	1.79E+00
Pgk1-rs7	5.00E+02	1.32E−02	2.25E−01	1.58E+00
Tyrobp	1.88E+02	9.84E−03	2.09E−01	2.62E+00
Gm5537	5.58E+02	1.17E−02	2.19E−01	1.59E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Slc7a8	4.67E+01	1.65E−02	2.41E−01	2.89E+00
Armc6	6.56E+01	3.68E−02	3.10E−01	1.54E+00
Fam69a	1.81E+02	3.29E−04	9.70E−02	1.66E+00
Gcnt1	3.90E+01	6.25E−03	1.81E−01	2.81E+00
Ccl22	2.26E+01	2.84E−02	2.83E−01	3.27E+00
Sprr2a2	1.35E+03	6.12E−04	1.01E−01	2.83E+01
Pirb	7.96E+01	2.93E−02	2.85E−01	2.92E+00
Myo1g	5.57E+01	4.37E−02	3.26E−01	2.24E+00
Ddah1	2.20E+01	2.39E−02	2.67E−01	4.12E+00
Ms4a6c	4.63E+01	1.62E−02	2.40E−01	3.36E+00
Neto2	1.22E+01	7.31E−03	1.85E−01	2.24E+00
Il1rl1	1.93E+01	2.39E−02	2.67E−01	3.21E+00
Ptprj	1.25E+02	1.13E−02	2.16E−01	1.51E+00
Sdf2l1	8.91E+01	1.90E−02	2.53E−01	1.89E+00
Sprr2a3	7.74E+01	5.39E−04	9.70E−02	3.08E+01
Pira2	1.72E+01	4.88E−03	1.67E−01	5.17E+00
Serpinb1a	4.03E+02	4.35E−02	3.26E−01	1.77E+00
Gm9025	2.82E+01	3.00E−02	2.86E−01	2.17E+00
Flot2	3.35E+02	2.20E−02	2.63E−01	1.82E+00
Il2rg	2.43E+01	3.86E−02	3.15E−01	3.01E+00
Nfkbie	3.26E+01	1.59E−02	2.38E−01	1.74E+00
Thy1	8.20E+02	1.03E−02	2.09E−01	2.42E+00
Tmprss11g	4.99E+01	6.90E−03	1.84E−01	2.67E+00
Clec4a1	5.67E+01	3.25E−02	2.95E−01	2.57E+00
Zyx	4.88E+02	3.28E−02	2.96E−01	1.52E+00
Ecscr	7.33E+01	4.97E−02	3.38E−01	2.39E+00
Pdia3	2.30E+03	2.49E−03	1.42E−01	1.56E+00
2610528A11Rik	3.03E+02	5.30E−04	9.70E−02	1.95E+02
Tlr2	5.09E+01	4.91E−02	3.37E−01	1.56E+00
Impdh2	2.79E+02	2.43E−04	9.70E−02	1.70E+00
Krt6b	9.71E+02	1.63E−03	1.30E−01	2.84E+01
Fscn1	9.94E+01	5.80E−03	1.77E−01	3.12E+00
Tmem173	5.77E+01	1.69E−02	2.44E−01	2.91E+00
Cdhr1	5.32E+01	1.08E−04	9.12E−02	4.82E+01
Ifitm1	6.70E+01	2.95E−03	1.48E−01	3.26E+00
Cytip	5.53E+01	1.17E−02	2.19E−01	1.72E+00
Psmb10	1.52E+02	2.89E−02	2.84E−01	1.57E+00
Marcks	3.94E+02	2.22E−02	2.63E−01	1.52E+00
Pcbp3	2.45E+01	5.12E−03	1.69E−01	2.23E+00
Cfl1	2.01E+03	1.55E−03	1.30E−01	1.70E+00
Hck	1.58E+01	4.45E−03	1.64E−01	3.18E+00
Tnfrsf13b	1.79E+01	3.38E−02	3.00E−01	2.71E+00
Traf1	1.33E+01	2.52E−02	2.71E−01	2.54E+00
Ap1m1	3.61E+02	1.70E−03	1.30E−01	1.53E+00
Jam1	2.09E+01	3.51E−02	3.03E−01	1.63E+00
Vav1	2.92E+01	1.33E−02	2.25E−01	2.43E+00
Csf2rb	1.09E+02	1.10E−02	2.14E−01	2.27E+00
Impdh1	1.57E+02	2.19E−03	1.37E−01	1.62E+00
Irf8	3.21E+01	2.87E−02	2.84E−01	2.17E+00
Slc7a11	7.83E+01	1.87E−03	1.30E−01	2.47E+00
Igsf6	1.94E+01	1.37E−02	2.27E−01	3.35E+00
Cd300a	2.59E+01	2.02E−02	2.58E−01	2.81E+00
Dynlt1b	2.52E+02	9.72E−03	2.07E−01	1.62E+00
Laptm5	2.92E+02	2.87E−02	2.84E−01	1.96E+00
Ccl12	2.35E+01	6.88E−03	1.84E−01	9.89E+00
Ldha	3.49E+03	2.87E−02	2.84E−01	1.51E+00
Tagln2	1.10E+03	3.16E−03	1.48E−01	1.60E+00
Irak4	6.75E+01	1.09E−02	2.13E−01	1.54E+00
Fyb	3.08E+01	9.37E−03	2.05E−01	2.20E+00
Cxcl1	2.67E+01	5.21E−04	9.70E−02	1.31E+01
Nme1	4.78E+02	2.33E−03	1.40E−01	1.85E+00
Ripor2	1.85E+01	1.83E−02	2.51E−01	2.27E+00
Ncf4	4.40E+01	2.91E−02	2.84E−01	2.05E+00
Impdh2-ps	7.61E+02	5.07E−04	9.70E−02	1.71E+00
Alg8	2.43E+01	5.03E−03	1.67E−01	1.92E+00
Mthfd2	4.07E+01	4.38E−02	3.26E−01	1.90E+00
Flvcr1	8.70E+01	1.35E−02	2.26E−01	1.54E+00
Ncf2	3.28E+01	3.34E−02	2.98E−01	1.93E+00
Dusp6	1.79E+02	3.18E−02	2.93E−01	1.78E+00
Flna	1.39E+03	3.94E−02	3.15E−01	1.68E+00
Etv4	3.57E+01	1.29E−02	2.24E−01	1.78E+00
Rab31	2.88E+02	4.64E−03	1.65E−01	2.07E+00
Bak1	1.33E+02	1.05E−02	2.11E−01	1.58E+00
Lgals9	4.93E+02	1.10E−03	1.16E−01	2.58E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Gm3839	1.15E+01	4.20E−02	3.22E−01	2.53E+00
Prss12	1.39E+02	8.73E−03	1.99E−01	1.90E+00
Hyou1	4.35E+02	4.51E−03	1.64E−01	1.57E+00
1810055G02Rik	1.34E+02	4.12E−02	3.20E−01	1.51E+00
Gm5837	1.14E+02	6.56E−03	1.82E−01	1.51E+00
Ripk3	4.69E+01	9.61E−03	2.07E−01	3.15E+00
Mmp9	6.44E+01	2.34E−02	2.67E−01	1.64E+00
Ran	1.04E+03	1.17E−03	1.19E−01	1.64E+00
Gsdmc	1.25E+02	2.91E−03	1.48E−01	4.77E+00
Me2	7.01E+01	3.19E−02	2.93E−01	2.03E+00
Ccl24	1.77E+01	2.03E−02	2.58E−01	5.13E+00
Lrrc59	5.81E+02	4.04E−04	9.70E−02	1.61E+00
Gmfg	2.50E+01	3.57E−02	3.06E−01	1.77E+00
Ddx39	3.46E+02	8.84E−04	1.11E−01	1.72E+00
Tubb5	2.95E+03	1.10E−02	2.14E−01	2.01E+00
Gmfg-ps	3.56E+01	4.32E−02	3.24E−01	1.71E+00
Dhfr	1.31E+02	7.84E−03	1.92E−01	1.56E+00
Gm4737	5.23E+02	1.84E−02	2.51E−01	1.68E+00
Gm11451	2.09E+01	1.95E−02	2.55E−01	2.16E+00
Csf2ra	4.93E+01	4.77E−02	3.34E−01	1.74E+00
Cdkn2d	1.24E+02	4.99E−03	1.67E−01	1.56E+00
Lrp8	4.18E+01	3.10E−04	9.70E−02	2.56E+00
Evi2b	2.81E+01	4.52E−02	3.28E−01	2.70E+00
Pgk1	5.29E+02	2.82E−02	2.83E−01	1.69E+00
Spi1	8.95E+01	3.31E−02	2.97E−01	2.16E+00
Sorcs2	4.03E+01	4.56E−02	3.29E−01	2.15E+00
Crispld2	1.11E+03	3.30E−03	1.50E−01	2.16E+00
AC154572.2	5.38E+01	4.30E−02	3.23E−01	1.55E+00
Ier5l	3.26E+01	1.88E−02	2.53E−01	2.09E+00
Ruvbl2	1.69E+02	1.54E−03	1.30E−01	1.63E+00
Parp12	8.76E+01	6.96E−03	1.84E−01	1.54E+00
AC123061.1	3.70E+01	4.53E−02	3.29E−01	1.67E+00
Osmr	2.05E+02	4.29E−03	1.63E−01	1.83E+00
Dtymk	1.43E+02	1.84E−02	2.51E−01	1.75E+00
Gm6180	9.49E+01	5.39E−03	1.72E−01	1.74E+00
Gm5851	9.09E+00	1.07E−02	2.12E−01	2.58E+00
Gm2564	2.21E+01	1.21E−02	2.20E−01	3.89E+00
Apol8	2.75E+01	2.33E−03	1.40E−01	2.46E+00
Lcn2	2.92E+02	9.67E−03	2.07E−01	8.26E+00
Hnrnpa3	9.53E+02	1.27E−02	2.23E−01	1.50E+00
Eno1	5.06E+02	1.19E−03	1.20E−01	2.04E+00
Csf2rb2	7.09E+01	3.42E−02	3.01E−01	1.76E+00
Bcl3	5.31E+01	4.51E−03	1.64E−01	5.59E+00
Ngf	1.84E+01	7.12E−03	1.85E−01	3.69E+00
Hpgd	2.17E+02	2.34E−02	2.67E−01	1.53E+00
Cks1b	1.47E+02	3.47E−03	1.54E−01	1.62E+00
Lsm4	1.98E+02	2.21E−02	2.63E−01	1.55E+00
H13	6.32E+02	1.23E−03	1.20E−01	1.50E+00
Fam162a	1.70E+02	1.17E−02	2.19E−01	1.81E+00
Eno1b	1.75E+03	7.07E−04	1.05E−01	1.88E+00
Txn1	8.38E+02	5.09E−04	9.70E−02	1.55E+00
Marcksl1	1.50E+02	4.96E−04	9.70E−02	1.92E+00
Vcan	1.54E+02	3.92E−02	3.15E−01	2.86E+00
Hmox1	9.55E+02	1.90E−03	1.31E−01	1.91E+00
Il4ra	3.07E+02	6.55E−03	1.82E−01	1.95E+00
Crlf2	3.39E+01	1.69E−02	2.44E−01	1.92E+00
Gm15725	3.82E+01	2.85E−02	2.84E−01	2.00E+00
Enkd1	2.62E+01	1.04E−02	2.10E−01	1.80E+00
Snrpa	2.82E+02	6.65E−03	1.82E−01	1.51E+00
Gins1	4.26E+01	1.92E−02	2.55E−01	1.88E+00
Ifi35	1.96E+02	2.39E−02	2.67E−01	1.53E+00
Gm15590	1.42E+01	4.46E−02	3.28E−01	1.99E+00
Gjb1	1.03E+01	4.49E−02	3.28E−01	1.96E+00
Ranbp1	3.45E+02	3.64E−03	1.55E−01	1.57E+00
Brca2	9.93E+01	9.35E−04	1.13E−01	2.56E+00
Slc39a14	9.67E+01	2.39E−03	1.41E−01	1.95E+00
Arf2	3.56E+02	2.93E−02	2.85E−01	1.57E+00
Gpr132	1.04E+01	4.78E−02	3.34E−01	1.77E+00
Cad	2.46E+02	3.64E−03	1.55E−01	1.67E+00
Serpinc1	1.40E+01	1.74E−02	2.47E−01	1.98E+00
Tslp	1.96E+01	2.74E−02	2.81E−01	1.62E+00
Snrpf	1.18E+02	5.22E−03	1.70E−01	1.57E+00
Hsp90aa1	8.11E+02	4.44E−03	1.64E−01	1.51E+00
Gm6992	1.30E+01	4.43E−03	1.64E−01	2.58E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

1110038B12Rik	6.80E+01	1.47E−02	2.33E−01	1.50E+00
Gm12758	2.09E+01	2.15E−02	2.62E−01	2.14E+00
Gm11847	5.18E+01	2.49E−02	2.70E−01	1.77E+00
Dusp2	1.09E+01	1.41E−02	2.28E−01	2.25E+00
Cenps	7.19E+01	1.64E−02	2.41E−01	1.64E+00
Gm17383	3.70E+01	2.56E−02	2.73E−01	2.60E+00
2610203C20Rik	1.13E+02	3.94E−02	3.15E−01	1.57E+00
Alg3	5.95E+01	3.22E−03	1.48E−01	1.62E+00
Gm5844	1.03E+02	1.31E−02	2.25E−01	1.57E+00
Cenpt	7.41E+01	5.15E−03	1.69E−01	1.71E+00
Pglyrp1	1.35E+01	1.80E−02	2.50E−01	2.60E+00
Pold2	2.44E+02	1.99E−02	2.57E−01	1.57E+00
Slc16a14	1.38E+02	2.32E−02	2.66E−01	1.50E+00
Nup43	8.94E+01	3.14E−03	1.48E−01	1.70E+00
Acy1	6.13E+01	1.39E−02	2.28E−01	1.57E+00
Fhl2	2.24E+01	9.21E−03	2.04E−01	1.98E+00
Mcm3	2.79E+02	2.99E−02	2.86E−01	1.79E+00
Gm20390	3.17E+02	4.84E−03	1.67E−01	1.83E+00
Pfkl	2.14E+02	2.96E−02	2.86E−01	1.54E+00
Gm26809	8.67E+01	1.36E−04	9.70E−02	2.14E+00
Mmp3	2.61E+02	8.43E−03	1.97E−01	4.04E+00
Ints7	1.06E+02	3.89E−02	3.15E−01	1.53E+00
Orc1	3.19E+01	1.25E−02	2.20E−01	2.08E+00
Slc19a1	9.69E+01	1.94E−02	2.55E−01	1.53E+00
Rbm14	2.04E+02	3.62E−03	1.55E−01	1.58E+00
Gemin6	5.88E+01	1.78E−02	2.49E−01	1.52E+00
Aldh18a1	1.28E+02	2.26E−02	2.65E−01	1.62E+00
Dhrs13	2.46E+01	6.82E−03	1.84E−01	2.39E+00
Mcm4	3.38E+02	2.13E−02	2.62E−01	1.51E+00
Lsm2	8.84E+01	2.68E−03	1.46E−01	1.66E+00
Pop1	5.15E+01	3.84E−03	1.58E−01	1.79E+00
Chil1	2.16E+03	4.32E−03	1.63E−01	2.93E+00
Nup93	2.32E+02	4.05E−03	1.62E−01	1.56E+00
Slc29a2	4.36E+01	6.81E−03	1.84E−01	2.38E+00
Vstm2a	9.31E+00	2.41E−02	2.67E−01	1.99E+00
Cdt1	1.24E+02	3.34E−02	2.98E−01	1.61E+00
Rad51	7.52E+01	3.31E−02	2.97E−01	1.90E+00
Mcm6	4.00E+02	3.61E−02	3.07E−01	1.84E+00
Ercc6l	4.30E+01	4.75E−02	3.34E−01	1.87E+00
Ccne1	3.17E+01	2.26E−02	2.65E−01	2.01E+00
Casp6	8.71E+01	2.83E−02	2.83E−01	1.51E+00
Abcg2	2.24E+02	1.62E−03	1.30E−01	1.66E+00
Gm5855	1.17E+01	6.87E−03	1.84E−01	2.34E+00
Gm6977	5.53E+01	4.47E−02	3.28E−01	1.69E+00
Tbl3	2.19E+02	1.60E−03	1.30E−01	1.58E+00
BC100530	7.99E+01	2.73E−02	2.81E−01	1.93E+01
Rpp40	4.22E+01	1.54E−02	2.37E−01	1.55E+00
Lyar	1.62E+02	4.42E−03	1.64E−01	1.53E+00
Clec2l	2.17E+01	3.35E−03	1.51E−01	3.76E+00
Sprr2h	4.07E+01	1.29E−02	2.24E−01	7.43E+00
Ppia	3.97E+03	3.64E−03	1.55E−01	1.50E+00
Ndc1	1.34E+02	9.31E−03	2.05E−01	1.54E+00
Bfsp1	1.48E+01	2.35E−02	2.67E−01	1.90E+00
Skap2	4.01E+02	1.47E−03	1.29E−01	1.50E+00
Smyd5	1.15E+02	2.39E−03	1.41E−01	1.60E+00
Car12	2.72E+02	2.84E−03	1.48E−01	2.26E+00
Casp3	1.40E+02	4.46E−02	3.28E−01	1.52E+00
Fbxo10	9.27E+01	2.90E−02	2.84E−01	1.60E+00
Lsm5	3.60E+01	3.32E−02	2.97E−01	1.61E+00
Gstcd	6.05E+01	1.74E−02	2.47E−01	1.64E+00
Stom	5.92E+02	6.92E−03	1.84E−01	1.66E+00
Gm8203	3.02E+02	5.83E−04	9.70E−02	1.59E+00
Gm13461	2.84E+02	6.90E−03	1.84E−01	1.64E+00
Pgm3	6.75E+01	2.46E−02	2.69E−01	1.51E+00
Erh	2.54E+02	7.60E−03	1.88E−01	1.54E+00
Fam171a2	1.20E+02	3.53E−04	9.70E−02	2.36E+00
Xdh	3.95E+02	4.86E−03	1.67E−01	1.55E+00
Nfyb	2.65E+02	4.29E−03	1.63E−01	1.61E+00
Hbegf	6.68E+01	1.45E−02	2.31E−01	1.78E+00
Myof	4.58E+02	2.93E−02	2.85E−01	1.57E+00
Prss27	5.47E+01	1.71E−02	2.46E−01	2.14E+00
Slc14a1	2.12E+01	8.28E−03	1.96E−01	3.46E+00
Entpd7	3.80E+01	5.03E−03	1.67E−01	1.74E+00
Gm7899	1.79E+01	4.70E−02	3.34E−01	2.05E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Gm12988	1.34E+01	2.38E−02	2.67E−01	1.84E+00
Tpcn2	9.41E+01	6.44E−03	1.82E−01	1.61E+00
Srm	3.12E+02	2.90E−03	1.48E−01	1.60E+00
Has3	2.28E+01	1.64E−02	2.41E−01	4.85E+00
Wdhd1	7.23E+01	4.28E−02	3.23E−01	1.76E+00
Gm13092	1.22E+02	3.27E−02	2.95E−01	1.59E+00
Socs3	3.30E+02	2.97E−03	1.48E−01	1.98E+00
Anapc15-ps	8.79E+00	3.30E−02	2.97E−01	1.73E+00
Fosl1	1.73E+01	4.43E−02	3.28E−01	1.72E+00
Nfkbid	1.15E+01	3.99E−02	3.16E−01	1.64E+00
Pim2	3.55E+01	1.39E−02	2.28E−01	1.60E+00
Ada	4.45E+01	1.62E−02	2.40E−01	1.76E+00
Gm5791	1.93E+01	2.07E−02	2.60E−01	2.18E+00
Gm11675	6.42E+01	4.76E−02	3.34E−01	1.55E+00
Sema4c	1.95E+02	2.51E−03	1.42E−01	1.52E+00
Tes	1.05E+02	6.69E−03	1.82E−01	1.54E+00
Lrp11	2.50E+01	3.62E−02	3.07E−01	1.54E+00
Tyms	2.24E+02	4.88E−02	3.36E−01	1.53E+00
Mtcl1	4.53E+01	2.00E−02	2.57E−01	2.78E+00
Rfng	3.04E+02	8.59E−04	1.09E−01	1.53E+00
Snhg4	1.31E+02	1.59E−02	2.38E−01	1.61E+00
Ndnf	9.79E+01	4.44E−02	3.28E−01	3.12E+00
Gm3379	3.54E+01	2.22E−02	2.63E−01	1.93E+00
Trip13	4.31E+01	1.12E−02	2.16E−01	1.86E+00
Sprr2g	1.50E+01	3.00E−02	2.86E−01	6.51E+00
Gpr176	1.05E+01	2.27E−02	2.66E−01	2.59E+00
Panx1	1.73E+02	1.97E−03	1.31E−01	1.64E+00
Stat3	1.34E+03	4.24E−03	1.63E−01	1.64E+00
Gemin4	4.19E+01	4.68E−02	3.33E−01	2.10E+00
Slc9a1	7.23E+02	7.90E−04	1.08E−01	1.58E+00
Gm6210	5.01E+01	4.00E−02	3.16E−01	1.87E+00
Eeflakmt4	5.38E+01	1.44E−02	2.30E−01	1.51E+00
Gm5620	1.74E+01	3.96E−02	3.15E−01	1.67E+00
Dnph1	1.53E+02	9.13E−03	2.03E−01	1.52E+00
Gm12666	1.17E+01	4.36E−02	3.26E−01	1.63E+00
S100a9	3.12E+02	2.90E−02	2.84E−01	1.76E+01
Mrto4	1.67E+02	6.54E−03	1.82E−01	1.54E+00
Stfa3	1.83E+01	7.01E−03	1.84E−01	5.45E+00
Nkain1	1.22E+01	4.62E−03	1.65E−01	2.87E+00
Psmg4	7.14E+01	5.49E−03	1.72E−01	1.50E+00
S100a8	1.94E+02	1.37E−02	2.27E−01	1.22E+01
Ampd3	1.73E+02	1.74E−02	2.47E−01	1.70E+00
Duxbl2	1.76E+01	2.24E−02	2.63E−01	1.75E+00
Rab15	3.41E+02	2.48E−02	2.70E−01	1.62E+00
Gm27219	3.66E+01	2.15E−02	2.62E−01	1.71E+00
Hmgb1-ps3	1.22E+01	3.76E−02	3.13E−01	1.96E+00
Noc4l	1.88E+02	1.99E−03	1.31E−01	1.78E+00
Gm12722	1.10E+01	4.77E−02	3.34E−01	1.63E+00
Dsg1c	7.44E+01	2.07E−03	1.32E−01	2.04E+00
1700052K11Rik	6.55E+01	4.96E−02	3.38E−01	1.55E+00
Krt6a	1.25E+03	2.14E−03	1.36E−01	3.99E+00
Hirip3	1.12E+02	2.12E−02	2.62E−01	1.64E+00
Pgam1	9.91E+02	2.48E−03	1.42E−01	1.63E+00
B4galnt4	1.07E+01	4.00E−02	3.16E−01	1.83E+00
Rpl10-ps5	8.71E+01	1.61E−02	2.40E−01	1.68E+00
Hrh2	1.09E+01	2.93E−03	1.48E−01	2.72E+00
AC131178.1	2.54E+01	1.76E−02	2.48E−01	1.99E+00
Gadl1	7.43E+02	1.32E−02	2.25E−01	1.71E+00
BC055324	3.24E+01	3.50E−02	3.03E−01	1.56E+00
Gm6063	1.46E+01	4.49E−02	3.28E−01	1.93E+00
Trex1	1.69E+02	2.64E−02	2.78E−01	1.54E+00
Galnt6	8.87E+01	5.31E−03	1.71E−01	2.60E+00
Gm3448	3.70E+01	3.41E−02	3.01E−01	1.89E+00
Nat8l	5.68E+02	2.80E−02	2.83E−01	1.66E+00
AC022775.2	1.95E+01	2.54E−02	2.73E−01	1.59E+00
Gm6793	2.30E+01	3.60E−02	3.06E−01	1.97E+00
Mgat5b	1.84E+01	9.60E−04	1.14E−01	3.43E+00
Rpl29	4.19E+01	2.29E−02	2.66E−01	1.51E+00
Gm11805	9.02E+00	3.77E−02	3.13E−01	1.72E+00
Pla2g7	1.06E+02	3.05E−02	2.90E−01	1.58E+00
AC154176.1	1.50E+02	3.09E−02	2.90E−01	1.62E+00
Top2a	3.70E+02	2.35E−02	2.67E−01	1.96E+00
H2afx	1.38E+02	1.79E−03	1.30E−01	1.90E+00
Gtse1	4.83E+01	1.03E−03	1.14E−01	2.30E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Gm12933	9.99E+00	2.85E−02	2.84E−01	2.18E+00
Enah	3.35E+02	1.80E−02	2.50E−01	1.51E+00
Sbno2	6.21E+02	1.80E−02	2.50E−01	1.53E+00
Tmem266	1.99E+01	7.37E−03	1.85E−01	2.19E+00
Sprr2e	1.87E+01	4.12E−02	3.20E−01	7.70E+00
Slpi	6.30E+01	1.39E−02	2.28E−01	5.25E+00
Aldh1a3	2.09E+01	8.71E−03	1.99E−01	2.52E+00
Kcnh1	1.81E+02	2.89E−02	2.84E−01	2.08E+00
Cxcr2	5.99E+01	2.04E−02	2.58E−01	3.05E+00
Rpl32-ps	2.85E+01	4.88E−02	3.36E−01	1.52E+00
Prnd	1.11E+01	3.30E−02	2.97E−01	1.80E+00
Cdh3	3.06E+02	4.83E−02	3.35E−01	1.65E+00
Gpx2	7.00E+01	1.62E−02	2.40E−01	2.34E+00
Grwd1	1.86E+02	1.62E−02	2.40E−01	1.56E+00
Cenpw	3.70E+01	1.98E−02	2.56E−01	1.72E+00
Nop56	3.64E+02	7.01E−03	1.84E−01	1.65E+00
Trp53i11	4.41E+02	3.23E−02	2.95E−01	1.57E+00
Tctn3	4.25E+01	1.81E−02	2.50E−01	1.54E+00
Gls2	1.11E+01	4.39E−02	3.26E−01	1.70E+00
Gpcpd1	5.26E+02	5.81E−03	1.77E−01	1.58E+00
Gpatch4	2.11E+02	1.83E−02	2.51E−01	1.61E+00
Shank1	1.21E+01	3.30E−02	2.97E−01	1.65E+00
Atp1a1	3.80E+03	3.26E−04	9.70E−02	1.95E+00
Dctd	5.11E+01	1.33E−02	2.25E−01	1.58E+00
Ly6k	2.85E+01	6.90E−04	1.05E−01	3.05E+00
Rrp12	1.71E+02	1.86E−02	2.52E−01	1.54E+00
Gch1	3.89E+01	2.92E−02	2.84E−01	1.58E+00
Il13ra2	2.07E+01	2.45E−02	2.69E−01	2.24E+00
Ccnf	7.57E+01	1.80E−02	2.50E−01	1.56E+00
Rp17a-ps10	1.33E+01	3.03E−02	2.88E−01	1.68E+00
Plbd1	9.06E+02	1.25E−02	2.20E−01	1.57E+00
Lrrc4	2.92E+01	2.30E−02	2.66E−01	3.11E+00
Tdg-ps	7.95E+01	4.43E−03	1.64E−01	1.57E+00
Gm8666	4.81E+01	4.42E−02	3.28E−01	1.52E+00
Gpr35	3.53E+01	4.74E−02	3.34E−01	1.67E+00
Itpk1	1.47E+02	3.03E−02	2.88E−01	1.54E+00
Nolc1	3.74E+02	6.02E−03	1.80E−01	1.52E+00
Incenp	1.22E+02	3.98E−02	3.16E−01	1.63E+00
Oplah	5.00E+02	1.14E−02	2.17E−01	1.50E+00
Nt5dc2	3.10E+02	6.29E−03	1.82E−01	1.65E+00
Tubb3	3.04E+01	2.63E−03	1.46E−01	2.40E+00
Txn-ps1	1.37E+01	4.48E−02	3.28E−01	1.82E+00
AI506816	2.81E+01	5.48E−03	1.72E−01	2.05E+00
Gm15452	1.42E+01	4.10E−02	3.19E−01	1.67E+00
Depdc1b	1.71E+01	3.68E−02	3.10E−01	1.87E+00
Epb4113	1.75E+02	1.49E−03	1.29E−01	1.52E+00
Btbd19	9.47E+01	1.24E−02	2.20E−01	1.51E+00
Igsf3	1.77E+02	2.30E−03	1.40E−01	1.71E+00
Dusp9	1.28E+01	2.46E−02	2.69E−01	2.04E+00
Cd44	7.00E+02	3.82E−04	9.70E−02	1.76E+00
Gm45902	3.26E+01	2.80E−02	2.83E−01	1.74E+00
Wfdc12	1.09E+02	1.08E−02	2.13E−01	4.99E+00
Tdh	8.38E+01	1.64E−02	2.41E−01	3.18E+00
Rps13-ps2	5.42E+01	2.04E−02	2.58E−01	1.83E+00
Poc1a	4.29E+01	1.47E−02	2.33E−01	1.68E+00
Gja1	9.24E+02	3.97E−02	3.16E−01	1.62E+00
9330102E08Rik	2.34E+01	1.14E−02	2.17E−01	1.74E+00
2700038G22Rik	1.48E+01	2.27E−02	2.66E−01	1.89E+00
Rpl27	1.05E+02	3.76E−03	1.57E−01	1.70E+00
Cdca8	1.05E+02	4.48E−02	3.28E−01	1.64E+00
Stx11	3.97E+01	2.07E−02	2.60E−01	1.60E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Fam167a	5.88E+01	6.34E−03	1.82E−01	3.53E+00
Pinx1	6.70E+01	1.88E−02	2.53E−01	1.54E+00
Cks2	5.38E+01	2.41E−02	2.67E−01	1.56E+00
Gm10182	1.40E+02	4.39E−02	3.26E−01	1.57E+00

Gene ID	Fold change (Naive-control*Bites vs. Naive-control*No bites)	LSMean (Naive-control*Bites) (Naive-control*Bites vs. Naive-control*No bites)	LSMean (Naive-control*No bites) (Naive-control*Bites vs. Naive-control*No bites)
Serpine1	5.59E+00	1.56E+01	2.80E+00
Chil3	2.01E+02	2.03E+01	1.01E−01
Ly6c1	2.03E+00	6.95E+01	3.42E+01
Cc19	8.69E+00	3.82E+01	4.39E+00
Il1b	2.41E+01	1.01E+01	4.18E−01
Msr1	1.15E+01	1.45E+01	1.26E+00
Ccl2	3.01E+01	2.64E+01	8.78E−01
Ly6a	2.49E+00	2.32E+02	9.31E+01
Ifitm3	3.15E+00	1.93E+02	6.13E+01
Hsd11b1	1.77E+00	1.35E+01	7.66E+00
Cd53	3.29E+00	2.63E+01	7.98E+00
Ccl7	2.07E+01	3.17E+01	1.53E+00
Ccl8	3.02E+00	5.51E+01	1.82E+01
Hp	2.92E+00	9.19E+01	3.15E+01
Lilrb4a	7.41E+00	1.75E+01	2.37E+00
Ms4a6d	6.10E+00	1.98E+01	3.25E+00
Ccl6	1.67E+00	4.04E+01	2.41E+01
Adm	3.22E+00	9.74E+00	3.03E+00
Lyve1	4.01E+00	3.01E+01	7.50E+00
Slfn2	4.01E+00	1.37E+01	3.41E+00
Wfdc17	4.79E+00	1.90E+01	3.96E+00
Akr1b8	2.32E+00	1.67E+01	7.23E+00
Lrg1	2.23E+00	1.24E+01	5.55E+00
Icam1	2.78E+00	2.64E+01	9.52E+00
Cxcl14	2.10E+00	4.97E+01	2.37E+01
Ifitm2	1.87E+00	2.97E+02	1.58E+02
Ctsb	1.58E+00	4.42E+02	2.79E+02
Upp1	4.35E+00	2.60E+00	5.98E−01
Bst1	3.15E+00	5.58E+00	1.77E+00
Timp1	1.32E+01	3.57E+01	2.70E+00
Ccnd3	1.77E+00	6.52E+01	3.68E+01
Csf1	2.09E+00	4.33E+01	2.07E+01
Li1r4b	5.52E+00	1.34E+01	2.43E+00
Ifi204	2.96E+00	1.85E+00	6.25E−01
Ctla2a	3.49E+00	2.27E+01	6.51E+00
Capn2	1.72E+00	6.65E+01	3.87E+01
Tmsb10	2.56E+00	6.42E+01	2.51E+01
C5ar1	5.38E+00	2.54E+00	4.72E−01
Serpina3m	6.61E+00	6.98E+00	1.06E+00
Ccr5	1.09E+01	4.69E+00	4.30E−01
Gsta4	4.54E+00	1.28E+01	2.82E+00
Ddr2	2.70E+00	7.94E+01	2.94E+01
Ifi207	2.14E+00	2.99E+00	1.40E+00
Cfb	2.05E+00	1.64E+01	8.00E+00
AC160962.1	4.65E+00	3.39E+00	7.28E−01
Gm6560	1.92E+00	1.05E+02	5.48E+01
Fcgr2b	2.79E+00	2.66E+01	9.51E+00
Ccrl	7.47E+00	1.10E+01	1.47E+00
AB124611	4.62E+00	2.61E+00	5.66E−01
Spp1	6.08E+00	2.74E+01	4.52E+00
Hspa5	1.79E+00	4.19E+02	2.34E+02
Trim46	1.92E+00	1.03E+00	5.37E−01
Clec7a	8.27E+00	6.73E+00	8.13E−01
Dok2	3.96E+00	9.02E+00	2.28E+00
Srgn	4.53E+00	2.15E+01	4.76E+00
Sprr1b	2.37E+01	3.02E+01	1.27E+00
Calr	2.12E+00	5.11E+02	2.41E+02
Clec5a	3.67E+00	2.96E+00	8.07E−01
Ms4a4a	5.15E+00	6.36E+00	1.24E+00
Pxdc1	1.51E+00	1.27E+01	8.39E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Pdpn	2.62E+00	1.13E+01	4.30E+00
Serpina3n	6.74E+00	4.71E+02	6.98E+01
Ptafr	2.74E+00	3.49E+00	1.27E+00
Mrc1	3.22E+00	5.31E+01	1.65E+01
Tmem8	4.00E+00	7.84E+00	1.96E+00
Plaur	5.19E+00	9.07E+00	1.75E+00
Gm15922	4.81E+00	4.46E+00	9.28E−01
Cd163	2.30E+00	2.34E+01	1.01E+01
Samhd1	2.42E+00	5.01E+01	2.07E+01
Lcp2	2.68E+00	3.08E+00	1.15E+00
Ifnar2	1.67E+00	1.84E+01	1.10E+01
Mfsd10	1.64E+00	3.05E+01	1.87E+01
Ccr2	6.36E+00	2.89E+01	4.55E+00
Tnfaip2	1.56E+00	1.32E+01	8.48E+00
Cd68	2.29E+00	2.15E+01	9.41E+00
Lbp	2.45E+00	4.15E+01	1.70E+01
Lrrc25	3.85E+00	5.87E+00	1.52E+00
Anxa3	2.61E+00	5.16E+00	1.97E+00
Hdc	3.52E+00	7.59E+00	2.16E+00
Lyz2	2.37E+00	1.75E+02	7.42E+01
Cebpd	1.96E+00	1.87E+01	9.54E+00
C1ec4d	2.17E+01	7.92E+00	3.65E−01
Tnfrsf1b	3.77E+00	1.21E+01	3.21E+00
Manf	1.86E+00	8.35E+01	4.49E+01
Hk3	5.51E+00	2.57E+00	4.66E−01
Cyp7b1	3.99E+00	8.66E+00	2.17E+00
Parm1	1.96E+00	5.05E+00	2.58E+00
Msn	1.90E+00	1.31E+02	6.90E+01
Plek	3.14E+00	2.08E+01	6.63E+00
Tlr13	4.59E+00	7.40E+00	1.61E+00
Sema3a	2.07E+00	8.41E+00	4.07E+00
Slc27a3	3.11E+00	7.11E+01	2.29E+01
Csf3r	1.39E+01	8.48E+00	6.08E−01
Nek6	1.54E+00	1.59E+01	1.03E+01
Tubb6	2.76E+00	3.15E+01	1.14E+01
Capns1	1.65E+00	1.68E+02	1.02E+02
Lyn	2.74E+00	1.26E+01	4.60E+00
Krt16	4.32E+01	3.07E+02	7.09E+00
Apbb1ip	2.50E+00	1.03E+01	4.13E+00
Sirpb1c	1.59E+01	9.34E+00	5.86E−01
Gm27029	2.33E+00	1.85E+00	7.93E−01
Fcer1g	3.38E+00	2.86E+01	8.45E+00
Ptx3	5.03E+00	4.54E+00	9.03E−01
Cd14	3.77E+00	1.30E+01	3.44E+00
Cd7	2.41E+00	1.94E+00	8.05E−01
Mpeg1	2.62E+00	2.64E+01	1.01E+01
Cpne2	1.92E+00	2.54E+01	1.32E+01
Pdia4	1.69E+00	6.09E+01	3.60E+01
Creld2	1.86E+00	3.65E+01	1.97E+01
Atrip	1.65E+00	1.83E+00	1.11E+00
C3ar1	3.00E+00	8.24E+00	2.75E+00
Svep1	2.98E+00	3.87E+01	1.30E+01
Gm3788	3.38E+00	2.10E+00	6.20E−01
Rnasel	1.70E+00	9.91E+00	5.82E+00
Thbs1	1.59E+00	2.04E+02	1.28E+02
C1qb	2.05E+00	4.70E+01	2.29E+01
Ftl1	1.63E+00	3.83E+02	2.35E+02
Ptprc	1.89E+00	1.59E+01	8.43E+00
Angptl4	2.15E+00	1.07E+01	5.01E+00
Relt	3.00E+00	4.45E+00	1.48E+00
Pdia6	1.73E+00	1.44E+02	8.35E+01
Serpina3e-ps	4.57E+00	3.06E+00	6.68E−01
Clec4n	4.75E+00	1.13E+01	2.37E+00
Wisp2	3.16E+00	3.67E+01	1.16E+01
Fgr	3.83E+00	5.17E+00	1.35E+00
Layn	2.54E+00	2.00E+00	7.87E−01
Pcdhb22	2.10E+00	5.66E+00	2.70E+00
Adam8	2.74E+00	3.00E+01	1.09E+01
Lgmn	2.26E+00	1.46E+02	6.44E+01
March1	1.53E+00	2.99E+00	1.95E+00
Clec4a2	5.46E+00	1.22E+01	2.23E+00
Dab2	2.56E+00	7.26E+01	2.83E+01
Lcp1	2.15E+00	4.34E+01	2.02E+01
Cd300lb	4.52E+00	3.01E+00	6.67E−01

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Slco2a1	1.54E+00	7.37E+01	4.78E+01
Slc11a1	3.01E+00	2.36E+00	7.86E−01
Ceacam1	2.64E+00	3.62E+00	1.37E+00
Emilin2	3.08E+00	2.39E+01	7.76E+00
Dnajb11	1.56E+00	7.40E+01	4.75E+01
Rnf141	1.52E+00	5.76E+01	3.80E+01
Nlrp3	4.64E+00	2.18E+00	4.70E−01
Itgb2	3.05E+00	1.58E+01	5.18E+00
Mceemp1	5.17E+00	2.41E+00	4.66E−01
Tmem150a	1.73E+00	6.77E+00	3.92E+00
Cyba	2.16E+00	2.35E+01	1.09E+01
Itgal	2.65E+00	2.65E+00	1.00E+00
Gm9844	2.40E+00	1.58E+01	6.59E+00
Slc15a3	1.84E+00	8.85E+00	4.80E+00
Pfn1	1.63E+00	2.80E+02	1.72E+02
Fam49b	1.86E+00	2.77E+01	1.49E+01
Ssbp4	1.50E+00	2.09E+01	1.39E+01
Cyth4	3.25E+00	1.31E+01	4.03E+00
Gda	2.17E+00	4.60E+01	2.12E+01
Syk	1.88E+00	1.32E+01	7.00E+00
Samsn1	3.22E+00	2.15E+00	6.68E−01
Nqo1	2.30E+00	2.66E+01	1.16E+01
Pik3r5	2.30E+00	4.93E+00	2.14E+00
Tpsab1	2.82E+00	3.19E+01	1.13E+01
Hsp90b1	1.56E+00	2.94E+02	1.89E+02
Mgp	2.61E+00	1.57E+02	6.01E+01
F630028O10Rik	5.60E+00	3.34E+00	5.97E−01
AI662270	2.76E+00	3.93E+00	1.42E+00
Cd200r1	3.25E+00	2.68E+00	8.25E−01
Pf4	3.06E+00	2.90E+01	9.49E+00
Fth1	1.60E+00	8.98E+02	5.60E+02
Smim3	1.68E+00	9.30E+00	5.53E+00
Sash3	2.86E+00	3.44E+00	1.20E+00
Cd48	1.93E+00	5.05E+00	2.62E+00
Mcoln2	2.57E+00	4.01E+00	1.56E+00
Adgrg3	2.84E+00	2.36E+00	8.32E−01
Coro1a	2.72E+00	4.10E+01	1.51E+01
Pkm	1.79E+00	6.66E+02	3.71E+02
Pgk1-rs7	1.58E+00	7.17E+01	4.53E+01
Tyrobp	2.62E+00	3.24E+01	1.24E+01
Gm5537	1.59E+00	8.07E+01	5.07E+01
Slc7a8	2.89E+00	7.92E+00	2.74E+00
Armc6	1.54E+00	8.89E+00	5.77E+00
Fam69a	1.66E+00	3.03E+01	1.83E+01
Gcnt1	2.81E+00	6.91E+00	2.45E+00
Ccl22	3.27E+00	2.99E+00	9.14E−01
Sprr2a2	2.83E+01	4.92E+02	1.74E+01
Pirb	2.92E+00	1.24E+01	4.25E+00
Myo1g	2.24E+00	8.08E+00	3.61E+00
Ddah1	4.12E+00	3.60E+00	8.74E−01
Ms4a6c	3.36E+00	8.35E+00	2.49E+00
Neto2	2.24E+00	1.93E+00	8.63E−01
Il1rl1	3.21E+00	2.81E+00	8.75E−01
Ptprj	1.51E+00	1.79E+01	1.19E+01
Sdf2l1	1.89E+00	1.35E+01	7.16E+00
Sprr2a3	3.08E+01	2.89E+01	9.40E−01
Pira2	5.17E+00	3.76E+00	7.26E−01
Serpinb1a	1.77E+00	5.57E+01	3.15E+01
Gm9025	2.17E+00	4.03E+00	1.85E+00
Flot2	1.82E+00	4.82E+01	2.65E+01
Il2rg	3.01E+00	3.64E+00	1.21E+00
Nfkbie	1.74E+00	4.85E+00	2.79E+00
Thy1	2.42E+00	1.41E+02	5.83E+01
Tmprss11g	2.67E+00	8.58E+00	3.21E+00
Clec4a1	2.57E+00	8.87E+00	3.46E+00
Zyx	1.52E+00	6.58E+01	4.32E+01
Ecscr	2.39E+00	1.03E+01	4.30E+00
Pdia3	1.56E+00	3.57E+02	2.28E+02
2610528A11Rik	1.95E+02	1.39E+02	7.12E−01
Tlr2	1.56E+00	6.58E+00	4.23E+00
Impdh2	1.70E+00	4.59E+01	2.70E+01
Krt6b	2.84E+01	3.27E+02	1.15E+01
Fscn1	3.12E+00	1.84E+01	5.90E+00
Tmem173	2.91E+00	9.67E+00	3.33E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Cdhr1	4.82E+01	2.33E+01	4.84E−01
Ifitm1	3.26E+00	1.36E+01	4.17E+00
Cytip	1.72E+00	8.14E+00	4.73E+00
Psmb10	1.57E+00	2.14E+01	1.37E+01
Marcks	1.52E+00	5.74E+01	3.77E+01
Pcbp3	2.23E+00	4.12E+00	1.85E+00
Cfl1	1.70E+00	3.31E+02	1.94E+02
Hck	3.18E+00	3.04E+00	9.57E−01
Tnfrsf13b	2.71E+00	2.70E+00	9.96E−01
Traf1	2.54E+00	1.96E+00	7.73E−01
Ap1m1	1.53E+00	5.52E+01	3.61E+01
Jaml	1.63E+00	2.86E+00	1.76E+00
Vav1	2.43E+00	4.93E+00	2.03E+00
Csf2rb	2.27E+00	1.80E+01	7.93E+00
Impdh1	1.62E+00	2.50E+01	1.54E+01
Irf8	2.17E+00	5.10E+00	2.36E+00
Slc7a11	2.47E+00	1.52E+01	6.15E+00
Igsf6	3.35E+00	3.56E+00	1.06E+00
Cd300a	2.81E+00	4.31E+00	1.53E+00
Dynlt1b	1.62E+00	3.86E+01	2.39E+01
Laptm5	1.96E+00	4.40E+01	2.24E+01
Ccl12	9.89E+00	6.08E+00	6.15E−01
Ldha	1.51E+00	4.92E+02	3.27E+02
Tagln2	1.60E+00	1.74E+02	1.09E+02
Irak4	1.54E+00	9.84E+00	6.38E+00
Fyb	2.20E+00	5.19E+00	2.36E+00
Cxcl1	1.31E+01	9.04E+00	6.89E−01
Nme1	1.85E+00	8.14E+01	4.39E+01
Ripor2	2.27E+00	2.92E+00	1.29E+00
Ncf4	2.05E+00	6.86E+00	3.35E+00
Impdh2-ps	1.71E+00	1.27E+02	7.42E+01
Alg8	1.92E+00	4.05E+00	2.11E+00
Mthfd2	1.90E+00	6.00E+00	3.15E+00
Flvcrl	1.54E+00	1.29E+01	8.39E+00
Ncf2	1.93E+00	4.90E+00	2.54E+00
Dusp6	1.78E+00	2.62E+01	1.48E+01
Flna	1.68E+00	1.99E+02	1.18E+02
Etv4	1.78E+00	5.37E+00	3.02E+00
Rab31	2.07E+00	4.88E+01	2.36E+01
Bak1	1.58E+00	2.02E+01	1.27E+01
Lgals9	2.58E+00	9.86E+01	3.82E+01
Gm3839	2.53E+00	1.70E+00	6.69E−01
Prss12	1.90E+00	2.25E+01	1.18E+01
Hyou1	1.57E+00	6.65E+01	4.25E+01
1810055G02Rik	1.51E+00	1.85E+01	1.23E+01
Gm5837	1.51E+00	1.73E+01	1.15E+01
Ripk3	3.15E+00	9.30E+00	2.95E+00
Mmp9	1.64E+00	9.20E+00	5.62E+00
Ran	1.64E+00	1.71E+02	1.04E+02
Gsdmc	4.77E+00	2.90E+01	6.08E+00
Me2	2.03E+00	1.10E+01	5.40E+00
Ccl24	5.13E+00	3.24E+00	6.31E−01
Lrrc59	1.61E+00	9.52E+01	5.92E+01
Gmfg	1.77E+00	3.57E+00	2.02E+00
Ddx39	1.72E+00	5.81E+01	3.37E+01
Tubb5	2.01E+00	4.95E+02	2.46E+02
Gmfg-ps	1.71E+00	5.06E+00	2.96E+00
Dhfr	1.56E+00	1.95E+01	1.25E+01
Gm4737	1.68E+00	8.02E+01	4.77E+01
Gm11451	2.16E+00	3.35E+00	1.55E+00
Csf2ra	1.74E+00	7.54E+00	4.34E+00
Cdkn2d	1.56E+00	1.92E+01	1.23E+01
Lrp8	2.56E+00	8.36E+00	3.26E+00
Evi2b	2.70E+00	4.61E+00	1.71E+00
Pgk1	1.69E+00	7.93E+01	4.70E+01
Spi1	2.16E+00	1.47E+01	6.78E+00
Sorcs2	2.15E+00	6.15E+00	2.86E+00
Crispld2	2.16E+00	1.94E+02	8.97E+01
AC154572.2	1.55E+00	7.70E+00	4.98E+00
Ier5l	2.09E+00	5.47E+00	2.62E+00
Ruvbl2	1.63E+00	2.72E+01	1.67E+01
Parp12	1.54E+00	1.32E+01	8.63E+00
AC123061.1	1.67E+00	5.30E+00	3.17E+00
Osmr	1.83E+00	3.47E+01	1.90E+01

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Dtymk	1.75E+00	2.24E+01	1.27E+01
Gm6180	1.74E+00	1.58E+01	9.09E+00
Gm5851	2.58E+00	1.81E+00	6.99E−01
Gm2564	3.89E+00	4.66E+00	1.20E+00
Apol8	2.46E+00	5.24E+00	2.13E+00
Lcn2	8.26E+00	8.19E+01	9.91E+00
Hnrnpa3	1.50E+00	1.45E+02	9.67E+01
Eno1	2.04E+00	9.34E+01	4.59E+01
Csf2rb2	1.76E+00	1.07E+01	6.05E+00
Bcl3	5.59E+00	1.37E+01	2.46E+00
Ngf	3.69E+00	3.70E+00	1.00E+00
Hpgd	1.53E+00	3.26E+01	2.13E+01
Cks1b	1.62E+00	2.40E+01	1.48E+01
Lsm4	1.55E+00	3.05E+01	1.97E+01
H13	1.50E+00	9.97E+01	6.63E+01
Fam162a	1.81E+00	2.80E+01	1.55E+01
Eno1b	1.88E+00	3.12E+02	1.66E+02
Txn1	1.55E+00	1.38E+02	8.91E+01
Marcksl1	1.92E+00	2.71E+01	1.42E+01
Vcan	2.86E+00	2.83E+01	9.88E+00
Hmox1	1.91E+00	1.71E+02	8.95E+01
Il4ra	1.95E+00	5.34E+01	2.74E+01
Crlf2	1.92E+00	5.52E+00	2.87E+00
Gm15725	2.00E+00	5.95E+00	2.98E+00
Enkd1	1.80E+00	4.37E+00	2.43E+00
Snrpa	1.51E+00	4.47E+01	2.95E+01
Gins1	1.88E+00	6.83E+00	3.62E+00
Ifi35	1.53E+00	2.93E+01	1.92E+01
Gm15590	1.99E+00	2.19E+00	1.10E+00
Gjb1	1.96E+00	1.56E+00	7.98E−01
Ranbp1	1.57E+00	5.49E+01	3.49E+01
Brca2	2.56E+00	1.93E+01	7.55E+00
Slc39a14	1.95E+00	1.76E+01	9.01E+00
Arf2	1.57E+00	5.40E+01	3.44E+01
Gpr132	1.77E+00	1.59E+00	8.96E−01
Cad	1.67E+00	3.92E+01	2.35E+01
Serpinc1	1.98E+00	2.28E+00	1.15E+00
Tslp	1.62E+00	2.73E+00	1.69E+00
Snrpf	1.57E+00	1.87E+01	1.20E+01
Hsp90aa1	1.51E+00	1.27E+02	8.46E+01
Gm6992	2.58E+00	2.61E+00	1.01E+00
1110038B12Rik	1.50E+00	1.06E+01	7.05E+00
Gm12758	2.14E+00	3.60E+00	1.68E+00
Gm11847	1.77E+00	8.10E+00	4.56E+00
Dusp2	2.25E+00	2.13E+00	9.45E−01
Cenps	1.64E+00	1.10E+01	6.71E+00
Gm17383	2.60E+00	6.52E+00	2.51E+00
2610203C20Rik	1.57E+00	1.72E+01	1.09E+01
Alg3	1.62E+00	9.64E+00	5.96E+00
Gm5844	1.57E+00	1.66E+01	1.06E+01
Cenpt	1.71E+00	1.23E+01	7.15E+00
Pglyrp1	2.60E+00	2.66E+00	1.02E+00
Pold2	1.57E+00	3.72E+01	2.38E+01
Slc16a14	1.50E+00	2.41E+01	1.61E+01
Nup43	1.70E+00	1.47E+01	8.66E+00
Acy1	1.57E+00	9.59E+00	6.09E+00
Fhl2	1.98E+00	4.08E+00	2.06E+00
Mcm3	1.79E+00	4.47E+01	2.50E+01
Gm20390	1.83E+00	5.62E+01	3.07E+01
Pfkl	1.54E+00	3.22E+01	2.09E+01
Gm26809	2.14E+00	1.72E+01	8.06E+00
Mmp3	4.04E+00	6.56E+01	1.62E+01
Ints7	1.53E+00	1.59E+01	1.04E+01
Orc1	2.08E+00	5.60E+00	2.69E+00
Slc19a1	1.53E+00	1.46E+01	9.57E+00
Rbm14	1.58E+00	3.26E+01	2.07E+01
Gemin6	1.52E+00	8.96E+00	5.88E+00
Aldh18a1	1.62E+00	2.02E+01	1.25E+01
Dhrs13	2.39E+00	5.01E+00	2.10E+00
Mcm4	1.51E+00	5.11E+01	3.39E+01
Lsm2	1.66E+00	1.49E+01	9.00E+00
Pop1	1.79E+00	8.74E+00	4.88E+00
Chil1	2.93E+00	4.85E+02	1.66E+02
Nup93	1.56E+00	3.72E+01	2.39E+01

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Slc29a2	2.38E+00	8.24E+00	3.47E+00
Vstm2a	1.99E+00	1.57E+00	7.86E−01
Cdt1	1.61E+00	1.93E+01	1.20E+01
Rad51	1.90E+00	1.24E+01	6.55E+00
Mcm6	1.84E+00	6.43E+01	3.49E+01
Ercc6l	1.87E+00	7.10E+00	3.80E+00
Ccne1	2.01E+00	5.56E+00	2.77E+00
Casp6	1.51E+00	1.30E+01	8.58E+00
Abcg2	1.66E+00	3.83E+01	2.30E+01
Gm5855	2.34E+00	2.21E+00	9.44E−01
Gm6977	1.69E+00	8.99E+00	5.33E+00
Tbl3	1.58E+00	3.58E+01	2.27E+01
BC100530	1.93E+01	2.68E+01	1.39E+00
Rpp40	1.55E+00	6.65E+00	4.28E+00
Lyar	1.53E+00	2.59E+01	1.70E+01
Clec2l	3.76E+00	5.58E+00	1.48E+00
Sprr2h	7.43E+00	1.22E+01	1.64E+00
Ppia	1.50E+00	6.35E+02	4.22E+02
Ndc1	1.54E+00	2.12E+01	1.38E+01
Bfsp1	1.90E+00	2.57E+00	1.36E+00
Skap2	1.50E+00	7.17E+01	4.78E+01
Smyd5	1.60E+00	1.92E+01	1.20E+01
Car12	2.26E+00	6.44E+01	2.85E+01
Casp3	1.52E+00	2.10E+01	1.39E+01
Fbxo10	1.60E+00	1.40E+01	8.71E+00
Lsm5	1.61E+00	5.77E+00	3.58E+00
Gstcd	1.64E+00	9.84E+00	6.00E+00
Stom	1.66E+00	9.74E+01	5.88E+01
Gm8203	1.59E+00	5.21E+01	3.28E+01
Gm13461	1.64E+00	4.69E+01	2.87E+01
Pgm3	1.51E+00	1.03E+01	6.78E+00
Erh	1.54E+00	4.10E+01	2.65E+01
Fam171a2	2.36E+00	2.41E+01	1.02E+01
Xdh	1.55E+00	6.32E+01	4.08E+01
Nfyb	1.61E+00	4.35E+01	2.71E+01
Hbegf	1.78E+00	1.10E+01	6.19E+00
Myof	1.57E+00	7.10E+01	4.53E+01
Prss27	2.14E+00	1.01E+01	4.73E+00
Slc14a1	3.46E+00	4.84E+00	1.40E+00
Entpd7	1.74E+00	6.59E+00	3.79E+00
Gm7899	2.05E+00	3.22E+00	1.57E+00
Gm12988	1.84E+00	2.26E+00	1.23E+00
Tpcn2	1.61E+00	1.55E+01	9.64E+00
Srm	1.60E+00	5.26E+01	3.30E+01
Has3	4.85E+00	5.99E+00	1.23E+00
Wdhd1	1.76E+00	1.15E+01	6.56E+00
Gm13092	1.59E+00	1.99E+01	1.25E+01
Socs3	1.98E+00	6.09E+01	3.08E+01
Anapc15-ps	1.73E+00	1.48E+00	8.54E−01
Fosl1	1.72E+00	2.62E+00	1.52E+00
Nfkbid	1.64E+00	1.84E+00	1.12E+00
Pim2	1.60E+00	5.79E+00	3.63E+00
Ada	1.76E+00	7.47E+00	4.25E+00
Gm5791	2.18E+00	3.62E+00	1.66E+00
Gm11675	1.55E+00	1.03E+01	6.67E+00
Sema4c	1.52E+00	3.19E+01	2.10E+01
Tes	1.54E+00	1.70E+01	1.10E+01
Lrp11	1.54E+00	3.74E+00	2.44E+00
Tyms	1.53E+00	3.44E+01	2.25E+01
Mtcl1	2.78E+00	9.61E+00	3.45E+00
Rfng	1.53E+00	4.98E+01	3.26E+01
Snhg4	1.61E+00	2.49E+01	1.54E+01
Ndnf	3.12E+00	2.30E+01	7.37E+00
Gm3379	1.93E+00	6.41E+00	3.32E+00
Trip13	1.86E+00	7.69E+00	4.13E+00
Sprr2g	6.51E+00	4.66E+00	7.15E−01
Gpr176	2.59E+00	2.19E+00	8.47E−01
Panx1	1.64E+00	2.94E+01	1.79E+01
Stat3	1.64E+00	2.28E+02	1.39E+02
Gemin4	2.10E+00	7.39E+00	3.52E+00
Slc9a1	1.58E+00	1.20E+02	7.58E+01
Gm6210	1.87E+00	8.75E+00	4.67E+00
Eef1akmt4	1.51E+00	8.52E+00	5.63E+00
Gm5620	1.67E+00	2.78E+00	1.66E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Dnph1	1.52E+00	2.48E+01	1.64E+01
Gm12666	1.63E+00	1.96E+00	1.20E+00
S100a9	1.76E+01	1.19E+02	6.74E+00
Mrto4	1.54E+00	2.72E+01	1.76E+01
Stfa3	5.45E+00	5.02E+00	9.20E−01
Nkain1	2.87E+00	2.51E+00	8.77E−01
Psmg4	1.50E+00	1.16E+01	7.70E+00
S100a8	1.22E+01	6.75E+01	5.51E+00
Ampd3	1.70E+00	2.89E+01	1.70E+01
Duxbl2	1.75E+00	2.82E+00	1.61E+00
Rab15	1.62E+00	6.56E+01	4.04E+01
Gm27219	1.71E+00	6.41E+00	3.74E+00
Hmgb1-ps3	1.96E+00	2.20E+00	1.12E+00
Noc4l	1.78E+00	3.35E+01	1.88E+01
Gm12722	1.63E+00	1.81E+00	1.11E+00
Dsg1c	2.04E+00	1.31E+01	6.39E+00
1700052K11Rik	1.55E+00	1.03E+01	6.69E+00
Krt6a	3.99E+00	3.43E+02	8.58E+01
Hirip3	1.64E+00	1.82E+01	1.11E+01
Pgam1	1.63E+00	1.70E+02	1.04E+02
B4galnt4	1.83E+00	1.81E+00	9.87E−01
Rpl10-ps5	1.68E+00	1.54E+01	9.15E+00
Hrh2	2.72E+00	2.19E+00	8.06E−01
AC131178.1	1.99E+00	4.69E+00	2.35E+00
Gadl1	1.71E+00	1.33E+02	7.81E+01
BC055324	1.56E+00	5.06E+00	3.25E+00
Gm6063	1.93E+00	2.60E+00	1.34E+00
Trex1	1.54E+00	2.68E+01	1.73E+01
Galnt6	2.60E+00	2.01E+01	7.71E+00
Gm3448	1.89E+00	7.58E+00	4.01E+00
Nat8l	1.66E+00	1.07E+02	6.49E+01
AC022775.2	1.59E+00	3.33E+00	2.09E+00
Gm6793	1.97E+00	4.34E+00	2.21E+00
Mgat5b	3.43E+00	4.53E+00	1.32E+00
Rpl29	1.51E+00	6.90E+00	4.56E+00
Gm11805	1.72E+00	1.63E+00	9.46E−01
Pla2g7	1.58E+00	1.72E+01	1.09E+01
AC154176.1	1.62E+00	2.60E+01	1.60E+01
Top2a	1.96E+00	7.01E+01	3.58E+01
H2afx	1.90E+00	2.64E+01	1.39E+01
Gtse1	2.30E+00	1.01E+01	4.37E+00
Gm12933	2.18E+00	1.96E+00	8.98E−01
Enah	1.51E+00	5.55E+01	3.68E+01
Sbno2	1.53E+00	9.96E+01	6.50E+01
Tmem266	2.19E+00	4.45E+00	2.03E+00
Sprr2e	7.70E+00	6.61E+00	8.59E−01
Slpi	5.25E+00	1.97E+01	3.75E+00
Aldh1a3	2.52E+00	4.26E+00	1.69E+00
Kcnh1	2.08E+00	4.04E+01	1.94E+01
Cxcr2	3.05E+00	1.48E+01	4.83E+00
Rpl32-ps	1.52E+00	5.03E+00	3.31E+00
Prnd	1.80E+00	1.97E+00	1.09E+00
Cdh3	1.65E+00	5.78E+01	3.50E+01
Gpx2	2.34E+00	1.73E+01	7.39E+00
Grwd1	1.56E+00	3.09E+01	1.98E+01
Cenpw	1.72E+00	6.62E+00	3.86E+00
Nop56	1.65E+00	6.31E+01	3.82E+01
Trp53i11	1.57E+00	7.86E+01	5.00E+01
Tctn3	1.54E+00	6.83E+00	4.45E+00
Gls2	1.70E+00	1.86E+00	1.10E+00
Gpcpd1	1.58E+00	8.83E+01	5.58E+01
Gpatch4	1.61E+00	3.57E+01	2.22E+01
Shank1	1.65E+00	2.02E+00	1.22E+00
Atp1a1	1.95E+00	7.45E+02	3.81E+02
Dctd	1.58E+00	8.57E+00	5.44E+00
Ly6k	3.05E+00	7.01E+00	2.30E+00
Rrp12	1.54E+00	2.91E+01	1.88E+01
Gch1	1.58E+00	6.69E+00	4.25E+00
Il13ra2	2.24E+00	4.34E+00	1.93E+00
Ccnf	1.56E+00	1.28E+01	8.21E+00
Rpl7a-ps10	1.68E+00	2.46E+00	1.46E+00
Plbd1	1.57E+00	1.60E+02	1.02E+02
Lrrc4	3.11E+00	8.15E+00	2.62E+00
Tdg-ps	1.57E+00	1.39E+01	8.82E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Gm8666	1.52E+00	7.81E+00	5.14E+00
Gpr35	1.67E+00	6.13E+00	3.67E+00
Itpk1	1.54E+00	2.41E+01	1.56E+01
Nolc1	1.52E+00	6.28E+01	4.12E+01
Incenp	1.63E+00	2.14E+01	1.31E+01
Oplah	1.50E+00	8.39E+01	5.58E+01
Nt5dc2	1.65E+00	5.77E+01	3.49E+01
Tubb3	2.40E+00	6.40E+00	2.67E+00
Txn-ps1	1.82E+00	2.55E+00	1.40E+00
AI506816	2.05E+00	6.04E+00	2.95E+00
Gm15452	1.67E+00	2.66E+00	1.59E+00
Depdc1b	1.87E+00	3.33E+00	1.78E+00
Epb4113	1.52E+00	2.95E+01	1.94E+01
Btbd19	1.51E+00	1.59E+01	1.06E+01
Igsf3	1.71E+00	3.18E+01	1.86E+01
Dusp9	2.04E+00	2.48E+00	1.21E+00
Cd44	1.76E+00	1.30E+02	7.39E+01
Gm45902	1.74E+00	5.89E+00	3.38E+00

TABLE 2-continued

List of upregulated genes at the bite site of mice treated with control (naïve) serum.

Wfdc12	4.99E+00	3.58E+01	7.17E+00
Tdh	3.18E+00	2.23E+01	7.01E+00
Rps13-ps2	1.83E+00	1.00E+01	5.49E+00
Poc1a	1.68E+00	7.80E+00	4.63E+00
Gja1	1.62E+00	1.63E+02	1.00E+02
9330102E08Rik	1.74E+00	4.30E+00	2.48E+00
2700038G22Rik	1.89E+00	2.88E+00	1.52E+00
Rpl27	1.70E+00	1.91E+01	1.13E+01
Cdca8	1.64E+00	1.92E+01	1.17E+01
Stx11	1.60E+00	6.82E+00	4.28E+00
Fam167a	3.53E+00	1.59E+01	4.51E+00
Pinx1	1.54E+00	1.14E+01	7.40E+00
Cks2	1.56E+00	9.48E+00	6.08E+00
Gm10182	1.57E+00	2.43E+01	1.55E+01

Control-resting skin: n = 2, Control-bitten skin: n = 2, AgBR1 antiserum-bitten skin: n = 2 biologically independent samples.
Normalized read counts were statistically modeled using Partek Flow's Gene Specific Analysis (GSA) approach.

TABLE 3

Oligonucleotide primers used in the experiments.

Oligonucleotide primers for qRT-PCR	
Zika virus	F: TTGGTCATGATACTGCTGATTGC (SEQ ID NO: 130) R: CCTTCCACAAAGTCCCTATTGC (SEQ ID NO: 131)
Mosquito Rp49	F: GCTATGACAAGCTTGCCCCCA (SEQ ID NO: 132) R: TCATCAGCACCTCCAGCT (SEQ ID NO: 133)
Mouse βactin	F: GATGACGATATCGCTGCGCTG (SEQ ID NO: 134) R: GTACGACCAGAGGCATACAGG (SEQ ID NO: 135)
Mouse Tnfa	F: TGGAACTGGCAGAAGAGGCACT (SEQ ID NO: 136) R: GAGATAGCAAATCGGCTGACGG (SEQ ID NO: 137)
Mouse Il1b	F: GCTTCAGGCAGGCAGTATCAC (SEQ ID NO: 138) R: CGACAGCACGAGGCTTTTT (SEQ ID NO: 139)
Mouse Il6	F: ATGAAGTTCCTCTCTGCAAGAGACT (SEQ ID NO: 140) R: CACTAGGTTTGCCGAGTAGATCTC (SEQ ID NO: 141)
Mosquito AgBR1	F: CGTCAACTTGGCTTCGTTCG (SEQ ID NO: 142) R: GATGCCGGATTTCTCCACCA (SEQ ID NO: 143)
Oligonucleotide primers for cloning into the expression vector	
AgBR1	F: CTCGCTCGGGAGATCTAACAATGCCACTACCGGCCCAAAGGTCCTC (SEQ ID NO: 144) R: GCCCTCTAGACTCGAGCAGCCTATACTTAGCAGCCCTCAG (SEQ ID NO: 145)
SP	F:CTCGCTCGGGAGATCTCACCCAATTCCAGCCGAAGATCCCGCCAAGC (SEQ ID NO: 146) R:CCCTCTAGACTCGAGACCAAAAGCCTTCACCATGACCTTCGGATAG (SEQ ID NO: 147)
D7Bclu	F: CTCGCTCGGGAGATCTGCACCTTTATGGGATGCAAAGGATCCAGAGC (SEQ ID NO: 148) R: GCCCTCTAGACTCGAGGCTACACTGGATCTTGTCGATATCG (SEQ ID NO: 149)
Oligonucleotide primers for dsRNA preparation	
dsAgBR1 RNA	F: TAATACGACTCACTATAGGGGATGGACAGATGTCTCTTCGTG (SEQ ID NO: 150) R: TAATACGACTCACTATAGGGCCAAATCCAATCCATCGAAA (SEQ ID NO: 151)

TABLE 3-continued

Oligonucleotide primers used in the experiments.

dsGFP RNA	F: TAATACGACTCACTATAGGGGTGAGCAAGGGCGAGGAG (SEQ ID NO: 152)
	R: TAATACGACTCACTATAGGGCATGATATAGACGTTGTGGCTGTT (SEQ ID NO: 153)

TABLE 4

List of GSEA enriched pathway at bite sites in mice treated with control serum using hallmark gene sets

	GS follow link to MSigDB	NES	FDR q-val
1	HALLMARK_INFLAMMATORY_RESPONSE	2.5049036	0
2	HALLMARK_ALLOGRAFT_REJECTION	2.3367434	0
3	HALLMARK_IL6_JAK_STAT3_SIGNALING	2.016875	8.00E−04
4	HALLMARK_TNFA_SIGNALING_VIA_NFKB	1.8812603	0.001689706

TABLE 4-continued

List of GSEA enriched pathway at bite sites in mice treated with control serum using hallmark gene sets

	GS follow link to MSigDB	NES	FDR q-val
5	HALLMARK_IL2_STAT5_SIGNALING	1.5615453	0.028370652

Control-resting skin: n = 2, Control-bitten skin: n = 2, AgBR1 antiserum-bitten skin: n = 2 biologically independent samples.

FDR statistics were performed based on study described in Subramanian, A. et al. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. Proc. Natl Acad. Sci. USA 102, 15545-15550 (2005).

TABLE 5

List of GSEA enriched pathway at bite sites in mice treated with control serum using KEGG gene sets

	GS follow link to MSigDB	NES	FDR q-val	LEADING EDGE
1	KEGG_CYTOKINE_CYTOKINE_RECEPTOR_INTERACTION	2.5147192	0	tags = 34%, list = 10%, signal = 37%
2	KEGG_HEMATOPOIETIC_CELL_LINEAGE	2.1477058	3.80E−04	tags = 34%, list = 12%, signal = 38%
3	KEGG_RIBOSOME	2.0992713	0.00114546	tags = 64%, list = 21%, signal = 80%
4	KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY	2.0794337	0.001266238	tags = 18%, list = 3%, signal = 18%
5	KEGG_TYPE_I_DIABETES_MELLITUS	2.047159	0.001789215	tags = 47%, list = 9%, signal = 52%

Control-resting skin: n = 2,

Control-bitten skin: n = 2,

AgBR1 antiserum-bitten skin: n = 2 biologically independent samples.

FDR statistics were performed based on study described in *Subramanian, A. et al.* Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proc. Natl Acad. Sci. USA* 102, 15545-15550 (2005).

TABLE 6

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICHMENT
	HALLMARK_INFLAMMATORY_RESPONSE		
SELL	selectin L (lymphocyte adhesion molecule 1)	4.533662319	Yes
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
IL18RAP	interleukin 18 receptor accessory protein	3.251766205	Yes
CSF3R	colony stimulating factor 3 receptor (granulocyte)	3.238983631	Yes

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
OSM	oncostatin M	2.948629141	Yes
MSR1	macrophage scavenger receptor 1	2.937763929	Yes
C5AR1	complement component 5a receptor 1	2.387494087	Yes
MEFV	Mediterranean fever	2.353091955	Yes
MARCO	macrophage receptor with collagenous structure	2.29198432	Yes
TNFRSF9	tumor necrosis factor receptor superfamily, member 9	2.029400826	Yes
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	1.842594028	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
CLEC5A	C-type lectin domain family 5, member A	1.796642661	Yes
BDKRB1	bradykinin receptor B1	1.789603353	Yes
PTAFR	platelet-activating factor receptor	1.573449492	Yes
PROK2	prokineticin 2	1.485739708	Yes
CCL22	chemokine (C-C motif) ligand 22	1.440871716	Yes
CSF3	colony stimulating factor 3 (granulocyte)	1.422928095	Yes
TLR1	toll-like receptor 1	1.34019506	Yes
PLAUR	plasminogen activator, urokinase receptor	1.308592319	Yes
FPR1	formyl peptide receptor 1	1.262866974	Yes
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B	1.259392858	Yes
SLAMF1	signaling lymphocytic activation molecule family member 1	1.241883397	Yes
CCL24	chemokine (C-C motif) ligand 24	1.233121157	Yes
GPR132	G protein-coStupled receptor 132	1.176985025	Yes
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	1.097683549	Yes
LCP2	lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	1.090578794	Yes
PIK3R5	phosphoinositide-3-kinase, regulatory subunit 5, p101	1.057828546	Yes
C3AR1	complement component 3a receptor 1	1.036981106	Yes
RGS1	regulator of G-protein signalling 1	0.960995197	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
CD14	CD14 molecule	0.848022759	Yes
CCRL2	chemokine (C-C motif) receptor-like 2	0.822621703	Yes
STAB1	stabilin 1	0.800862968	Yes
IL10	interleukin 10	0.777381659	Yes
TNFSF9	tumor necrosis factor (ligand) superfamily, member 9	0.771818101	Yes
ADM	adrenomedullin	0.746417522	Yes
ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	0.746375382	Yes
RTP4	receptor transporter protein 4	0.680959046	Yes
TLR2	toll-like receptor 2	0.671268702	Yes
CCL17	chemokine (C-C motif) ligand 17	0.664499223	Yes
BST2	bone marrow stromal cell antigen 2	0.6320346	Yes
CCL20	chemokine (C-C motif) ligand 20	0.625092983	Yes
CCR7	chemokine (C-C motif) receptor 7	0.594285488	Yes
CD82	CD82 molecule	0.569351971	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
TNFAIP6	tumor necrosis factor, alpha-induced protein 6	0.543578744	Yes
HBEGF	heparin-binding EGF-like growth factor	0.541148901	Yes
CD48	CD48 molecule	0.540921032	Yes
RGS16	regulator of G-protein signalling 16	0.526294231	Yes
SELE	selectin E (endothelial adhesion molecule 1)	0.494481832	Yes
CD40	CD40 molecule, TNF receptor superfamily member 5	0.492939293	Yes
LTA	lymphotoxin alpha (TNF superfamily, member 1)	0.44320941	No
HAS2	hyaluronan synthase 2	0.441198289	No
ITGA5	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	0.429049671	No
SLC4A4	solute carrier family 4, sodium bicarbonate cotransporter, member 4	0.396574855	No
CXCL9	chemokine (C-X-C motif) ligand 9	0.391491205	No
IL10RA	interleukin 10 receptor, alpha	0.343504012	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
GCH1	GTP cyclohydrolase 1 (dopa-responsive dystonia)	0.327480644	No
LCK	lymphocyte-specific protein tyrosine kinase	0.318335414	No
IFITM1	interferon induced transmembrane protein 1 (9-27)	0.315781265	No
PDPN	podoplanin	0.294152737	No
PTGIR	prostaglandin I2 (prostacyclin) receptor (IP)	0.285321265	No
OLR1	oxidised low density lipoprotein (lectin-like) receptor 1	0.284122884	No
INHBA	inhibin, beta A (activin A, activin AB alpha polypeptide)	0.280317694	No
ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	0.256395549	No
CCL7	chemokine (C-C motif) ligand 7	0.251811057	No
CXCL10	chemokine (C-X-C motif) ligand 10	0.226761773	No
IRF1	interferon regulatory factor 1	0.214157283	No
OSMR	oncostatin M receptor	0.207781732	No
LAMP3	lysosomal-associated membrane protein 3	0.205396608	No
SLC28A2	solute carrier family 28 (sodium-coupled nucleoside transporter), member 2	0.192293972	No
EBI3	Epstein-Barr virus induced gene 3	0.188898429	No
SLC7A2	solute carrier family 7 (cationic amino acid transporter, y+ system), member 2	0.175343886	No
ICAM4	intercellular adhesion molecule 4 (Landsteiner-Wiener blood group)	0.169187918	No
CD69	CD69 molecule	0.166904241	No
ADRM1	adhesion regulating molecule 1	0.161846325	No
PTGER4	prostaglandin E receptor 4 (subtype EP4)	0.143603638	No
NDP	Norrie disease (pseudoglioma)	0.107874334	No
SCARF1	scavenger receptor class F, member 1	0.093449399	No
IL15RA	interleukin 15 receptor, alpha	0.084517181	No
CXCL11	chemokine (C-X-C motif) ligand 11	0.079039596	No
CYBB	cytochrome b-245, beta polypeptide (chronic granulomatous disease)	0.067997418	No
IFNAR1	interferon (alpha, beta and omega) receptor 1	0.059620846	No
IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	0.046017136	No
TPBG	trophoblast glycoprotein	0.045252148	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
CXCR6	chemokine (C-X-C motif) receptor 6	0.031615365	No
GPC3	glypican 3	0.026109839	No
EIF2AK2	eukaryotic translation initiation factor 2-alpha kinase 2	0.021446833	No
CHST2	carbohydrate (N-acetylglucosamine-6-0) sulfotransferase 2	0.006915596	No
EDN1	endothelin 1	0.002488923	No
P2RX4	purinergic receptor P2X, ligand-gated ion channel, 4	0.002422775	No
PTPRE	protein tyrosine phosphatase, receptor type, E	−0.01096273	No
PTGER2	prostaglandin E receptor 2 (subtype EP2), 53kDa	−0.01937426	No
TACR3	tachykinin receptor 3	−0.02168826	No
NPFFR2	neuropeptide FF receptor 2	−0.03000635	No
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	−0.03587324	No
DCBLD2	discoidin, CUB and LCCL domain containing 2	−0.04324392	No
IL15	interleukin 15	−0.04502484	No
IL1R1	interleukin 1 receptor, type I	−0.05148519	No
FZD5	frizzled homolog 5 (Drosophila)	−0.05248347	No
ADORA2B	adenosine A2b receptor	−0.07098219	No
CMKLR1	chemokine-like receptor 1	−0.07226631	No
TLR3	toll-like receptor 3	−0.0735488	No
CDKN1A	cyclin-dependent kinase inhibitor 1A p21, Cip1)	−0.08443426	No
KCNA3	potassium voltage-gated channel, shaker-related subfamily, member 3	−0.09990013	No
MMP14	matrix metallopeptidase 14 (membrane-inserted)	−0.10503554	No
HRH1	histamine receptor H1	−0.11474121	No
IRAK2	interleukin-1 receptor-associated kinase 2	−0.13551585	No
ATP2B1	ATPase, Ca++ transporting, plasma membrane 1	−0.14145075	No
SCN1B	sodium channel, voltage-gated, type I, beta	−0.14982769	No
SLC31A2	solute carrier family 31 (copper transporters), member 2	−0.15675473	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
PVR	poliovirus receptor	−0.15986347	No
SLC11A2	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 2	−0.16051796	No
KLF6	Kruppel-like factor 6	−0.16283926	No
ITGB8	integrin, beta 8	−0.16627799	No
PDE4B	phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4 dunce homolog, Drosophila)	−0.16894662	No
MXD1	MAX dimerization protein 1	−0.16998833	No
BTG2	BTG family, member 2	−0.17541341	No
SLC7A1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	−0.17681299	No
RIPK2	receptor-interacting serine-threonine kinase 2	−0.1842809	No
SRI	sorcin	−0.19541027	No
P2RX7	purinergic receptor P2X, ligand-gated ion channel, 7	−0.1960772	No
P2RY2	purinergic receptor P2Y, G-protein coupled, 2	−0.19852374	No
LDLR	low density lipoprotein receptor (familial hypercholesterolemia)	−0.20240238	No
HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	−0.20901471	No
AHR	aryl hydrocarbon receptor	−0.21279255	No
CX3CL1	chemokine (C-X3-C motif) ligand 1	−0.22508623	No
MET	met proto-oncogene (hepatocyte growth factor receptor)	−0.2252703	No
LY6E	lymphocyte antigen 6 complex, locus E	−0.22614777	No
NMI	N-myc (and STAT) interactor	−0.22712676	No
SEMA4D	sema domain, immunoglobulin domain (Ig), transmembrane domain (TM) and short cytoplasmic domain, (semaphorin) 4D	−0.22815116	No
IL1A	interleukin 1, alpha	−0.22882077	No
ABI1	abl-interactor 1	−0.22907911	No
GNA15	guanine nucleotide binding protein (G protein), alpha 15 (Gq class)	−0.23037907	No
SPHK1	sphingosine kinase 1	−0.23109274	No
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	−0.25809258	No
ACVR2A	activin A receptor, type IIA	−0.26500779	No
AQP9	aquaporin 9	−0.2774868	No
IRF7	interferon regulatory factor 7	−0.28254756	No
ACVR1B	activin A receptor, type IB	−0.29110909	No
IL7R	interleukin 7 receptor	−0.30657914	No
SLC31A1	solute carrier family 31 (copper transporters), member 1	−0.30956858	No
KIF1B	kinesin family member 1B	−0.31039682	No
IL2RB	interleukin 2 receptor, beta	−0.31792504	No
TAPBP	TAP binding protein (tapasin)	−0.32166621	No
GNAI3	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 3	−0.32649222	No
RELA	v−rel reticuloendotheliosis viral oncogene homolog A, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3, p65 (avian)	−0.32651395	No
ATP2A2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	−0.32773513	No
ABCA1	ATP-binding cassette, sub-family A (ABC1), member 1	−0.33476061	No
RAF1	v-raf-1 murine leukemia viral oncogene homolog 1	−0.3348152	No
PCDH7	BH-protocadherin (brain-heart)	−0.34278125	No
CD55	CD55 molecule, decay accelerating factor for complement (Cromer blood group)	−0.34951958	No
TACR1	tachykinin receptor 1	−0.36803696	No
RASGRP1	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	−0.37512192	No
PSEN1	presenilin 1 (Alzheimer disease 3)	−0.38747761	No
ATP2C1	ATPase, Ca++ transporting, type 2C, member 1	−0.39031595	No
CALCRL	calcitonin receptor-like	−0.41768777	No
SLC1A2	solute carrier family 1 (glial high affinity glutamate transporter), member 2	−0.48958847	No
IL18	interleukin 18 (interferon-gamma-inducing factor)	−0.5164243	No
EMP3	epithelial membrane protein 3	−0.51683706	No
GABBR1	gamma-aminobutyric acid (GABA) B receptor, 1	−0.54345095	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
AXL	AXL receptor tyrosine kinase	−0.57041121	No
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	−0.57849312	No
GP1BA	glycoprotein Ib (platelet), alpha polypeptide	−0.59780264	No
TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	−0.65267819	No
FFAR2	free fatty acid receptor 2	−0.66044772	No
NMUR1	neuromedin U receptor 1	−0.66688561	No
HPN	hepsin (transmembrane protease, serine 1)	−0.68898129	No
KCNJ2	potassium inwardly-rectifying channel, subfamily J, member 2	−0.70222563	No
TIMP1	TIMP metallopeptidase inhibitor 1	−0.70523745	No
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10	−0.78845328	No
IL18R1	interleukin 18 receptor 1	−0.81675339	No
RHOG	ras homolog gene family, member G (rhoG)	−0.9650324	No
EREG	epiregulin	−1.24036241	No
ROS1	v-ros UR2 sarcoma virus oncogene homolog 1 (avian)	−1.97980785	No
	HALLMARK_ALLOGRAFT_REJECTION		
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
IL18RAP	interleukin 18 receptor accessory protein	3.251766205	Yes
STAT4	signal transducer and activator of transcription 4	3.148304939	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	2.667121887	Yes
CCR1	chemokine (C-C motif) receptor 1	2.132987738	Yes
CCR5	chemokine (C-C motif) receptor 5	2.054755688	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
ITGAL	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	1.800091743	Yes
CD7	CD7 molecule	1.628337383	Yes
FGR	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog	1.552860975	Yes
CCL22	chemokine (C-C motif) ligand 22	1.440871716	Yes
TLR1	toll-like receptor 1	1.34019506	Yes
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	1.315529704	Yes
CCL4	chemokine (C-C motif) ligand 4	1.303452969	Yes
GPR65	G protein-coupled receptor 65	1.301272631	Yes
CCR2	chemokine (C-C motif) receptor 2	1.17247808	Yes
PRF1	perforin 1 (pore forming protein)	1.171788573	Yes
IGSF6	immunoglobulin superfamily, member 6	1.100607872	Yes
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	1.097683549	Yes
LCP2	lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	1.090578794	Yes
IL2RG	interleukin 2 receptor, gamma (severe combined immunodeficiency)	1.083326221	Yes
DYRK3	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3	1.04365015	Yes
IRF8	interferon regulatory factor 8	0.984531879	Yes
TLR6	toll-like receptor 6	0.974328399	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
SOCS1	suppressor of cytokine signaling 1	0.912176847	Yes
FYB	FYN binding protein (FYB-120/130)	0.841911793	Yes
STAB1	stabilin 1	0.800862968	Yes
CCL19	chemokine (C-C motif) ligand 19	0.784207284	Yes
ITGB2	integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	0.783176661	Yes
IL10	interleukin 10	0.777381659	Yes
BCL3	B-cell CLL/lymphoma 3	0.768477619	Yes
ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	0.746375382	Yes
MMP9	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	0.740974486	Yes
IL13	interleukin 13	0.6945768	Yes
IL11	interleukin 11	0.684957564	Yes
TLR2	toll-like receptor 2	0.671268702	Yes
GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2 (beta-1,6-N-acetylglucosaminyltransferase)	0.671001792	Yes
IL4	interleukin 4	0.65638262	Yes

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
CDKN2A	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	0.650471985	Yes
CD86	CD86 molecule	0.631752431	Yes
CD80	CD80 molecule	0.600226164	Yes
LTB	lymphotoxin beta (TNF superfamily, member 3)	0.579620421	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
WAS	Wiskott-Aldrich syndrome (eczema-thrombocytopenia)	0.525824308	Yes
PTPRC	protein tyrosine phosphatase, receptor type, C	0.522265971	Yes
RPS19	ribosomal protein S19	0.506382108	Yes
CD40	CD40 molecule, TNF receptor superfamily member 5	0.492939293	Yes
NCF4	neutrophil cytosolic factor 4, 40kDa	0.465533584	Yes
LY86	lymphocyte antigen 86	0.449851602	Yes
FCGR2B	Fc fragment of IgG, low affinity IIb, receptor (CD32)	0.436047524	Yes
HCLS1	hematopoietic cell-specific Lyn substrate 1	0.427405208	Yes
CD3D	CD3d molecule, delta (CD3-TCR complex)	0.415081888	Yes
CXCL9	chemokine (C-X-C motif) ligand 9	0.391491205	Yes
CXCR3	chemokine (C-X-C motif) receptor 3	0.380579948	Yes
BRCA1	breast cancer 1, early onset	0.38035053	Yes
RPL9	ribosomal protein L9	0.372396767	Yes
CD8A	CD8a molecule	0.337146819	No
SIT1	signaling threshold regulating transmembrane adaptor 1	0.334993273	No
CD28	CD28 molecule	0.331128299	No
LCK	lymphocyte-specific protein tyrosine kinase	0.318335414	No
IFNAR2	interferon (alpha, beta and omega) receptor 2	0.281477422	No
INHBA	inhibin, beta A (activin A, activin AB alpha polypeptide)	0.280317694	No
UBE2N	ubiquitin-conjugating enzyme E2N (UBC13 homolog, yeast)	0.279983729	No
CCL7	chemokine (C-C motif) ligand 7	0.251811057	No
CD79A	CD79a molecule, immunoglobulin-associated alpha	0.249655664	No
MAP4K1	mitogen-activated protein kinase kinase kinase kinase 1	0.249342158	No
ETS1	v-ets erythroblastosis virus E26 oncogene homolog 1 (avian)	0.217027962	No
FAS	Fas (TNF receptor superfamily, member 6)	0.173293099	No
ST8SIA4	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	0.147267297	No
RPL39	ribosomal protein L39	0.145141497	No
GLMN	glomulin, FKBP associated protein	0.138915822	No
CRTAM	cytotoxic and regulatory T cell molecule	0.132859111	No
ZAP70	zeta-chain (TCR) associated protein kinase 70kDa	0.127061605	No
TGFB1	transforming growth factor, beta 1 (Camurati-Engelmann disease)	0.120179698	No
SPI1	spleen focus forming virus (SFFV) proviral integration oncogene spi1	0.119634412	No
STAT1	signal transducer and activator of transcription 1, 91kDa	0.050059285	No
IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	0.046017136	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
CCL11	chemokine (C-C motif) ligand 11	0.039969306	No
CD3E	CD3e molecule, epsilon (CD3-TCR complex)	0.002899456	No
APBB1	amyloid beta (A4) precursor protein-binding, family B, member 1 (Fe65)	−0.002237323	No
GBP2	guanylate binding protein 2, interferon-inducible	−0.031019775	No
TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	−0.033033174	No
CD3G	CD3g molecule, gamma (CD3-TCR complex)	−0.033679064	No
SOCS5	suppressor of cytokine signaling 5	−0.042330034	No
INHBB	inhibin, beta B (activin AB beta polypeptide)	−0.043366853	No
IL15	interleukin 15	−0.045024838	No
CXCL13	chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant)	−0.045578849	No
IL12RB1	interleukin 12 receptor, beta 1	−0.050351642	No
CD74	CD74 molecule, major histocompatibility complex, class II invariant chain	−0.073090956	No
TLR3	toll-like receptor 3	−0.073548801	No
TAP2	transporter 2, ATP-binding cassette, sub-family B (MDR/TAP)	−0.081326358	No
UBE2D1	ubiquitin-conjugating enzyme E2D 1 (UBC4/5 homolog, yeast)	−0.089536563	No
ELF4	E74-like factor 4 (ets domain transcription factor)	−0.119385988	No
CD4	CD4 molecule	−0.128431112	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
PTPN6	protein tyrosine phosphatase, non-receptor type 6	−0.134158283	No
IL16	interleukin 16 (lymphocyte chemoattractant factor)	−0.139530182	No
MAP3K7	mitogen-activated protein kinase kinase kinase 7	−0.140273616	No
RPS9	ribosomal protein S9	−0.145742506	No
EIF4G3	eukaryotic translation initiation factor 4 gamma, 3	−0.146932095	No
PRKCG	protein kinase C, gamma	−0.148039475	No
TPD52	tumor protein D52	−0.149961919	No
MRPL3	mitochondrial ribosomal protein L3	−0.158919781	No
EGFR	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	−0.164786458	No
IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta	−0.167352051	No
JAK2	Janus kinase 2 (a protein tyrosine kinase)	−0.167714015	No
CCND2	cyclin D2	−0.172594517	No
HDAC9	histone deacetylase 9	−0.17316395	No
AARS	alanyl-tRNA synthetase	−0.175502419	No
IL27RA	interleukin 27 receptor, alpha	−0.177759618	No
IFNGR1	interferon gamma receptor 1	−0.181889921	No
RIPK2	receptor-interacting serine-threonine kinase 2	−0.184280902	No
MTIF2	mitochondrial translational initiation factor 2	−0.19249332	No
HIF1A	hypoxia-inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	−0.209014714	No
CFP	complement factor properdin	−0.21020171	No
F2R	coagulation factor II (thrombin) receptor	−0.219984412	No
ABI1	abl-interactor 1	−0.229079112	No
B2M	beta-2-microglobulin	−0.230768695	No
LY75	lymphocyte antigen 75	−0.23181951	No
TGFB2	transforming growth factor, beta 2	−0.233885586	No
CD47	CD47 molecule	−0.250719309	No
ITK	IL2-inducible T-cell kinase	−0.254682004	No
CSK	c-src tyrosine kinase	−0.260919124	No
DARS	aspartyl-tRNA synthetase	−0.26485461	No
ACVR2A	activin A receptor, type IIA	−0.265007794	No
IRF4	interferon regulatory factor 4	−0.281879067	No
IRF7	interferon regulatory factor 7	−0.282547563	No
TRAF2	TNF receptor-associated factor 2	−0.292227983	No
NCK1	NCK adaptor protein 1	−0.300779611	No
GALNT1	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 1 (GalNAc-T1)	−0.308693349	No
DEGS1	degenerative spermatocyte homolog 1, lipid desaturase (Drosophila)	−0.309142411	No
IL2RB	interleukin 2 receptor, beta	−0.317925036	No
TAPBP	TAP binding protein (tapasin)	−0.321666211	No
ACHE	acetylcholinesterase (Yt blood group)	−0.328164309	No
CD247	CD247 molecule	−0.337787271	No
IL7	interleukin 7	−0.356599182	No
CD2	CD2 molecule	−0.376374722	No
BCL10	B-cell CLL/lymphoma 10	−0.387535632	No
PSMB10	proteasome (prosome, macropain) subunit, beta type, 10	−0.392836064	No
IL2RA	interleukin 2 receptor, alpha	−0.422955573	No
CCND3	cyclin D3	−0.436431259	No
NPM1	nucleophosmin (nucleolar phosphoprotein B23, numatrin)	−0.437718987	No
EIF5A	eukaryotic translation initiation factor 5A	−0.440881759	No
ABCE1	ATP-binding cassette, sub-family E (OABP), member 1	−0.462895155	No
KLRD1	killer cell lectin-like receptor subfamily D, member 1	−0.488495886	No
WARS	tryptophanyl-tRNA synthetase	−0.497032523	No
NME1	non-metastatic cells 1, protein (NM23A) expressed in	−0.507820129	No
IL18	interleukin 18 (interferon-gamma-inducing factor)	−0.516424298	No
FLNA	filamin A, alpha (actin binding protein 280)	−0.591539323	No
TRAT1	T cell receptor associated transmembrane adaptor 1	−0.612580657	No
BCAT1	branched chain aminotransferase 1, cytosolic	−0.632505953	No
PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	−0.685499907	No
CD96	CD96 molecule	−0.696216106	No
TIMP1	TIMP metallopeptidase inhibitor 1	−0.705237448	No
CTSS	cathepsin S	−0.790032566	No
RARS	arginyl-tRNA synthetase	−0.869948447	No
CAPG	capping protein (actin filament), gelsolin-like	−0.915236473	No
AKT1	v-akt murine thymoma viral oncogene homolog 1	−0.990338564	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
THY1	Thy-1 cell surface antigen	−1.102289557	No
RPL3L	ribosomal protein L3-like	−1.196903586	No
EREG	epiregulin	−1.240362406	No
KRT1	keratin 1 (epidermolytic hyperkeratosis)	−1.605908155	No
	HALLMARK_IL6_JAK_STAT3_SIGNALING		
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
CSF3R	colony stimulating factor 3 receptor (granulocyte)	3.238983631	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	2.667189121	Yes
CCR1	chemokine (C-C motif) receptor 1	2.132987738	Yes
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B	1.259392858	Yes
IL2RG	interleukin 2 receptor, gamma (severe combined immunodeficiency)	1.083326221	Yes
PIK3R5	phosphoinositide-3-kinase, regulatory subunit 5, p101	1.057828546	Yes
CXCL3	chemokine (C-X-C motif) ligand 3	0.966697574	Yes
SOCS1	suppressor of cytokine signaling 1	0.912176847	Yes
CSF2RB	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	0.888966024	Yes
CD14	CD14 molecule	0.848022759	Yes
CSF2RA	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	0.78864789	Yes
CRLF2	cytokine receptor-like factor 2	0.754059553	Yes
TLR2	toll-like receptor 2	0.671268702	Yes
CD38	CD38 molecule	0.640005708	Yes
LTB	lymphotoxin beta (TNF superfamily, member 3)	0.579620421	Yes
CNTFR	ciliary neurotrophic factor receptor	0.557358146	Yes
CXCL9	chemokine (C-X-C motif) ligand 9	0.391491205	No
ITGB3	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	0.256395549	No
CCL7	chemokine (C-C motif) ligand 7	0.251811057	No
CXCL10	chemokine (C-X-C motif) ligand 10	0.226761773	No
IRF1	interferon regulatory factor 1	0.214157283	No
ACVRL1	activin A receptor type II-like 1	0.211801216	No
OSMR	oncostatin M receptor	0.207781732	No
EBI3	Epstein-Barr virus induced gene 3	0.188898429	No
FAS	Fas (TNF receptor superfamily, member 6)	0.173293099	No
ITGA4	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	0.159151196	No
TGFB1	transforming growth factor, beta 1 (Camurati-Engelmann disease)	0.120179698	No
IL15RA	interleukin 15 receptor, alpha	0.084517181	No
CXCL11	chemokine (C-X-C motif) ligand 11	0.079039596	No
STAT2	signal transducer and activator of transcription 2, 113kDa	0.064280972	No
IFNAR1	interferon (alpha, beta and omega) receptor 1	0.059620846	No
BAK1	BCL2-antagonist/killer 1	0.059363768	No
STAT1	signal transducer and activator of transcription 1, 91kDa	0.050059285	No
IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	0.046017136	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
IL17RB	interleukin 17 receptor B	0.030075336	No
CD9	CD9 molecule	0.026316533	No
IL3RA	interleukin 3 receptor, alpha (low affinity)	0.007537159	No
HAX1	HCLS1 associated protein X-1	−0.02173438	No
CXCL13	chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant)	−0.04557885	No
IL12RB1	interleukin 12 receptor, beta 1	−0.05035164	No
IL1R1	interleukin 1 receptor, type I	−0.05148519	No
IL9R	interleukin 9 receptor	−0.07257795	No
TNFRSF21	tumor necrosis factor receptor superfamily, member 21	−0.09369773	No
CBL	Cas-Br-M (murine) ecotropic retroviral transforming sequence	−0.10830661	No
CD36	CD36 molecule (thrombospondin receptor)	−0.11540288	No
PTPN11	protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	−0.14138806	No
TYK2	tyrosine kinase 2	−0.16118781	No
JUN	jun oncogene	−0.16524719	No
IL17RA	interleukin 17 receptor A	−0.17849953	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
IFNGR1	interferon gamma receptor 1	−0.18188992	No
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	−0.20624523	No
MAP3K8	mitogen-activated protein kinase kinase kinase 8	−0.2093222	No
PIM1	pim-1 oncogene	−0.21471494	No
IL1R2	interleukin 1 receptor, type II	−0.21576229	No
PTPN2	protein tyrosine phosphatase, non-receptor type 2	−0.21662436	No
PDGFC	platelet derived growth factor C	−0.21919613	No
PTPN1	protein tyrosine phosphatase, non-receptor type 1	−0.23609251	No
IL10RB	interleukin 10 receptor, beta	−0.26419479	No
STAM2	signal transducing adaptor molecule (SH3 domain and ITAM motif) 2	−0.28349385	No
ACVR1B	activin A receptor, type IB	−0.29110909	No
IL7	interleukin 7	−0.35659918	No
CD44	CD44 molecule (Indian blood group)	−0.41463488	No
IL13RA1	interleukin 13 receptor, alpha 1	−0.41913402	No
IL2RA	interleukin 2 receptor, alpha	−0.42295557	No
SOCS3	suppressor of cytokine signaling 3	−0.44126242	No
LEPR	leptin receptor	−0.48937947	No
TNFRSF12A	tumor necrosis factor receptor superfamily, member 12A	−0.51185614	No
GRB2	growth factor receptor-bound protein 2	−0.56912065	No
CSF2	colony stimulating factor 2 (granulocyte-macrophage)	−0.62405962	No
LTBR	lymphotoxin beta receptor (TNFR superfamily, member 3)	−0.67464828	No
PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	−0.68549991	No
A2M	alpha-2-macroglobulin	−0.77927083	No
MYD88	myeloid differentiation primary response gene (88)	−0.79646552	No
IL18R1	interleukin 18 receptor 1	−0.81675339	No
STAT3	signal transducer and activator of transcription 3 (acute-phase response factor)	−0.89553529	No
TNFRSF1A	tumor necrosis factor receptor superfamily, member lA	−0.96931034	No
HMOX1	heme oxygenase (decycling) 1	−1.15975845	No
	HALLMARK_TNFA_SIGNALING_VIA_NFKB		
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	2.667189121	Yes
TNFRSF9	tumor necrosis factor receptor superfamily, member 9	2.029400826	Yes
CXCL2	chemokine (C-X-C motif) ligand 2	1.990867496	Yes
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	1.842594028	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
PTX3	pentraxin-related gene, rapidly induced by IL-1 beta	1.801822662	Yes
PLAUR	plasminogen activator, urokinase receptor	1.308592319	Yes
CCL4	chemokine (C-C motif) ligand 4	1.303452969	Yes
TRAF1	TNF receptor-associated factor 1	1.300272942	Yes
PLEK	pleckstrin	1.008932829	Yes
CXCL3	chemokine (C-X-C motif) ligand 3	0.966697574	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
DUSP2	dual specificity phosphatase 2	0.894410133	Yes
IL23A	interleukin 23, alpha subunit p19	0.838799894	Yes
CCRL2	chemokine (C-C motif) receptor-like 2	0.822621703	Yes
SLC2A6	solute carrier family 2 (facilitated glucose transporter), member 6	0.820073187	Yes
FOSL1	FOS-like antigen 1	0.779859602	Yes
TNFSF9	tumor necrosis factor (ligand) superfamily, member 9	0.771818101	Yes
BCL3	B-cell CLL/lymphoma 3	0.768477619	Yes
ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	0.746375382	Yes
NFKBIE	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, epsilon	0.742087662	Yes
CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	0.70218122	Yes
PTGS2	prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase)	0.696858883	Yes
TLR2	toll-like receptor 2	0.671268702	Yes
KLF4	Kruppel-like factor 4 (gut)	0.639784276	Yes
CCL20	chemokine (C-C motif) ligand 20	0.625092983	Yes
NR4A3	nuclear receptor subfamily 4, group A, member 3	0.624355614	Yes

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
CD80	CD80 molecule	0.600226164	Yes
AREG	amphiregulin (schwannoma-derived growth factor)	0.548579574	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
TNFAIP6	tumor necrosis factor, alpha-induced protein 6	0.543578744	Yes
PHLDA2	pleckstrin homology-like domain, family A, member 2	0.543070078	Yes
HBEGF	heparin-binding EGF-like growth factor	0.541148901	Yes
B4GALT5	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 5	0.432685524	No
FUT4	fucosyltransferase 4 (alpha (1,3) fucosyltransferase, myeloid-specific)	0.386936367	No
TNC	tenascin C (hexabrachion)	0.34414199	No
GCH1	GTP cyclohydrolase 1 (dopa-responsive dystonia)	0.327480644	No
OLR1	oxidised low density lipoprotein (lectin-like) receptor 1	0.284122884	No
INHBA	inhibin, beta A (activin A, activin AB alpha polypeptide)	0.280317694	No
CLCF1	cardiotrophin-like cytokine factor 1	0.26978004	No
TNFAIP2	tumor necrosis factor, alpha-induced protein 2	0.231159508	No
PHLDA1	pleckstrin homology-like domain, family A, member 1	0.226918563	No
CXCL10	chemokine (C-X-C motif) ligand 10	0.226761773	No
DUSP4	dual specificity phosphatase 4	0.222908363	No
IRF1	interferon regulatory factor 1	0.214157283	No
NFIL3	nuclear factor, interleukin 3 regulated	0.181677267	No
NR4A2	nuclear receptor subfamily 4, group A, member 2	0.1683653	No
CD69	CD69 molecule	0.166904241	No
PTGER4	prostaglandin E receptor 4 (subtype EP4)	0.143603638	No
SERPINB2	serpin peptidase inhibitor, clade B (ovalbumin), member 2	0.129979178	No
PANX1	pannexin 1	0.12138366	No
FOSB	FBJ murine osteosarcoma viral oncogene homolog B	0.113320433	No
TNFAIP3	tumor necrosis factor, alpha-induced protein 3	0.100990877	No
BTG1	B-cell translocation gene 1, anti-proliferative	0.100179978	No
IL15RA	interleukin 15 receptor, alpha	0.084517181	No
CXCL11	chemokine (C-X-C motif) ligand 11	0.079039596	No
SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	0.069677271	No
IFIT2	interferon-induced protein with tetratricopeptide repeats 2	0.05142466	No
IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	0.046017136	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
STAT5A	signal transducer and activator of transcription 5A	0.015167505	No
ATF3	activating transcription factor 3	0.007687764	No
EGR3	early growth response 3	0.003858579	No
EDN1	endothelin 1	0.002488923	No
F2RL1	coagulation factor II (thrombin) receptor-like 1	−0.00567373	No
PTPRE	protein tyrosine phosphatase, receptor type, E	−0.01096273	No
GFPT2	glutamine -fructose -6-phosphate transaminase 2	−0.02297758	No
IER5	immediate early response 5	−0.02526059	No
TANK	TRAF family member-associated NFKB activator	−0.02547635	No
TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	−0.03303317	No
GADD45B	growth arrest and DNA-damage-inducible, beta	−0.03472245	No
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	−0.03587324	No
KLF10	Kruppel-like factor 10	−0.03688239	No
GEM	GTP binding protein overexpressed in skeletal muscle	−0.04264625	No
DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	−0.05442556	No
PER1	period homolog 1 (Drosophila)	−0.05708625	No
BCL6	B-cell CLL/lymphoma 6 (zinc finger protein 51)	−0.06102759	No
BIRC3	baculoviral IAP repeat-containing 3	−0.06623559	No
LAMB3	laminin, beta 3	−0.07300156	No
ZC3H12A	zinc finger CCCH-type containing 12A	−0.07837815	No
FOS	v-fos FBJ murine osteosarcoma viral oncogene homolog	−0.08169513	No
CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	−0.08443426	No
CCNL1	cyclin Ll	−0.08534243	No
MAP2K3	mitogen-activated protein kinase kinase 3	−0.09317061	No
ZBTB10	zinc finger and BTB domain containing 10	−0.10083003	No
TIPARP	TCDD-inducible poly(ADP-ribose) polymerase	−0.10120153	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
TRIP10	thyroid hormone receptor interactor 10	−0.11554773	No
SERPINB8	serpin peptidase inhibitor, clade B (ovalbumin), member 8	−0.1231901	No
BMP2	bone morphogenetic protein 2	−0.14009446	No
ATP2B1	ATPase, Ca++ transporting, plasma membrane 1	−0.14145075	No
SOD2	superoxide dismutase 2, mitochondrial	−0.14157586	No
GADD45A	growth arrest and DNA-damage-inducible, alpha	−0.14824487	No
DDX58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58	−0.15164469	No
FJX1	four jointed box 1 (Drosophila)	−0.15888149	No
KLF6	Kruppel-like factor 6	−0.16283926	No
DUSP1	dual specificity phosphatase 1	−0.16306108	No
JUN	jun oncogene	−0.16524719	No
REL	v-rel reticuloendotheliosis viral oncogene homolog (avian)	−0.16811736	No
PDE4B	phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4 dunce homolog, Drosophila)	−0.16894662	No
MXD1	MAX dimerization protein 1	−0.16998833	No
BTG2	BTG family, member 2	−0.17541341	No
TNIP2	TNFAIP3 interacting protein 2	−0.18125953	No
RIPK2	receptor-interacting serine-threonine kinase 2	−0.1842809	No
NR4A1	nuclear receptor subfamily 4, group A, member 1	−0.19607757	No
JAG 1	jagged 1 (Alagille syndrome)	−0.19851652	No
LDLR	low density lipoprotein receptor (familial hypercholesterolemia)	−0.20240238	No
NFKB2	nuclear factor of kappa light polypeptide gene enhancer in B-cells 2 (p49/p100)	−0.20358734	No
IFIH1	interferon induced with helicase C domain 1	−0.20616461	No
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	−0.20624523	No
SLC16A6	solute carrier family 16, member 6 (monocarboxylic acid transporter 7)	−0.20754693	No
MAP3K8	mitogen-activated protein kinase kinase kinase 8	−0.2093222	No
RELB	v-rel reticuloendotheliosis viral oncogene homolog B, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3 (avian)	−0.21800217	No
G0S2	G0/Glswitch 2	−0.22224158	No
ETS2	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	−0.22630355	No
IL1A	interleukin 1, alpha	−0.22882077	No
MARCKS	myristoylated alanine-rich protein kinase C substrate	−0.22976576	No
SPHK1	sphingosine kinase 1	−0.23109274	No
FOSL2	FOS-like antigen 2	−0.23224656	No
TRIB1	tribbles homolog 1 (Drosophila)	−0.24160028	No
EGR2	early growth response 2 (Krox-20 homolog, Drosophila)	−0.2432663	No
TNFAIP8	tumor necrosis factor, alpha-induced protein8	−0.24982262	No
PDLIM5	PDZ and LIM domain 5	−0.25230208	No
RHOB	ras homolog gene family, member B	−0.25625306	No
CFLAR	CASP8 and FADD-like apoptosis regulator	−0.25688204	No
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	−0.25809258	No
NFE2L2	nuclear factor (erythroid-derived 2)-like 2	−0.25833997	No
SMAD3	SMAD, mothers against DPP homolog 3 (Drosophila)	−0.26333848	No
PLK2	polo-like kinase 2 (Drosophila)	−0.26362717	No
TNIP1	TNFAIP3 interacting protein 1	−0.27545539	No
SAT1	spermidine/spermine N1-acetyltransferase 1	−0.27614322	No
EHD1	EH-domain containing 1	−0.28172371	No
KYNU	kynureninase (L-kynurenine hydrolase)	−0.28701586	No
CCND1	cyclin D1	−0.28974119	No
SNN	stannin	−0.2964263	No
IRS2	insulin receptor substrate 2	−0.30096406	No
EIF1	eukaryotic translation initiation factor 1	−0.3023158	No
PLAU	plasminogen activator, urokinase	−0.30320007	No
IL7R	interleukin 7 receptor	−0.30657914	No
MAFF	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)	−0.31840307	No
RELA	v-rel reticuloendotheliosis viral oncogene homolog A, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3, p65 (avian)	−0.32651395	No
ABCA1	ATP-binding cassette, sub-family A (ABC1), member 1	−0.33476061	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
PNRC1	proline-rich nuclear receptor coactivator 1	−0.3378354	No
NFAT5	nuclear factor of activated T-cells 5, tonicity-responsive	−0.33818045	No
DUSP5	dual specificity phosphatase 5	−0.3400479	No
NINJ1	ninjurin 1	−0.37850687	No
KLF9	Kruppel-like factor 9	−0.39027402	No
MCL1	myeloid cell leukemia sequence 1 (BCL2-related)	−0.40117186	No
HES1	hairy and enhancer of split 1, (Drosophila)	−0.40132076	No
LITAF	lipopolysaccharide-induced TNF factor	−0.40729272	No
CEBPB	CCAAT/enhancer binding protein (C/EBP), beta	−0.41097072	No
CD44	CD44 molecule (Indian blood group)	−0.41463488	No
SPSB1	splA/ryanodine receptor domain and SOCS box containing 1	−0.42047217	No
PFKFB3	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	−0.43228999	No
PPP1R15A	protein phosphatase 1, regulatory (inhibitor) subunit 15A	−0.43424553	No
BIRC2	baculoviral IAP repeat-containing 2	−0.4354732	No
TSC22D1	TSC22 domain family, member 1	−0.43681926	No
SOCS3	suppressor of cytokine signaling 3	−0.44126242	No
ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	−0.44699806	No
TUBB2A	tubulin, beta 2A	−0.47803786	No
EGR1	early growth response 1	−0.48577189	No
IER3	immediate early response 3	−0.49368548	No
EFNA1	ephrin-A1	−0.4986856	No
CD83	CD83 molecule	−0.50458539	No
SQSTM1	sequestosome 1	−0.50716919	No
B4GALT1	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 1	−0.51576161	No
IL18	interleukin 18 (interferon-gamma-inducing factor)	−0.5164243	No
KLF2	Kruppel-like factor 2 (lung)	−0.519408047	No
CYR61	cysteine-rich, angiogenic inducer, 61	−0.564450562	No
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	−0.578493118	No
CSF2	colony stimulating factor 2 (granulocyte-macrophage)	−0.624059618	No
IER2	immediate early response 2	−0.680687428	No
YRDC	yrdC domain containing (*E. coli*)	−0.685481429	No
SDC4	syndecan 4 (amphiglycan, ryudocan)	−0.915015876	No
ZFP36	zinc finger protein 36, C3H type, homolog (mouse)	−0.918698609	No
MSC	musculin (activated B-cell factor-1)	−1.425963402	No
JUNB	jun B proto-oncogene	−1.767692924	No
	HALLMARK_IL2_STATS_SIGNALING		
SELL	selectin L (lymphocyte adhesion molecule 1)	4.533662319	Yes
MUC1	mucin 1, cell surface associated	2.119087458	Yes
TNFRSF9	tumor necrosis factor receptor superfamily, member 9	2.029400826	Yes
SERPINC1	serpin peptidase inhibitor, clade C (antithrombin), member 1	2.011505842	Yes
AHCY	S-adenosylhomocysteine hydrolase	1.540450335	Yes
IL1RL1	interleukin 1 receptor-like 1	1.417232871	Yes
BATF	basic leucine zipper transcription factor, ATF-like	1.339311957	Yes
GPR65	G protein-coupled receptor 65	1.301272631	Yes
TRAF1	TNF receptor-associated factor 1	1.300272942	Yes
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B	1.259392858	Yes
ENO3	enolase 3 (beta, muscle)	1.107318997	Yes
CCNE1	cyclin E1	1.016289473	Yes
IRF8	interferon regulatory factor 8	0.984531879	Yes
SLC29A2	solute carrier family 29 (nucleoside transporters), member 2	0.945622802	Yes
RHOH	ras homolog gene family, member H	0.934723258	Yes
SOCS1	suppressor of cytokine signaling 1	0.912176847	Yes
CD79B	CD79b molecule, immunoglobulin-associated beta	0.805104673	Yes
IL10	interleukin 10	0.777381659	Yes
CTLA4	cytotoxic T-lymphocyte-associated protein 4	0.773720741	Yes
PLSCR1	phospholipid scramblase 1	0.761682391	Yes
TLR7	toll-like receptor 7	0.725582063	Yes
IL13	interleukin 13	0.6945768	Yes
CD86	CD86 molecule	0.631752431	Yes
LTB	lymphotoxin beta (TNF superfamily, member 3)	0.579620421	Yes
ETV4	ets variant gene 4 (E1A enhancer binding protein, E1AF)	0.579223096	Yes
MAP6	microtubule-associated protein 6	0.574204385	Yes

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
CDC6	CDC6 cell division cycle 6 homolog (*S. cerevisiae*)	0.569661617	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
CD48	CD48 molecule	0.540921032	Yes
APLP1	amyloid beta (A4) precursor-like protein 1	0.531183481	Yes
RGS16	regulator of G-protein signalling 16	0.526294231	Yes
ICOS	inducible T-cell co-stimulator	0.480524778	No
SHE	Src homology 2 domain containing E	0.421151727	No
AGER	advanced glycosylation end product-specific receptor	0.402864873	No
TNFSF11	tumor necrosis factor (ligand) superfamily, member 11	0.372757733	No
SLC39A8	solute carrier family 39 (zinc transporter), member 8	0.364194393	No
IL10RA	interleukin 10 receptor, alpha	0.343504012	No
GPX4	glutathione peroxidase 4 (phospholipid hydroperoxidase)	0.319138467	No
SPP1	secreted phosphoprotein 1 (osteopontin, bone sialoprotein I, early T-lymphocyte activation 1)	0.311187059	No
GALM	galactose mutarotase (aldose 1-epimerase)	0.300109804	No
PRAF2	PRA1 domain family, member 2	0.275571346	No
UMPS	uridine monophosphate synthetase (orotate phosphoribosyl transferase and orotidine-5'-decarboxylase)	0.234596103	No
TNFRSF8	tumor necrosis factor receptor superfamily, member	0.232401714	No
SPRY4	sprouty homolog 4 (Drosophila)	0.231738269	No
PHLDA1	pleckstrin homology-like domain, family A, member 1	0.226918563	No
CXCL10	chemokine (C-X-C motif) ligand 10	0.226761773	No
LRRC8C	leucine rich repeat containing 8 family, member C	0.22627607	No
CST7	cystatin F (leukocystatin)	0.22475262	No
CASP3	caspase 3, apoptosis-related cysteine peptidase	0.213040709	No
NFIL3	nuclear factor, interleukin 3 regulated	0.181677267	No
AKAP2	A kinase (PRKA) anchor protein 2	0.180033192	No
SELP	selectin P (granule membrane protein 140kDa, antigen CD62)	0.175435156	No
AMACR	alpha-methylacyl-CoA racemase	0.139369324	No
ST3GAL4	ST3 beta-galactoside alpha-2,3-sialyltransferase 4	0.134488985	No
GBP4	guanylate binding protein 4	0.095500618	No
P4HA1	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide I	0.09174899	No
SYT11	synaptotagmin XI	0.088011898	No
XBP1	X-box binding protein 1	0.087087706	No
ADAM19	ADAM metallopeptidase domain 19 (meltrin beta)	0.073120117	No
SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	0.069677271	No
PENK	proenkephalin	0.058247235	No
CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	0.05285516	No
SWAP70	—	0.047020242	No
PLAGL1	pleiomorphic adenoma gene-like 1	0.045933478	No
PRKCH	protein kinase C, eta	0.043467484	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
SNX9	sorting nexin 9	0.031658247	No
F2RL2	coagulation factor II (thrombin) receptor-like 2	0.016297607	No
ENPP1	ectonucleotide pyrophosphatase/phosphodiesterase 1	0.012228195	No
IL3RA	interleukin 3 receptor, alpha (low affinity)	0.007537159	No
P2RX4	purinergic receptor P2X, ligand-gated ion channel, 4	0.002422775	No
TNFRSF4	tumor necrosis factor receptor superfamily, member 4	−0.00651959	No
FGL2	fibrinogen-like 2	−0.00713548	No
ITGA6	integrin, alpha 6	−0.00743946	No
PTGER2	prostaglandin E receptor 2 (subtype EP2), 53kDa	−0.01937426	No
GADD45B	growth arrest and DNA-damage-inducible, beta	−0.03472245	No
PTCH1	patched homolog 1 (Drosophila)	−0.06307594	No
BCL2	B-cell CLL/lymphoma 2	−0.06359753	No
IKZF4	IKAROS family zinc finger 4 (Eos)	−0.07420553	No
TNFRSF21	tumor necrosis factor receptor superfamily, member 21	−0.09369773	No
POU2F1	POU domain, class 2, transcription factor 1	−0.09776106	No
TIAM1	T-cell lymphoma invasion and metastasis 1	−0.09797619	No
NFKBIZ	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	−0.10177696	No
RABGAP1L	RAB GTPase activating protein 1-like	−0.1046719	No
SOCS2	suppressor of cytokine signaling 2	−0.10708491	No
FURIN	furin (paired basic amino acid cleaving enzyme)	−0.10786293	No
NRP1	neuropilin 1	−0.10988839	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
AHNAK	AHNAK nucleoprotein (desmoyokin)	−0.12126806	No
IGF1R	insulin-like growth factor 1 receptor	−0.12401183	No
DHRS3	dehydrogenase/reductase (SDR family) member 3	−0.12833633	No
ALCAM	activated leukocyte cell adhesion molecule	−0.12868702	No
RORA	RAR-related orphan receptor A	−0.13175237	No
BMP2	bone morphogenetic protein 2	−0.14009446	No
ARL4A	ADP-ribosylation factor-like 4A	−0.14104421	No
SLC1A5	solute carrier family 1 (neutral amino acid transporter), member 5	−0.14482026	No
NCOA3	nuclear receptor coactivator 3	−0.14673433	No
HIPK2	homeodomain interacting protein kinase 2	−0.14735302	No
CYFIP1	cytoplasmic FMR1 interacting protein 1	−0.15203957	No
KLF6	Kruppel-like factor 6	−0.16283926	No
NDRG1	N-myc downstream regulated gene 1	−0.16343482	No
SH3BGRL2	SH3 domain binding glutamic acid-rich protein like 2	−0.16945736	No
MXD1	MAX dimerization protein 1	−0.16998833	No
NT5E	5'-nucleotidase, ecto (CD73)	−0.17018586	No
CDCP1	CUB domain containing protein 1	−0.17038067	No
CCND2	cyclin D2	−0.17259452	No
IFNGR1	interferon gamma receptor 1	−0.18188992	No
TGM2	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	−0.18499345	No
CDC42SE2	CDC42 small effector 2	−0.19735253	No
BMPR2	bone morphogenetic protein receptor, type II (serine/threonine kinase)	−0.2040211	No
PTRH2	peptidyl-tRNA hydrolase 2	−0.20548932	No
PDCD2L	programmed cell death 2-like	−0.20793679	No
MAP3K8	mitogen-activated protein kinase kinase kinase 8	−0.2093222	No
SPRED2	sprouty-related, EVH1 domain containing 2	−0.21080628	No
ITGAV	integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	−0.21208024	No
AHR	aryl hydrocarbon receptor	−0.21279255	No
IGF2R	insulin-like growth factor 2 receptor	−0.21324262	No
PIM1	pim-1 oncogene	−0.21471494	No
IL1R2	interleukin 1 receptor, type II	−0.21576229	No
SNX14	sorting nexin 14	−0.22292101	No
DCPS	decapping enzyme, scavenger	−0.22333506	No
COL6A1	collagen, type VI, alpha 1	−0.2306418	No
SMPDL3A	sphingomyelin phosphodiesterase, acid-like 3A	−0.2336476	No
PUS1	pseudouridylate synthase 1	−0.23526376	No
RHOB	ras homolog gene family, member B	−0.25625306	No
BCL2L1	BCL2-like 1	−0.26874608	No
IRF6	interferon regulatory factor 6	−0.26956779	No
MYO1E	myosin IE	−0.27304026	No
IRF4	interferon regulatory factor 4	−0.28187907	No
IKZF2	IKAROS family zinc finger 2 (Helios)	−0.28325367	No
HK2	hexokinase 2	−0.29201287	No
TNFRSF18	tumor necrosis factor receptor superfamily, member 18	−0.29958081	No
HUWE1	HECT, UBA and WWE domain containing 1	−0.30141243	No
S100A1	S100 calcium binding protein A1	−0.30719495	No
IL2RB	interleukin 2 receptor, beta	−0.31792504	No
MAFF	v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian)	−0.31840307	No
ITGAE	integrin, alpha E (antigen CD103, human mucosal lymphocyte antigen 1; alpha polypeptide)	−0.32581159	No
TWSG1	twisted gastrulation homolog 1 (Drosophila)	−0.3268795	No
ECM1	extracellular matrix protein 1	−0.32777062	No
ITIH5	inter-alpha (globulin) inhibitor H5	−0.32929945	No
MAPKAPK2	mitogen-activated protein kinase-activated protein kinase 2	−0.33747	No
GATA1	GATA binding protein 1 (globin transcription factor 1)	−0.34819636	No
COCH	coagulation factor C homolog, cochlin (Limulus polyphemus)	−0.35349667	No
FAM126B	family with sequence similarity 126, member B	−0.37080041	No
GABARAPL1	GABA(A) receptor-associated protein like 1	−0.37952036	No
UCK2	uridine-cytidine kinase 2	−0.39549923	No
CISH	cytokine inducible SH2-containing protein	−0.40262353	No
CTSZ	cathepsin Z	−0.41291174	No
CD44	CD44 molecule (Indian blood group)	−0.41463488	No
LRIG1	leucine-rich repeats and immunoglobulin-like domains 1	−0.41774288	No
IL2RA	interleukin 2 receptor, alpha	−0.42295557	No

TABLE 6-continued

Gene List in gene sets of enriched pathway in Table 4.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
PHTF2	putative homeodomain transcription factor 2	−0.43087524	No
FAH	fumarylacetoacetate hydrolase (fumarylacetoacetase)	−0.43588102	No
CCND3	cyclin D3	−0.43643126	No
MYO1C	myosin IC	−0.44808453	No
ODC1	ornithine decarboxylase 1	−0.46056387	No
ANXA4	annexin A4	−0.47317448	No
CD83	CD83 molecule	−0.50458539	No
CKAP4	cytoskeleton-associated protein 4	−0.51768428	No
MYC	v-myc myelocytomatosis viral oncogene homolog (avian)	−0.57849312	No
CD81	CD81 molecule	−0.58255219	No
CSF2	colony stimulating factor 2 (granulocyte-macrophage)	−0.62405962	No
CAPN3	calpain 3, (p94)	−0.63329792	No
SYNGR2	synaptogyrin 2	−0.63514042	No
GUCY1B3	guanylate cyclase 1, soluble, beta 3	−0.64079314	No
CCR4	chemokine (C-C motif) receptor 4	−0.64653838	No
PRNP	prion protein (p27-30) (Creutzfeldt-Jakob disease, Gerstmann-Strausler-Scheinker syndrome, fatal familial insomnia)	−0.76452804	No
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10	−0.78845328	No
IL18R1	interleukin 18 receptor 1	−0.81675339	No
CAPG	capping protein (actin filament), gelsolin-like	−0.91523647	No
EMP1	epithelial membrane protein 1	−0.96930897	No
IFITM3	interferon induced transmembrane protein 3 (I-8U)	−1.08716643	No
GSTO1	glutathione S-transferase omega 1	−1.18441701	No
RNH1	ribonuclease/angiogenin inhibitor 1	−1.19759107	No
RRAGD	Ras-related GTP binding D	−1.36585367	No

TABLE 7

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
	HALLMARK_INFLAMMATORY_RESPONSE		
PPBP	pro-platelet basic protein (chemokine (C-X-C motif) ligand 7)	3.837641716	Yes
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
CCL1	chemokine (C-C motif) ligand 1	3.329092503	Yes
IL18RAP	interleukin 18 receptor accessory protein	3.251766205	Yes
CSF3R	colony stimulating factor 3 receptor (granulocyte)	3.238983631	Yes
OSM	oncostatin M	2.948629141	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	2.667189121	Yes
CCR1	chemokine (C-C motif) receptor 1	2.132987738	Yes
CCR5	chemokine (C-C motif) receptor 5	2.054755688	Yes
TNFRSF9	tumor necrosis factor receptor superfamily, member 9	2.029400826	Yes
CXCL2	chemokine (C-X-C motif) ligand 2	1.990867496	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
CXCL5	chemokine (C-X-C motif) ligand 5	1.754894018	Yes
CCL3	chemokine (C-C motif) ligand 3	1.564267635	Yes
TNFSF8	tumor necrosis factor (ligand) superfamily, member 8	1.533434033	Yes
TNFSF14	tumor necrosis factor (ligand) superfamily, member 14	1.530670643	Yes
TPO	thyroid peroxidase	1.496503949	Yes
CCL22	chemokine (C-C motif) ligand 22	1.440871716	Yes
CSF3	colony stimulating factor 3 (granulocyte)	1.422928095	Yes
IL21R	interleukin 21 receptor	1.375825167	Yes

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	1.315529704	Yes
CCL4	chemokine (C-C motif) ligand 4	1.303452969	Yes
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B	1.259392858	Yes
CCL24	chemokine (C-C motif) ligand 24	1.233121157	Yes
CCR2	chemokine (C-C motif) receptor 2	1.17247808	Yes
IL2RG	interleukin 2 receptor, gamma (severe combined immunodeficiency)	1.083326221	Yes
IFNK	interferon, kappa	0.981288373	Yes
TNFRSF13B	tumor necrosis factor receptor superfamily, member 13B	0.980329454	Yes
CXCL3	chemokine (C-X-C motif) ligand 3	0.966697574	Yes
XCR1	chemokine (C motif) receptor 1	0.960530758	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
CSF2RB	colony stimulating factor 2 receptor, beta, low-affinity (granulocyte-macrophage)	0.888966024	Yes
IL24	interleukin 24	0.877363384	Yes
IL23A	interleukin 23, alpha subunit p19	0.838799894	Yes
IL17B	interleukin 17B	0.823239386	Yes
AMH	anti-Mullerian hormone	0.818140507	Yes
CSF2RA	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	0.78864789	Yes
CCL19	chemokine (C-C motif) ligand 19	0.784207284	Yes
IL10	interleukin 10	0.777381659	Yes
TNFSF9	tumor necrosis factor (ligand) superfamily, member 9	0.771818101	Yes
CCL25	chemokine (C-C motif) ligand 25	0.763763368	Yes
CRLF2	cytokine receptor-like factor 2	0.754059553	Yes
IL19	interleukin 19	0.750038803	Yes
CCR9	chemokine (C-C motif) receptor 9	0.745218694	Yes
IL17A	interleukin 17A	0.707072496	Yes
IL13	interleukin 13	0.6945768	Yes
TNFSF4	tumor necrosis factor (ligand) superfamily, member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa)	0.689626753	Yes
IL11	interleukin 11	0.684957564	Yes
CCL17	chemokine (C-C motif) ligand 17	0.664499223	Yes
IL4	interleukin 4	0.65638262	Yes
TNFRSF10B	tumor necrosis factor receptor superfamily, member 10b	0.651966751	Yes
CCL20	chemokine (C-C motif) ligand 20	0.625092983	Yes
VEGFC	vascular endothelial growth factor C	0.620482028	Yes
CCR7	chemokine (C-C motif) receptor 7	0.594285488	Yes
LTB	lymphotoxin beta (TNF superfamily, member 3)	0.579620421	Yes
CNTFR	ciliary neurotrophic factor receptor	0.557358146	Yes
IL20RB	interleukin 20 receptor beta	0.556012034	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
CD40	CD40 molecule, TNF receptor superfamily member 5	0.492939293	Yes
CXCR4	chemokine (C-X-C motif) receptor 4	0.484079331	Yes
TSLP	—	0.474735647	Yes
CX3CR1	chemokine (C-X3-C motif) receptor 1	0.444680154	Yes
LTA	lymphotoxin alpha (TNF superfamily, member 1)	0.44320941	Yes
FLT4	fms-related tyrosine kinase 4	0.435430467	Yes
CXCL9	chemokine (C-X-C motif) ligand 9	0.391491205	No
CXCR3	chemokine (C-X-C motif) receptor 3	0.380579948	No
TNFSF11	tumor necrosis factor (ligand) superfamily, member 11	0.372757733	No
CCL28	chemokine (C-C motif) ligand 28	0.358908564	No
IL10RA	interleukin 10 receptor, alpha	0.343504012	No
TNFRSF25	tumor necrosis factor receptor superfamily, member 25	0.331647813	No
IFNAR2	interferon (alpha, beta and omega) receptor 2	0.281477422	No
INHBA	inhibin, beta A (activin A, activin AB alpha polypeptide)	0.280317694	No

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
CLCF1	cardiotrophin-like cytokine factor 1	0.26978004	No
CCL7	chemokine (C-C motif) ligand 7	0.251811057	No
PDGFRA	platelet-derived growth factor receptor, alpha polypeptide	0.249525964	No
TNFRSF8	tumor necrosis factor receptor superfamily, member 8	0.232401714	No
CXCL10	chemokine (C-X-C motif) ligand 10	0.226761773	No
ACVRL1	activin A receptor type II-like 1	0.211801216	No
OSMR	oncostatin M receptor	0.207781732	No
FAS	Fas (TNF receptor superfamily, member 6)	0.173293099	No
TNFRSF11A	tumor necrosis factor receptor superfamily, member 11a, NFKB activator	0.15901272	No
TNFRSF14	tumor necrosis factor receptor superfamily, member 14 (herpesvirus entry mediator)	0.15240927	No
KDR	kinase insert domain receptor (a type III receptor tyrosine kinase)	0.150256053	No
TGFB1	transforming growth factor, beta 1 (Camurati-Engelmann disease)	0.120179698	No
TNFSF12	tumor necrosis factor (ligand) superfamily, member 12	0.112915978	No
HGF	hepatocyte growth factor (hepapoietin A; scatter factor)	0.098659903	No
IL25	interleukin 25	0.094349928	No
IL15RA	interleukin 15 receptor, alpha	0.084517181	No
CXCL11	chemokine (C-X-C motif) ligand 11	0.079039596	No
EDA	ectodysplasin A	0.07362695	No
CXCL12	chemokine (C-X-C motif) ligand 12 (stromal cell-derived factor 1)	0.070668168	No
IFNAR1	interferon (alpha, beta and omega) receptor 1	0.059620846	No
FLT1	fms-related tyrosine kinase 1 (vascular endothelial growth factor/vascular permeability factor receptor)	0.050929114	No
IFNGR2	interferon gamma receptor 2 (interferon gamma transducer 1)	0.046017136	No
PDGFRB	platelet-derived growth factor receptor, beta polypeptide	0.045934543	No
CSF1	colony stimulating factor 1 (macrophage)	0.042810541	No
CCL11	chemokine (C-C motif) ligand 11	0.039969306	No
CXCR6	chemokine (C-X-C motif) receptor 6	0.031615365	No
IL17RB	interleukin 17 receptor B	0.030075336	No
TGFBR1	transforming growth factor, beta receptor I (activin A receptor type II-like kinase, 53kDa)	0.027430039	No
PRLR	prolactin receptor	0.015084264	No
IL3RA	interleukin 3 receptor, alpha (low affinity)	0.007537159	No
TNFRSF17	tumor necrosis factor receptor superfamily, member 17	7.15E−04	No
TNFRSF4	tumor necrosis factor receptor superfamily, member 4	−0.006519591	No
ACVR1	activin A receptor, type I	−0.006812894	No
TNFSF13B	tumor necrosis factor (ligand) superfamily, member 13b	−0.012086863	No
CCR3	chemokine (C-C motif) receptor 3	−0.012453511	No
IL22RA2	interleukin 22 receptor, alpha 2	−0.022728374	No
FLT3	fms-related tyrosine kinase 3	−0.036438417	No
INHBB	inhibin, beta B (activin AB beta polypeptide)	−0.043366853	No
IL15	interleukin 15	−0.045024838	No
CXCL13	chemokine (C-X-C motif) ligand 13 (B-cell chemoattractant)	−0.045578849	No
CCR10	chemokine (C-C motif) receptor 10	−0.047813334	No
IL12RB1	interleukin 12 receptor, beta 1	−0.050351642	No
IL1R1	interleukin 1 receptor, type I	−0.051485192	No
CCR8	chemokine (C-C motif) receptor 8	−0.062265944	No
TGFB3	transforming growth factor, beta 3	−0.069080003	No
IL9R	interleukin 9 receptor	−0.072577946	No
KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	−0.07663402	No
IL23R	interleukin 23 receptor	−0.083718598	No

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
TNFRSF21	tumor necrosis factor receptor superfamily, member 21	−0.093697727	No
NGFR	nerve growth factor receptor (TNFR superfamily, member 16)	−0.105525017	No
IL1RAP	interleukin 1 receptor accessory protein	−0.112636082	No
BMPR1B	bone morphogenetic protein receptor, type IB	−0.112772785	No
CCR6	chemokine (C-C motif) receptor 6	−0.119453743	No
GDF5	growth differentiation factor 5 (cartilage-derived morphogenetic (protein-1)	−0.139077023	No
BMP2	bone morphogenetic protein 2	−0.140094459	No
TNFRSF19	tumor necrosis factor receptor superfamily, member 19	−0.163563892	No
EGFR	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	−0.164786458	No
BMPR1A	bone morphogenetic protein receptor, type IA	−0.169454694	No
IL17RA	interleukin 17 receptor A	−0.178499535	No
IFNGR1	interferon gamma receptor 1	−0.181889921	No
CXCL16	chemokine (C-X-C motif) ligand 16	−0.20063293	No
BMPR2	bone morphogenetic protein receptor, type II (serine/threonine kinase)	−0.204021096	No
AMHR2	anti-Mullerian hormone receptor, type II	−0.204355285	No
CSF1R	colony stimulating factor 1 receptor, formerly McDonough feline sarcoma viral (v-fms) oncogene homolog	−0.204763398	No
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	−0.206245229	No
IL1R2	interleukin 1 receptor, type II	−0.215762287	No
PDGFC	platelet derived growth factor C	−0.219196126	No
CX3CL1	chemokine (C-X3-C motif) ligand 1	−0.225086227	No
MET	met proto-oncogene (hepatocyte growth factor receptor)	−0.225270301	No
ILIA	interleukin 1, alpha	−0.228820771	No
TGFB2	transforming growth factor, beta 2	−0.233885586	No
PDGFB	platelet-derived growth factor beta polypeptide (simian sarcoma viral (v-sis) oncogene homolog)	−0.238625541	No
IL22RA1	interleukin 22 receptor, alpha 1	−0.240860581	No
GHR	growth hormone receptor	−0.260692686	No
IL10RB	interleukin 10 receptor, beta	−0.264194787	No
ACVR2A	activin A receptor, type IIA	−0.265007794	No
ACVR1B	activin A receptor, type IB	−0.291109085	No
IL20RA	interleukin 20 receptor, alpha	−0.291834027	No
PDGFA	platelet-derived growth factor alpha polypeptide	−0.293814242	No
TNFRSF11B	tumor necrosis factor receptor superfamily, member 11b (osteoprotegerin)	−0.294232696	No
TGFBR2	transforming growth factor, beta receptor II (70/80kDa)	−0.298537552	No
TNFRSF18	tumor necrosis factor receptor superfamily, member 18	−0.299580812	No
IL7R	interleukin 7 receptor	−0.306579143	No
VEGFB	vascular endothelial growth factor B	−0.315350085	No
IL2RB	interleukin 2 receptor, beta	−0.317925036	No
LIFR	leukemia inhibitory factor receptor alpha	−0.331205487	No
EDA2R	ectodysplasin A2 receptor	−0.346847653	No
EDAR	ectodysplasin A receptor	−0.348729432	No
CXCL14	chemokine (C-X-C motif) ligand 14	−0.354058266	No
CNTF	ciliary neurotrophic factor	−0.355169892	No
IL7	interleukin 7	−0.356599182	No
CTF1	cardiotrophin 1	−0.382776916	No
EPOR	erythropoietin receptor	−0.407475233	No
IL13RA1	interleukin 13 receptor, alpha 1	−0.419134021	No
IL2RA	interleukin 2 receptor, alpha	−0.422955573	No
LEPR	leptin receptor	−0.489379466	No
BMP7	bone morphogenetic protein 7 (osteogenic protein 1)	−0.494219154	No
IL12RB2	interleukin 12 receptor, beta 2	−0.511588156	No

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
TNFRSF12A	tumor necrosis factor receptor superfamily, member 12A	−0.511856139	No
IL18	interleukin 18 (interferon-gamma-inducing factor)	−0.516424298	No
IL20	interleukin 20	−0.517831087	No
MPL	myeloproliferative leukemia virus oncogene	−0.612580657	No
CSF2	colony stimulating factor 2 (granulocyte-macrophage)	−0.624059618	No
CCR4	chemokine (C-C motif) receptor 4	−0.646538377	No
TNFSF15	tumor necrosis factor (ligand) superfamily, member 15	−0.652678192	No
LEP	leptin (obesity homolog, mouse)	−0.674438477	No
LTBR	lymphotoxin beta receptor (TNFR superfamily, member 3)	−0.674648285	No
PF4	platelet factor 4 (chemokine (C-X-C motif) ligand 4)	−0.685499907	No
XCL1	chemokine (C motif) ligand 1	−0.706809223	No
TNFSF13	tumor necrosis factor (ligand) superfamily, member 13	−0.743143797	No
IL5	interleukin 5 (colony-stimulating factor, eosinophil)	−0.77403909	No
TNFSF18	tumor necrosis factor (ligand) superfamily, member 18	−0.779219151	No
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10	−0.788453281	No
IL18R1	interleukin 18 receptor 1	−0.816753387	No
TNFRSF1A	tumor necrosis factor receptor superfamily, member 1A	−0.969310343	No
EGF	epidermal growth factor (beta-urogastrone)	−1.048612952	No
TNFRSF13C	tumor necrosis factor receptor superfamily, member 13C	−1.065307021	No
ACVR2B	activin A receptor, type IIB	−1.067408323	No
	KEGG_HEMATOPOIETIC_CELL_LINEAGE		
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
IL18RAP	interleukin 18 receptor accessory protein	3.251766205	Yes
STAT4	signal transducer and activator of transcription 4	3.148304939	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	2.667121887	Yes
CCR1	chemokine (C-C motif) receptor 1	2.132987738	Yes
CCR5	chemokine (C-C motif) receptor 5	2.054755688	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
ITGAL	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	1.800091743	Yes
CD7	CD7 molecule	1.628337383	Yes
FGR	Gardner-Rasheed feline sarcoma viral (v-fgr) oncogene homolog	1.552860975	Yes
CCL22	chemokine (C-C motif) ligand 22	1.440871716	Yes
TLR1	toll-like receptor 1	1.34019506	Yes
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	1.315529704	Yes
CCL4	chemokine (C-C motif) ligand 4	1.303452969	Yes
GPR65	G protein-coupled receptor 65	1.301272631	Yes
CCR2	chemokine (C-C motif) receptor 2	1.17247808	Yes
PRF1	perforin 1 (pore forming protein)	1.171788573	Yes
IGSF6	immunoglobulin superfamily, member 6	1.100607872	Yes
LYN	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	1.097683549	Yes
LCP2	lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	1.090578794	Yes
IL2RG	interleukin 2 receptor, gamma (severe combined immunodeficiency)	1.083326221	Yes
DYRK3	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 3	1.04365015	Yes

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
IRF8	interferon regulatory factor 8	0.984531879	Yes
TLR6	toll-like receptor 6	0.974328399	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
SOCS1	suppressor of cytokine signaling 1	0.912176847	Yes
FYB	FYN binding protein (FYB-120/130)	0.841911793	Yes
STAB1	stabilin 1	0.800862968	Yes
CCL19	chemokine (C-C motif) ligand 19	0.784207284	Yes
ITGB2	integrin, beta 2 (complement component 3 receptor 3 and 4 subunit)	0.783176661	Yes
IL10	interleukin 10	0.777381659	Yes
BCL3	B-cell CLL/lymphoma 3	0.768477619	Yes
ICAM1	intercellular adhesion molecule 1 (CD54), human rhinovirus receptor	0.746375382	Yes
MMP9	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	0.740974486	Yes
IL13	interleukin 13	0.6945768	Yes
IL11	interleukin 11	0.684957564	Yes
TLR2	toll-like receptor 2	0.671268702	Yes
GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2 (beta-1,6-N-acetylglucosaminyltransferase)	0.671001792	Yes
IL4	interleukin 4	0.65638262	Yes
CDKN2A	cyclin-dependent kinase inhibitor 2A (melanoma, p16, inhibits CDK4)	0.650471985	Yes
CD86	CD86 molecule	0.631752431	Yes
CD80	CD80 molecule	0.600226164	Yes
LTB	lymphotoxin beta (TNF superfamily, member 3)	0.579620421	Yes
LIF	leukemia inhibitory factor (cholinergic differentiation factor)	0.547570944	Yes
WAS	Wiskott-Aldrich syndrome (eczema-thrombocytopenia)	0.525824308	Yes
PTPRC	protein tyrosine phosphatase, receptor type, C	0.522265971	Yes
RPS19	ribosomal protein S19	0.506382108	Yes
CD40	CD40 molecule, TNF receptor superfamily member 5	0.492939293	Yes
NCF4	neutrophil cytosolic factor 4, 40kDa	0.465533584	Yes
LY86	lymphocyte antigen 86	0.449851602	Yes
FCGR2B	Fc fragment of IgG, low affinity IIb, receptor (CD32)	0.436047524	Yes
HCLS1	hematopoietic cell-specific Lyn substrate 1	0.427405208	Yes
CD3D	CD3d molecule, delta (CD3-TCR complex)	0.415081888	Yes
CXCL9	chemokine (C-X-C motif) ligand 9	0.391491205	Yes
CXCR3	chemokine (C-X-C motif) receptor 3	0.380579948	Yes
BRCA1	breast cancer 1, early onset	0.38035053	Yes
RPL9	ribosomal protein L9	0.372396767	Yes
	KEGG_RIBOSOME		
RPL17	ribosomal protein L17	1.672627926	Yes
RPL29	ribosomal protein L29	1.535640955	Yes
RPS21	ribosomal protein S21	1.305340767	Yes
RPS16	ribosomal protein S16	1.209875584	Yes
RPL7	ribosomal protein L7	1.179243684	Yes
RPS6	ribosomal protein S6	0.962560833	Yes
RPL35	ribosomal protein L35	0.879049003	Yes
RPL38	ribosomal protein L38	0.852828383	Yes
RPL11	ribosomal protein L11	0.769688666	Yes
RPL4	ribosomal protein L4	0.757808089	Yes
RPL32	ribosomal protein L32	0.755478978	Yes
RP515	ribosomal protein S15	0.75469929	Yes
RPL14	ribosomal protein L14	0.718787491	Yes
RPS25	ribosomal protein S25	0.702086389	Yes
RPL24	ribosomal protein L24	0.687731743	Yes
RPS8	ribosomal protein S8	0.68595165	Yes
RPS24	ribosomal protein S24	0.663855553	Yes
RPL21	ribosomal protein L21	0.640351593	Yes

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
RPS28	ribosomal protein S28	0.610872269	Yes
FAU	Finkel-Biskis-Reilly murine sarcoma virus (FBR-MuSV) ubiquitously expressed (fox derived); ribosomal protein S30	0.550771177	Yes
RPS5	ribosomal protein S5	0.538966238	Yes
RPL34	ribosomal protein L34	0.533506274	Yes
RPLPO	ribosomal protein, large, P0	0.522892892	Yes
RPL6	ribosomal protein L6	0.506569028	Yes
RPS19	ribosomal protein S19	0.506382108	Yes
RPS27A	ribosomal protein S27a	0.483083695	Yes
RPL7A	ribosomal protein L7a	0.443502933	Yes
RPL13	ribosomal protein L13	0.387363732	Yes
RPS13	ribosomal protein S13	0.383430898	Yes
RPLP2	ribosomal protein, large, P2	0.374124438	Yes
RPL9	ribosomal protein L9	0.372396767	Yes
RPS18	ribosomal protein S18	0.335394561	Yes
RPS15A	ribosomal protein S15a	0.329340279	Yes
RPL35A	ribosomal protein L35a	0.322530985	Yes
RPL37	ribosomal protein L37	0.275145084	Yes
RPL22L1	ribosomal protein L22-like 1	0.273913294	Yes
RPL30	ribosomal protein L30	0.266558886	Yes
RPL23A	ribosomal protein L23a	0.26068905	Yes
RPS7	ribosomal protein S7	0.257175088	Yes
RPS2	ribosomal protein S2	0.256049454	Yes
RPL18A	ribosomal protein L18a	0.228949845	Yes
RPS20	ribosomal protein S20	0.214455262	Yes
RPL36A	ribosomal protein L36a	0.185356036	Yes
RPS29	ribosomal protein S29	0.179608196	Yes
RPL12	ribosomal protein L12	0.177713573	Yes
RPS3	ribosomal protein S3	0.166580707	Yes
RPS26	ribosomal protein S26	0.166472122	Yes
RPL22	ribosomal protein L22	0.165959805	Yes
RPS17	ribosomal protein S17	0.152504608	Yes
RPL37A	ribosomal protein L37a	0.151727423	Yes
RPL39	ribosomal protein L39	0.145141497	Yes
RPS27	ribosomal protein S27 (metallopanstimulin 1)	0.138581008	Yes
RPL10	ribosomal protein L10	0.114015959	No
RPSA	ribosomal protein SA	0.113453649	No
RPS4X	ribosomal protein S4, X-linked	0.107207999	No
RPS12	ribosomal protein S12	0.095793545	No
RPL13A	ribosomal protein L13a	0.094446741	No
RPL27A	ribosomal protein L27a	0.065862156	No
RPL28	ribosomal protein L28	0.041829564	No
RPL5	ribosomal protein L5	0.024316726	No
RPL23	ribosomal protein L23	−0.010726028	No
RPS27L	ribosomal protein S27-like	−0.061738685	No
RPL31	ribosomal protein L31	−0.072339609	No
RPL3	ribosomal protein L3	−0.090979747	No
RPS23	ribosomal protein S23	−0.110026583	No
RPL10A	ribosomal protein L10a	−0.118189119	No
RPS9	ribosomal protein S9	−0.145742506	No
RPL41	ribosomal protein L41	−0.153432697	No
RPL18	ribosomal protein L18	−0.165799722	No
RPL26	ribosomal protein L26	−0.168741375	No
RPL36AL	ribosomal protein L36a-like	−0.17463319	No
RPS10	ribosomal protein S10	−0.186098009	No
RPL27	ribosomal protein L27	−0.269447058	No
RPS11	ribosomal protein S11	−0.335371464	No
UBA52	ubiquitin A-52 residue ribosomal protein fusion product 1	−0.479723126	No
RPL15	ribosomal protein L15	−0.572703719	No
MRPL13	mitochondrial ribosomal protein L13	−0.590085208	No
RPL8	ribosomal protein L8	−0.731413662	No

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
RPL36	ribosomal protein L36	−0.76863873	No
RPL19	ribosomal protein L19	−1.015113831	No
RPL3L	ribosomal protein L3-like	−1.196903586	No
	KEGG_NOD_LIKE_RECEPTOR_SIGNALING_PATHWAY		
IL1B	interleukin 1, beta	3.462865114	Yes
IL6	interleukin 6 (interferon, beta 2)	3.456357479	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	2.667189121	Yes
MEFV	Mediterranean fever	2.353091955	Yes
CXCL2	chemokine (C-X-C motif) ligand 2	1.990867496	Yes
CCL5	chemokine (C-C motif) ligand 5	1.827621102	Yes
CCL2	chemokine (C-C motif) ligand 2	0.932862163	Yes
CARD6	caspase recruitment domain family, member 6	0.672573209	No
CASP1	caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	0.499731153	No
CCL7	chemokine (C-C motif) ligand 7	0.251811057	No
PSTPIP1	proline-serine-threonine phosphatase interacting protein 1	0.226958573	No
MAPK11	mitogen-activated protein kinase 11	0.193452582	No
TNFAIP3	tumor necrosis factor, alpha-induced protein 3	0.100990877	No
MAPK9	mitogen-activated protein kinase 9	0.090808034	No
CCL11	chemokine (C-C motif) ligand 11	0.039969306	No
MAPK8	mitogen-activated protein kinase 8	0.032760639	No
PYCARD	PYD and CARD domain containing	−0.03229328	No
CASP8	caspase 8, apoptosis-related cysteine peptidase	−0.03536839	No
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	−0.03587324	No
SUGT1	SGT1, suppressor of G2 allele of SKP1 (*S. cerevisiae*)	−0.05679465	No
CARD9	caspase recruitment domain family, member 9	−0.06568909	No
BIRC3	baculoviral IAP repeat-containing 3	−0.06623559	No
MAPK3	mitogen-activated protein kinase 3	−0.12906235	No
TRIP6	thyroid hormone receptor interactor 6	−0.13364181	No
MAPK14	mitogen-activated protein kinase 14	−0.13693111	No
MAP3K7	mitogen-activated protein kinase kinase kinase 7	−0.14027362	No
IKBKB	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase beta	−0.16735205	No
TRAF6	TNF receptor-associated factor 6	−0.17263973	No
MAPK1	mitogen-activated protein kinase 1	−0.17270541	No
RIPK2	receptor-interacting serine-threonine kinase 2	−0.1842809	No
IKBKG	inhibitor of kappa light polypeptide gene enhancer in B-cells, kinase gamma	−0.19543105	No
MAPK10	mitogen-activated protein kinase 10	−0.25465888	No
HSP90AA1	heat shock protein 90kDa alpha (cytosolic), class A member 1	−0.25493035	No
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1 (p105)	−0.25809258	No
CHUK	conserved helix-loop-helix ubiquitous kinase	−0.32112595	No
RELA	v-rel reticuloendotheliosis viral oncogene homolog A, nuclear factor of kappa light polypeptide gene enhancer in B-cells 3, p65 (avian)	−0.32651395	No
HSP90AB1	heat shock protein 90kDa alpha (cytosolic), class B member 1	−0.35596654	No
NFKBIB	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta	−0.40253881	No
MAPK12	mitogen-activated protein kinase 12	−0.41511443	No
BIRC2	baculoviral IAP repeat-containing 2	−0.4354732	No

TABLE 7-continued

Gene List in gene sets of enriched pathway in Table 5.

GENE SYMBOL	GENE_TITLE	RANK METRIC SCORE	CORE ENRICH-MENT
MAPK13	mitogen-activated protein kinase 13	−0.45562434	No
HSP90B1	heat shock protein 90kDa beta (Grp94), member 1	−0.50010961	No
IL18	interleukin 18 (interferon-gamma-inducing factor)	−0.5164243	No
CCL8	chemokine (C-C motif) ligand 8	−1.63008225	No
	KEGG_TYPE_I DIABETES_MELLITUS		
IL1B	interleukin 1, beta	3.462865114	Yes
TNF	tumor necrosis factor (TNF superfamily, member 2)	2.751254082	Yes
GZMB	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	2.667121887	Yes
IL12A	interleukin 12A (natural killer cell stimulatory factor 1, cytotoxic lymphocyte maturation factor 1, p35)	1.315529704	Yes
PRF1	perforin 1 (pore forming protein)	1.171788573	Yes
CD86	CD86 molecule	0.631752431	Yes
CD80	CD80 molecule	0.600226164	Yes
LTA	lymphotoxin alpha (TNF superfamily, member 1)	0.44320941	Yes
CD28	CD28 molecule	0.331128299	No
FAS	Fas (TNF receptor superfamily, member 6)	0.173293099	No
PTPRN	protein tyrosine phosphatase, receptor type, N	0.112962097	No
GAD1	glutamate decarboxylase 1 (brain, 67kDa)	−0.03957521	No
ICA1	islet cell autoantigen 1, 69kDa	−0.0870818	No
ILIA	interleukin 1, alpha	−0.22882077	No
PTPRN2	protein tyrosine phosphatase, receptor type, N polypeptide 2	−0.23292804	No
CPE	carboxypeptidase E	−0.5967598	No
HSPD1	heat shock 60kDa protein 1 (chaperonin)	−0.8842746	No

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[0302] The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description. Such modifications are intended to fall within the scope of the appended claims.

[0303] All patents, applications, publications, test methods, literature, and other materials cited herein are hereby incorporated by reference in their entirety as if physically present in this specification.

SEQUENCE LISTING

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<212> TYPE: PRT
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<400> SEQUENCE: 1

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Gly Gln Met Ser Leu Arg Glu Gly Leu Gly Lys Ile Thr Val Thr Asp
        35                  40                  45

Ile Glu Leu Ala Leu Pro Phe Cys Thr His Leu Leu Tyr Gly Phe Ala
    50                  55                  60

Gly Val Asn Pro Glu Thr Tyr Arg Leu Lys Ala Leu Asp Glu Ser Leu
65                  70                  75                  80

Glu Leu Asp Ser Gly Lys Gly Gln Tyr Arg Leu Ala Thr Thr Leu Lys
                85                  90                  95

Arg Arg Tyr Pro Asn Leu Lys Val Leu Leu Ser Val Gly Gly Tyr Lys
            100                 105                 110
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Ser Ala Gly Ser Arg Thr Ala Phe Val Asn Ser Val Tyr Ser Thr Leu
    130                 135                 140

Lys Thr Tyr Asp Phe Asp Gly Leu Asp Leu Ala Trp Gln Phe Pro Gln
145                 150                 155                 160

Thr Lys Pro Lys Arg Ile Arg Gly Trp Thr Gly Lys Val Trp His Gly
                165                 170                 175

Phe Lys Lys Leu Phe Thr Gly Asp Ser Val Leu Asp Pro Lys Ala Asp
            180                 185                 190

Glu His Arg Glu Glu Phe Thr Ala Leu Val Arg Asp Leu Lys Asn Ala
        195                 200                 205

Leu Val Ala Asp Asn Phe Ile Leu Gly Leu Thr Val Leu Pro His Val
    210                 215                 220

Asn Glu Ser Ile Phe Met Asp Val Pro Leu Leu Lys Asp Asn Leu Asp
225                 230                 235                 240

Tyr Val Asn Leu Ala Ser Phe Asp Gln Gln Thr Pro Glu Arg Asn Pro
                245                 250                 255

Lys Glu Gly Asp Tyr Thr Ala Pro Ile Tyr Glu Pro Ser Glu Arg Val
            260                 265                 270

Glu Gly Asn Asn Val Asp Ala Glu Ala Ser Tyr Trp Gln Gly Thr Pro
        275                 280                 285

Ala Gly Lys Ile Val Ile Gly Ile Pro Thr Tyr Gly Arg Gly Trp Lys
    290                 295                 300

Leu Val Glu Lys Ser Gly Ile Thr Gly Val Pro Pro Ile Pro Ala Asp
305                 310                 315                 320

Gly Pro Ser Ile Pro Gly Pro His Ser Gly Ile Asn Gly Phe Tyr Ser
                325                 330                 335

Trp Ala Glu Val Cys Ala Lys Leu Pro Asn Pro Gly Asn Ala Asn Leu
            340                 345                 350

Gln Gly Ala Asp Gln Pro Leu Arg Lys Ile Gly Asp Pro Thr Arg Arg
        355                 360                 365

Phe Gly Ala Tyr Ala Phe Arg Ile Pro Asp Glu Asn Glu Glu His Gly
    370                 375                 380

Ile Trp Leu Ser Tyr Glu Asp Pro Asp Thr Ala Gly Asn Lys Ala Ala
385                 390                 395                 400

Tyr Val Lys Ala Lys Gly Leu Gly Gly Ile Ser Ile Phe Asp Leu Gly
                405                 410                 415

Asn Asp Asp Val Arg Gly Ala Cys Ala Gly Asp Lys Phe Pro Ile Leu
            420                 425                 430

Arg Ala Ala Lys Tyr Arg Leu
        435


<210> SEQ ID NO 2
<211> LENGTH: 312
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 2

Met Ser Pro Ser Lys Lys Ile Leu Val Leu Leu Phe Phe Pro Ile Leu
1               5                   10                  15

Leu Val Ser Ser His Pro Ile Pro Ala Glu Asp Pro Ala Lys Gln Cys
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            20                  25                  30

Asn Leu Ser Glu Asp Asp Leu Thr Lys Leu Lys Ala Ala Ile Ser Ser
        35                  40                  45

Ala Ser Ser Ala Lys Ala Ala Asn Glu Asp Ile Leu Pro Ser Thr Thr
    50                  55                  60

Leu Ala Ala Cys Pro Met Leu Lys Asn Phe Thr Glu Met Leu Lys Thr
65                  70                  75                  80

Val Ala Thr Asp Met Glu Val Leu Lys Thr Gln Gly Val Ser Asn Met
                85                  90                  95

Glu Val Gln Leu Leu Arg Glu Ser Phe Glu Glu Lys Leu Asn Asp Leu
            100                 105                 110

Ala Lys Asn Lys Asp Ile Phe Glu Arg Gln Ala Asn Gln Asp Thr Ser
        115                 120                 125

Lys Ala Glu Gly Glu Met Val Glu Lys Ile Asn Lys Leu Gln Leu Glu
    130                 135                 140

Met Ala Lys Leu Gln Glu Glu Ile Glu Glu Gln Thr Lys Gln Met Tyr
145                 150                 155                 160

Val Asp Met Ile Glu Tyr Ile Phe Glu Arg Leu Lys Met Asn Asp Thr
                165                 170                 175

Glu Ala Ile Asp Ser Tyr Ala Gln Ile Val Met Lys Thr Lys Met His
            180                 185                 190

Glu Leu Ile Met Lys Leu Lys Thr Asp Arg Leu Val Leu Trp Glu Met
        195                 200                 205

Val Lys Tyr Val Glu Gly Lys Lys Asn Lys Trp Val Gly Arg Lys Val
    210                 215                 220

Leu Asn Thr Ile Leu Asp Gln Val Asn Lys Leu Lys Leu Tyr Lys Pro
225                 230                 235                 240

Glu Glu Val Glu Ile Gly Lys Asn Ser Leu Val Val Val Trp Cys Trp
                245                 250                 255

Lys Phe Asn Ser Glu Thr Val Tyr Gly Thr Thr Asp Glu Asp Gln Lys
            260                 265                 270

Ser Phe His Leu Ala Lys Leu Phe Phe Pro Lys Glu Lys Gly Cys Lys
        275                 280                 285

Glu Cys Ala Asp Val Lys Ser Arg Thr Met Cys Asn Asn Asp Tyr Pro
    290                 295                 300

Lys Val Met Val Lys Ala Phe Gly
305                 310


<210> SEQ ID NO 3
<211> LENGTH: 316
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 3

Met Glu Thr Ser Leu Pro Ile Thr Val Val Phe Leu Ile Val Leu Ile
1               5                   10                  15

Thr Gly Ala Gln Thr Lys Pro Thr Gln Gly Ser Cys Thr Leu Thr Asp
            20                  25                  30

Glu Asp Ile Ser Asp Ile Lys Ser Ala Val Gln Lys Ala Ser Lys Ala
        35                  40                  45

Ala Val Asn Asp Ile Val Leu Asp Pro Thr Leu Ile Asp Lys Cys Pro
    50                  55                  60
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Met Leu Glu Lys Ile Thr Ala Ser Leu Lys Ser Val Ala Thr Glu Ile
65                  70                  75                  80

Val Gln Met Arg Asp Ser Ala Ile Ser Thr Asp Gln Val Asp Gln Leu
                85                  90                  95

Lys Gln Asn Phe Glu Asp Gln Val Asn Gln Ile Val Lys Ser Arg Asp
            100                 105                 110

Ile Phe Glu Lys Gln Ser Gly Thr Gln Ala Thr Lys Glu His Gly Glu
        115                 120                 125

Met Leu Glu Arg Met Thr Ala Leu Gln Val Lys Val Thr Glu Leu Glu
    130                 135                 140

Gln Gln Ile Ala Lys Gln Thr Ala Ser Met Tyr Glu Asp Met Ala Glu
145                 150                 155                 160

Leu Ile Phe Gln Arg Leu Gln Met Asn Ser Thr Glu Ser Val Arg Ser
                165                 170                 175

Tyr Thr Lys His Met Met Glu Glu Lys Leu Glu Glu Leu Met Asn Lys
            180                 185                 190

Leu Glu Thr Asn Tyr Arg Ile Tyr Leu Gly Ala Leu Arg Phe Leu Asn
        195                 200                 205

His Met Asn Asp Gln Glu Leu Ile Gly Lys Val Phe Asp Gly Ile Leu
    210                 215                 220

Lys Arg Leu Gly Asp Met Lys Ala Asp Ser Asp Asp Val Lys Glu Asn
225                 230                 235                 240

Gly Arg Asn Leu Leu Val Asn Leu Leu Cys Trp Thr Val Asn Asn Asp
                245                 250                 255

Phe Leu Gly Lys Lys Tyr Lys Glu Arg Gln Val Asp Leu Tyr Arg Met
            260                 265                 270

Ala Leu Lys Phe Tyr Pro Lys Thr Tyr Glu Lys Ala Ala Asn Glu Ala
        275                 280                 285

Asp Val Arg Ser Arg Gln Phe Cys Glu Glu Asn Phe Pro Ala Asn Leu
    290                 295                 300

Ile Thr Trp Phe Ala Val Ser Trp Asn Asp Arg Gly
305                 310                 315


<210> SEQ ID NO 4
<211> LENGTH: 332
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 4

Met Phe Pro Pro Arg Lys Phe Leu Leu Ser Ser Phe Ile Leu Ala Ala
1               5                   10                  15

Leu His Val Thr Ala Ala Pro Leu Trp Asp Ala Lys Asp Pro Glu Gln
            20                  25                  30

Leu Arg Phe Ile Thr Ser Arg Cys Met Glu Asp Trp Tyr Pro Lys Ala
        35                  40                  45

Lys Asn Pro Lys Ala Ala Leu Gln Asn Trp Leu Gly Trp Lys Leu Glu
    50                  55                  60

Pro Ser Asp Asp Gln Ala Thr Gln Cys Tyr Thr Lys Cys Val Leu Glu
65                  70                  75                  80

Lys Ile Gly Phe Tyr Glu Pro Gly Glu Lys Arg Phe Lys Gly Val Arg
                85                  90                  95

Val Met Gln Gln Trp Glu Thr Phe His Lys Tyr Leu Asn Ala Asp Arg
            100                 105                 110
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Glu Lys Val His Asp Leu Thr Ser Thr Phe Asp Phe Ile Pro Pro Leu
        115                 120                 125

Lys Ser Ser Ser Cys Ser Glu Val Phe Glu Ala Phe Lys Lys Val Asn
    130                 135                 140

Gly Lys His Ser Glu Thr Ile Arg Ala Ile Leu Phe Gly Lys Gly Glu
145                 150                 155                 160

Ser Ser Lys Lys Tyr Tyr Gln Glu Lys Gly Val Lys Ile Lys Gln Lys
                165                 170                 175

Glu Gln Ser Leu Phe Met His Cys Glu Ala Leu Asn Tyr Pro Lys Gly
            180                 185                 190

Ser Pro Gln Arg Lys Asp Leu Cys Gly Ile Arg Lys Tyr Gln Met Gly
        195                 200                 205

Ser Gly Ile Val Phe Glu Arg His Met Glu Cys Ile Phe Lys Gly Leu
    210                 215                 220

Arg Tyr Met Thr Ser Lys Asn Glu Leu Asp Val Asp Glu Ile Ala Arg
225                 230                 235                 240

Asp Phe Ile Val Val Lys Lys Lys Pro Asp Ala Met Lys Ala Met Met
                245                 250                 255

Lys Thr Cys Lys Ala Asn Leu Lys Glu Lys Asn Pro Gly Lys Ile Ala
            260                 265                 270

Val His Tyr Tyr Lys Cys Leu Met Asn Asp Ser Lys Val Thr Asn Asp
        275                 280                 285

Phe Lys Glu Ala Phe Asp Tyr Arg Glu Val Arg Ser Lys Asp Tyr Phe
    290                 295                 300

Ala Ala Leu Thr Gly Lys Leu Lys Pro Tyr Ser Arg Ser Asp Val Arg
305                 310                 315                 320

Lys Gln Val Asp Asp Ile Asp Lys Ile Gln Cys Ser
                325                 330


<210> SEQ ID NO 5
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 5

Met Lys Tyr Leu Leu Thr Phe Leu Met Ala Leu Ser Leu Val Asn Leu
1               5                   10                  15

Met Leu Thr Arg Pro Thr Pro Glu Asp Asp Gly Gly Thr Ser Glu Glu
            20                  25                  30

Pro Gln Thr Gln Glu Thr Thr Gly Ser Asp Glu Lys Asn Gly Ala Ser
        35                  40                  45

Glu Glu Pro Asn Ala Asp Asp Ala Ser Lys Pro Asp Asp Val Glu Glu
    50                  55                  60

Lys Gly Asp Asp Asp Thr Ala Lys Lys Glu Asp Asp Gly Glu Ser Lys
65                  70                  75                  80

Asp Gly Glu Gly Ser Glu Lys Ser Asp Lys Glu Lys Gly Glu Pro Lys
                85                  90                  95

Asn Asp Pro Arg Glu Thr Tyr Asn Lys Val Ile Glu Gln Leu Asp Gln
            100                 105                 110

Ile Lys Val Asp Asn Val Glu Asp Gly His Glu Arg Ser Glu Leu Ala
        115                 120                 125

Ala Asp Ile Gln Arg Tyr Leu Arg Asn Pro Ile Val Asp Val Ile Gly
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    130                 135                 140

Ser Ala Gly Asp Phe Ser Lys Ile Ala Lys Cys Phe Lys Ser Met Val
145                 150                 155                 160

Gly Asp Ala Lys Lys Ala Ile Glu Glu Asp Val Lys Gly Phe Lys Glu
                165                 170                 175

Cys Thr Ala Lys Lys Asp Ser Asn Ala Tyr Gln Cys Ser Gln Asp Arg
            180                 185                 190

Ser Thr Val Gln Asp Lys Ile Ala Lys Met Ser Ser Lys Ile Ala Ser
        195                 200                 205

Cys Val Ala Ser Asn Arg Ser
    210                 215


<210> SEQ ID NO 6
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 6

Asn Leu Lys Val Leu Leu Ser Val Gly Gly Tyr
1               5                   10


<210> SEQ ID NO 7
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 7

Phe Lys Val Gly Ala Leu Leu Phe Leu Ala Ala Leu Val Ser Ala
1               5                   10                  15


<210> SEQ ID NO 8
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 8

Thr Ala Leu Val Arg Asp Leu Lys Asn Ala Leu Val Ala Asp Asn Phe
1               5                   10                  15

Ile Leu Gly Leu Thr Val Leu Pro His Val Asn Glu Ser
            20                  25


<210> SEQ ID NO 9
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 9

Lys Ile Thr Val Thr Asp Ile Glu Leu Ala Leu Pro Phe Cys Thr His
1               5                   10                  15

Leu Leu Tyr Gly Phe Ala Gly Val
            20
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<210> SEQ ID NO 10
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 10

Thr Ala Phe Val Asn Ser Val Tyr Ser Thr Leu Lys Thr Tyr
1 5 10

<210> SEQ ID NO 11
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 11

Phe Met Asp Val Pro Leu Leu Lys Asp Asn Leu Asp Tyr Val Asn Leu
1 5 10 15

Ala Ser Phe

<210> SEQ ID NO 12
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 12

Ile Thr Gly Val Pro Pro Ile Pro Ala Asp Gly Pro
1 5 10

<210> SEQ ID NO 13
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 13

Arg Gly Ala Cys Ala Gly Asp Lys Phe Pro Ile Leu Arg Ala Ala Lys
1 5 10 15

<210> SEQ ID NO 14
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 14

Asn Ser Leu Val Val Val Trp Cys Trp Lys
1 5 10

<210> SEQ ID NO 15
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 15

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Lys Lys Ile Leu Val Leu Leu Phe Phe Pro Ile Leu Leu Val Ser Ser
1 5 10 15

His Pro Ile Pro Ala Glu
20

<210> SEQ ID NO 16
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 16

Leu Pro Ser Thr Thr Leu Ala Ala Cys Pro Met Leu
1 5 10

<210> SEQ ID NO 17
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 17

Thr Asp Arg Leu Val Leu Trp Glu Met Val Lys Tyr Val Glu
1 5 10

<210> SEQ ID NO 18
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 18

Ser Phe His Leu Ala Lys Leu Phe Phe Pro
1 5 10

<210> SEQ ID NO 19
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 19

Leu Asn Thr Ile Leu Asp Gln Val Asn Lys Leu Lys Leu Tyr Lys Pro
1 5 10 15

Glu Glu Val

<210> SEQ ID NO 20
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 20

Thr Lys Leu Lys Ala Ala Ile Ser Ser Ala Ser Ser Ala
1 5 10

<210> SEQ ID NO 21
<211> LENGTH: 12

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<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 21

Gln Met Tyr Val Asp Met Ile Glu Tyr Ile Phe Glu
1 5 10

<210> SEQ ID NO 22
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 22

Ser Leu Pro Ile Thr Val Val Phe Leu Ile Val Leu Ile Thr Gly
1 5 10 15

<210> SEQ ID NO 23
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 23

Asn Leu Leu Val Asn Leu Leu Cys Trp Thr Val
1 5 10

<210> SEQ ID NO 24
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 24

Ala Leu Gln Val Lys Val Thr Glu Leu Glu Gln Gln Ile Ala Lys Gln
1 5 10 15

<210> SEQ ID NO 25
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 25

Ile Lys Ser Ala Val Gln Lys Ala Ser Lys Ala Ala Val Asn Asp Ile
1 5 10 15

Val Leu Asp Pro Thr Leu Ile Asp Lys Cys Pro Met Leu
20 25

<210> SEQ ID NO 26
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 26

Ile Thr Ala Ser Leu Lys Ser Val Ala Thr Glu Ile Val

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1 5 10

<210> SEQ ID NO 27
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 27

Ala Asn Leu Ile Thr Trp Phe Ala Val Ser
1 5 10

<210> SEQ ID NO 28
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 28

Ile Gly Lys Val Phe Asp Gly Ile Leu Lys Arg
1 5 10

<210> SEQ ID NO 29
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 29

Glu Arg Gln Val Asp Leu Tyr Arg Met Ala Leu Lys Phe Tyr Pro Lys
1 5 10 15

Thr

<210> SEQ ID NO 30
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 30

Ala Thr Gln Cys Tyr Thr Lys Cys Val Leu Glu Lys Ile
1 5 10

<210> SEQ ID NO 31
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 31

Lys Ile Ala Val His Tyr Tyr Lys Cys Leu Met Asn Asp
1 5 10

<210> SEQ ID NO 32
<211> LENGTH: 21
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

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<400> SEQUENCE: 32

Arg Lys Phe Leu Leu Ser Ser Phe Ile Leu Ala Ala Leu His Val Thr
1 5 10 15

Ala Ala Pro Leu Trp
20

<210> SEQ ID NO 33
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 33

Arg Asp Phe Ile Val Val Lys Lys Lys
1 5

<210> SEQ ID NO 34
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 34

Thr Phe Asp Phe Ile Pro Pro Leu Lys Ser Ser Ser Cys Ser Glu Val
1 5 10 15

Phe Glu Ala Phe Lys Lys
20

<210> SEQ ID NO 35
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 35

Leu Phe Met His Cys Glu Ala Leu Asn Tyr Pro
1 5 10

<210> SEQ ID NO 36
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 36

Tyr Phe Ala Ala Leu Thr Gly Lys Leu Lys Pro Tyr
1 5 10

<210> SEQ ID NO 37
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 37

Lys Met Ser Ser Lys Ile Ala Ser Cys Val Ala Ser
1 5 10

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<210> SEQ ID NO 38
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 38

Leu Leu Thr Phe Leu Met Ala Leu Ser Leu Val Asn Leu Met Leu Thr
1 5 10 15

<210> SEQ ID NO 39
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 39

Ser Glu Leu Ala Ala Asp Ile Gln Arg Tyr Leu Arg Asn Pro Ile Val
1 5 10 15

Asp Val Ile Gly Ser Ala
20

<210> SEQ ID NO 40
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 40

Asn Lys Val Ile Glu Gln Leu Asp Gln Ile Lys Val Asp Asn Val
1 5 10 15

<210> SEQ ID NO 41
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 41

Phe Ser Lys Ile Ala Lys Cys Phe Lys Ser Met Val Gly
1 5 10

<210> SEQ ID NO 42
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 42

Ala Tyr Gln Cys Ser Gln Asp Arg Ser Thr Val Gln Asp Lys
1 5 10

<210> SEQ ID NO 43
<211> LENGTH: 291
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 43

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Met Asn Arg Gln Leu Trp Ile Ile Ile Phe Ala Ile Leu Cys Val Ala
1               5                  10                  15

Gln Ala Glu Glu Asp Asn Pro Thr Thr Glu Lys Met Glu Glu Leu Gly
            20                  25                  30

Ile Ala Thr Ile Asn Asn Phe Thr Arg Glu Phe Tyr Ser Tyr Val Glu
        35                  40                  45

Ala Val Ser Gln Val Leu Ala Asp Leu Glu Leu Thr Thr Thr Ala Ser
    50                  55                  60

Ile Thr Gln Ile Lys His Arg Ile Lys His Leu Leu Gln Glu Lys Cys
65                  70                  75                  80

Asn Leu Cys Ser Ala Lys Ala Glu Gly Pro Ala Leu Asp Gln Gly Tyr
                85                  90                  95

Val Thr Thr Ser Asn Gly Ser Val Ile Pro Val Ser Tyr Glu Gln Thr
            100                 105                 110

Arg Phe Gly Gly Gly Trp Ile Val Leu Met Gln Arg Tyr Asp Gly Thr
        115                 120                 125

Val Arg Phe Asn Arg Ser Trp Ala Glu Tyr Arg Asp Gly Phe Gly Met
    130                 135                 140

Val Gly His Glu Phe Trp Leu Gly Leu Glu Arg Ile His Gln Met Thr
145                 150                 155                 160

Lys Asp Ala Glu Tyr Glu Leu Met Ile Glu Met Gln Asp Phe Glu Gly
                165                 170                 175

Asn Tyr Lys Tyr Ala Gly Tyr Asp Ala Phe Ala Val Gly Pro Glu Glu
            180                 185                 190

Glu Arg Tyr Pro Leu Ala Lys Val Gly Lys Phe Asn Lys Thr Ala Tyr
        195                 200                 205

Val Asp Ser Phe Gly Lys His Arg Gly Tyr Gly Phe Ser Thr Tyr Asp
    210                 215                 220

Asn Asp Asp Asn Gly Cys Ser Asn Gln Tyr Gly Arg Gly Gly Trp Trp
225                 230                 235                 240

Tyr Tyr Arg Lys Ser Cys Phe Gly Ala Ser Leu Thr Gly Ile Trp Gln
                245                 250                 255

Asn Lys Gln Asp Trp Lys Ser Ile Ser Trp Val Trp Phe Ser Thr Glu
            260                 265                 270

Lys Lys Gln Val Pro Leu Lys Phe Ala Arg Met Met Met Arg Leu Lys
        275                 280                 285

Thr Ala Glu
    290


<210> SEQ ID NO 44
<211> LENGTH: 321
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 44

Met Lys Leu Pro Leu Leu Leu Ala Ile Val Thr Thr Phe Ser Val Val
1               5                  10                  15

Ala Ser Thr Gly Pro Phe Asp Pro Glu Glu Met Leu Phe Thr Phe Thr
            20                  25                  30

Arg Cys Met Glu Asp Asn Leu Glu Asp Gly Pro Asn Arg Leu Pro Met
        35                  40                  45

Leu Ala Lys Trp Lys Glu Trp Ile Asn Glu Pro Val Asp Ser Pro Ala
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    50                  55                  60

Thr Gln Cys Phe Gly Lys Cys Val Leu Val Arg Thr Gly Leu Tyr Asp
65                  70                  75                  80

Pro Val Ala Gln Lys Phe Asp Ala Ser Val Ile Gln Glu Gln Phe Lys
                85                  90                  95

Ala Tyr Pro Ser Leu Gly Glu Lys Ser Lys Val Glu Ala Tyr Ala Asn
            100                 105                 110

Ala Val Gln Gln Leu Pro Ser Thr Asn Asn Asp Cys Ala Ala Val Phe
        115                 120                 125

Lys Ala Tyr Asp Pro Val His Lys Ala His Lys Asp Thr Ser Lys Asn
    130                 135                 140

Leu Phe His Gly Asn Lys Glu Leu Thr Lys Gly Leu Tyr Glu Lys Leu
145                 150                 155                 160

Gly Lys Asp Ile Arg Gln Lys Lys Gln Ser Tyr Phe Glu Phe Cys Glu
                165                 170                 175

Asn Lys Tyr Tyr Pro Ala Gly Ser Asp Lys Arg Gln Gln Leu Cys Lys
            180                 185                 190

Ile Arg Gln Tyr Thr Val Leu Asp Asp Ala Leu Phe Lys Glu His Thr
        195                 200                 205

Asp Cys Val Met Lys Gly Ile Arg Tyr Ile Thr Lys Asn Asn Glu Leu
    210                 215                 220

Asp Ala Glu Glu Val Lys Arg Asp Phe Met Gln Val Asn Lys Asp Thr
225                 230                 235                 240

Lys Ala Leu Glu Lys Val Leu Asn Asp Cys Lys Ser Lys Glu Pro Ser
                245                 250                 255

Asn Ala Gly Glu Lys Ser Trp His Tyr Tyr Lys Cys Leu Val Glu Ser
            260                 265                 270

Ser Val Lys Asp Asp Phe Lys Glu Ala Phe Asp Tyr Arg Glu Val Arg
        275                 280                 285

Ser Gln Ile Tyr Ala Phe Asn Leu Pro Lys Lys Gln Val Tyr Ser Lys
    290                 295                 300

Pro Ala Val Gln Ser Gln Val Met Glu Ile Asp Gly Lys Gln Cys Pro
305                 310                 315                 320

Gln


<210> SEQ ID NO 45
<211> LENGTH: 339
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 45

Met Val Gln Phe Pro Val Leu Leu Ile Thr Leu Ser Leu Ala Phe Glu
1               5                   10                  15

Val His Ser Ser Tyr Ala Glu Asn Arg Arg Leu Gln Leu Val Arg Asp
            20                  25                  30

Ile Asp Gly Thr Gln Gln Leu Val Asn Pro Asn Pro Tyr Arg Val Leu
        35                  40                  45

Asn Ala His Leu Glu Arg Ser Phe Asn Ala Gln Ser Asp Ile Ile Phe
    50                  55                  60

Arg Leu Tyr Thr Arg Lys Asn Pro Glu Lys His Gln Ile Leu Lys Pro
65                  70                  75                  80

Asn Asp Thr Ser Ser Ile Leu Asn Ser Asn Phe Asn Ala Asp Leu Pro
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                85                  90                  95

Thr Arg Phe Leu Ile His Gly Trp Asn Gln Asn Gly Glu Ser Asp Ile
            100                 105                 110

Leu Ile Glu Leu Arg Arg Ser Tyr Leu Ser Val Glu Asp Phe Asn Val
        115                 120                 125

Ile Gly Val Asp Trp Gly Glu Gly Ala Leu Thr Ile Asn Tyr Val Met
    130                 135                 140

Ala Arg Lys Arg Val Glu Ser Val Gly Leu Val Thr Ser Gln Leu Ile
145                 150                 155                 160

Asp Thr Leu Val Asp Ala Ser Gly Val Ile Leu Asp Ser Ile Tyr Val
                165                 170                 175

Ile Gly His Ser Leu Gly Ala His Val Ala Gly Ile Val Gly Lys His
            180                 185                 190

Gln Arg Gly Gln Leu Asn Thr Ile Val Gly Leu Asp Pro Ala Gly Pro
        195                 200                 205

Leu Phe Ser Leu Asn Ser Ser Asp Ile Leu Asn Gln Asn His Ala Gln
    210                 215                 220

Tyr Val Glu Met Val Ser Thr Gly Ala Arg Leu Leu Gly Thr Tyr Glu
225                 230                 235                 240

Pro Leu Gly Asp Ala Asn Phe Tyr Pro Asn Gly Gly Leu Glu Gln Ala
                245                 250                 255

Gly Cys Gly Leu Asp Leu Phe Gly Ile Cys Ala His Ala Arg Ser Trp
            260                 265                 270

Ile Tyr Phe Ala Glu Thr Val Thr Asn Gly Lys Gly Phe Arg Gly Ile
        275                 280                 285

Lys Cys Ala Met Ile Glu Asp Leu Glu Gly Glu Thr Cys Asn Leu Ser
    290                 295                 300

Gly Leu Pro Asn Val Trp Met Gly Gly Glu Pro Ser Asn His Glu Arg
305                 310                 315                 320

Gly Val Lys Gly Ile Phe Met Val His Thr Asn Ser Glu Ala Pro Phe
                325                 330                 335

Ala Lys Asp


<210> SEQ ID NO 46
<211> LENGTH: 290
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 46

Met Ile Leu Gln Phe Trp Val Val Thr Phe Ser Val Leu Phe Ala Ala
1               5                   10                  15

Arg Ala Asp Glu Asn His Ser Ile Leu Ile Lys Leu Asn Asp Leu Asp
            20                  25                  30

His Arg Phe Thr Gln Met Phe Ser Gln Gln Phe Tyr Arg His Thr Gln
        35                  40                  45

Gln Val Thr Asp Arg Val Ser Ala Leu Lys Ile Ser Ile Asp Thr Asn
    50                  55                  60

Leu Leu Glu Leu Asp Gln Gln Ile Gln Gln Ala Leu Asp Gly Ile Gln
65                  70                  75                  80

Ser Asn Glu Ser Ser Ser Ser Ala Ser Ala Thr Lys Pro Pro Gly Leu
                85                  90                  95

Thr Thr Ile Pro Ile Gly Ser Glu Pro Arg Val Pro Ala Leu Tyr Glu
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            100                 105                 110

Arg Glu Arg Tyr Gly Gly Asp Trp Leu Val Val Met His Arg Tyr Asp
        115                 120                 125

Gly Ser Val Lys Phe Asp Arg Thr Trp Ala Glu Tyr Arg Asp Gly Phe
    130                 135                 140

Gly Met Val Gly Gln Glu Phe Trp Tyr Gly Leu Glu Arg Leu His Gln
145                 150                 155                 160

Leu Thr Lys Glu Lys Ser Tyr Glu Leu Met Val Glu Met Glu Asp Phe
                165                 170                 175

Asn Gly Ser Leu Lys Tyr Ala Trp Tyr Asp Lys Phe Val Val Gly Pro
            180                 185                 190

Glu Glu Gln Arg Tyr Ala Leu Val Glu Leu Gly Thr Phe Asn Gly Thr
        195                 200                 205

Thr Asp Gly Asp Ser Leu Lys Pro His Lys Gly Ser Gly Phe Ser Thr
    210                 215                 220

Tyr Asp Asn Asp Asp Phe Gly Cys Ser Asn Lys Tyr Ala Lys Gly Gly
225                 230                 235                 240

Trp Trp Tyr Tyr Ser Gly Lys Cys Tyr Gly Ser Ser Leu Thr Gly Ile
                245                 250                 255

Trp Lys Asn Glu Leu Ala Tyr Ser Ser Ile Val Trp Met Lys Phe Ser
            260                 265                 270

Asp Val Ser Asn Thr Pro Leu Lys Leu Val Arg Met Met Ile Arg Pro
        275                 280                 285

Lys Asn
    290


<210> SEQ ID NO 47
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 47

Leu Trp Ile Ile Ile Phe Ala Ile Leu Cys Val Ala Gln Ala
1               5                   10


<210> SEQ ID NO 48
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 48

Phe Tyr Ser Tyr Val Glu Ala Val Ser Gln Val Leu Ala Asp Leu Glu
1               5                   10                  15


<210> SEQ ID NO 49
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 49

Gly Ser Val Ile Pro Val Ser Tyr Glu
1               5
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<210> SEQ ID NO 50
<211> LENGTH: 22
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 50

Ile Thr Gln Ile Lys His Arg Ile Lys His Leu Leu Gln Glu Lys Cys
1 5 10 15

Asn Leu Cys Ser Ala Lys
20

<210> SEQ ID NO 51
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 51

Lys Lys Gln Val Pro Leu Lys Phe
1 5

<210> SEQ ID NO 52
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 52

Tyr Pro Leu Ala Lys Val Gly
1 5

<210> SEQ ID NO 53
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 53

Arg Lys Ser Cys Phe Gly Ala Ser Leu Thr Gly
1 5 10

<210> SEQ ID NO 54
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 54

Gly Trp Ile Val Leu Met Gln
1 5

<210> SEQ ID NO 55
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

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<400> SEQUENCE: 55

Leu Asp Gln Gly Tyr Val Thr Thr
1 5

<210> SEQ ID NO 56
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 56

Tyr Ala Gly Tyr Asp Ala Phe Ala Val Gly
1 5 10

<210> SEQ ID NO 57
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 57

Thr Ala Tyr Val Asp Ser Phe
1 5

<210> SEQ ID NO 58
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 58

Ile Ser Trp Val Trp Phe Ser
1 5

<210> SEQ ID NO 59
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 59

Trp Leu Gly Leu Glu Arg Ile
1 5

<210> SEQ ID NO 60
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 60

Pro Leu Leu Leu Ala Ile Val Thr Thr Phe Ser Val Val Ala Ser Thr
1 5 10 15

<210> SEQ ID NO 61
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence

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<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 61

Trp His Tyr Tyr Lys Cys Leu Val Glu Ser Ser
1 5 10

<210> SEQ ID NO 62
<211> LENGTH: 19
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 62

Pro Val Asp Ser Pro Ala Thr Gln Cys Phe Gly Lys Cys Val Leu Val
1 5 10 15

Arg Thr Gly

<210> SEQ ID NO 63
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 63

Cys Ala Ala Val Phe Lys Ala Tyr Asp Pro Val His Lys Ala
1 5 10

<210> SEQ ID NO 64
<211> LENGTH: 29
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 64

Tyr Arg Glu Val Arg Ser Gln Ile Tyr Ala Phe Asn Leu Pro Lys Lys
1 5 10 15

Gln Val Tyr Ser Lys Pro Ala Val Gln Ser Gln Val Met
20 25

<210> SEQ ID NO 65
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 65

Lys Val Glu Ala Tyr Ala Asn Ala Val Gln Gln Leu Pro
1 5 10

<210> SEQ ID NO 66
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 66

Tyr Asp Pro Val Ala Gln Lys Phe Asp Ala Ser Val Ile Gln Glu Gln

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1 5 10 15

Phe Lys Ala Tyr Pro Ser Leu
20

<210> SEQ ID NO 67
<211> LENGTH: 15
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 67

Gln Gln Leu Cys Lys Ile Arg Gln Tyr Thr Val Leu Asp Asp Ala
1 5 10 15

<210> SEQ ID NO 68
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 68

Leu Glu Lys Val Leu Asn Asp Cys
1 5

<210> SEQ ID NO 69
<211> LENGTH: 12
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 69

Tyr Phe Glu Phe Cys Glu Asn Lys Tyr Tyr Pro Ala
1 5 10

<210> SEQ ID NO 70
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 70

Phe Lys Glu His Thr Asp Cys Val Met Lys Gly
1 5 10

<210> SEQ ID NO 71
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 71

Phe Pro Val Leu Leu Ile Thr Leu Ser Leu Ala Phe Glu Val His Ser
1 5 10 15

Ser

<210> SEQ ID NO 72
<211> LENGTH: 44
<212> TYPE: PRT

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<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 72

Val Glu Ser Val Gly Leu Val Thr Ser Gln Leu Ile Asp Thr Leu Val
1 5 10 15

Asp Ala Ser Gly Val Ile Leu Asp Ser Ile Tyr Val Ile Gly His Ser
20 25 30

Leu Gly Ala His Val Ala Gly Ile Val Gly Lys His
35 40

<210> SEQ ID NO 73
<211> LENGTH: 23
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 73

Gln Ala Gly Cys Gly Leu Asp Leu Phe Gly Ile Cys Ala His Ala Arg
1 5 10 15

Ser Trp Ile Tyr Phe Ala Glu
20

<210> SEQ ID NO 74
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 74

Leu Gln Leu Val Arg Asp
1 5

<210> SEQ ID NO 75
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 75

Thr Gln Gln Leu Val Asn Pro Asn Pro Tyr Arg Val Leu Asn Ala His
1 5 10 15

<210> SEQ ID NO 76
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 76

Thr Ile Asn Tyr Val Met Ala Arg
1 5

<210> SEQ ID NO 77
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:

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<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 77

Ala Gln Tyr Val Glu Met Val
1 5

<210> SEQ ID NO 78
<211> LENGTH: 18
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 78

Asn Thr Ile Val Gly Leu Asp Pro Ala Gly Pro Leu Phe Ser Leu Asn
1 5 10 15

Ser Ser

<210> SEQ ID NO 79
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 79

Lys Gly Ile Phe Met Val His
1 5

<210> SEQ ID NO 80
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 80

Cys Asn Leu Ser Gly Leu Pro Asn Val
1 5

<210> SEQ ID NO 81
<211> LENGTH: 16
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 81

Asp Ile Leu Ile Glu Leu Arg Arg Ser Tyr Leu Ser Val Glu Asp Phe
1 5 10 15

<210> SEQ ID NO 82
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 82

Pro Thr Arg Phe Leu Ile His Gly
1 5

<210> SEQ ID NO 83

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<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 83

Ser Asp Ile Ile Phe Arg Leu Tyr
1 5

<210> SEQ ID NO 84
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 84

Gly Ile Lys Cys Ala Met Ile
1 5

<210> SEQ ID NO 85
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 85

Gly Ala Arg Leu Leu Gly Thr Tyr
1 5

<210> SEQ ID NO 86
<211> LENGTH: 13
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 86

Gln Phe Trp Val Val Thr Phe Ser Val Leu Phe Ala Ala
1 5 10

<210> SEQ ID NO 87
<211> LENGTH: 24
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 87

Leu Ala Tyr Ser Ser Ile Val Trp Met Lys Phe Ser Asp Val Ser Asn
1 5 10 15

Thr Pro Leu Lys Leu Val Arg Met
20

<210> SEQ ID NO 88
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 88

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Asp Trp Leu Val Val Met His Arg
1 5

<210> SEQ ID NO 89
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 89

Glu Pro Arg Val Pro Ala Leu Tyr
1 5

<210> SEQ ID NO 90
<211> LENGTH: 9
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 90

His Ser Ile Leu Ile Lys Leu Asn Asp
1 5

<210> SEQ ID NO 91
<211> LENGTH: 8
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 91

Arg Tyr Ala Leu Val Glu Leu Gly
1 5

<210> SEQ ID NO 92
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 92

Thr Asp Arg Val Ser Ala Leu Lys Ile Ser
1 5 10

<210> SEQ ID NO 93
<211> LENGTH: 11
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 93

Ser Gly Lys Cys Tyr Gly Ser Ser Leu Thr Gly
1 5 10

<210> SEQ ID NO 94
<211> LENGTH: 14
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

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<400> SEQUENCE: 94

Ser Leu Lys Tyr Ala Trp Tyr Asp Lys Phe Val Val Gly Pro
1 5 10

<210> SEQ ID NO 95
<211> LENGTH: 7
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 95

Leu Glu Arg Leu His Gln Leu
1 5

<210> SEQ ID NO 96
<211> LENGTH: 17
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 96

Asp Thr Asn Leu Leu Glu Leu Asp Gln Gln Ile Gln Gln Ala Leu Asp
1 5 10 15

Gly

<210> SEQ ID NO 97
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 97

Ser Gln Gln Phe Tyr Arg His Thr Gln Gln
1 5 10

<210> SEQ ID NO 98
<211> LENGTH: 6
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 98

Asp Gly Ser Val Lys Phe
1 5

<210> SEQ ID NO 99
<211> LENGTH: 10
<212> TYPE: PRT
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: Aedes aegypti

<400> SEQUENCE: 99

Pro Pro Gly Leu Thr Thr Ile Pro Ile Gly
1 5 10

<210> SEQ ID NO 100
<211> LENGTH: 651
<212> TYPE: PRT

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<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 100

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Met Ala Lys Ala Pro Ala Val Gly Ile Asp Leu Gly Thr Thr Tyr Ser
1               5                   10                  15

Cys Val Gly Val Phe Gln His Gly Lys Val Glu Ile Ile Ala Asn Asp
            20                  25                  30

Gln Gly Asn Arg Thr Thr Pro Ser Tyr Val Ala Phe Thr Asp Thr Glu
        35                  40                  45

Arg Leu Ile Gly Asp Ala Ala Lys Asn Gln Val Ala Met Asn Pro Thr
    50                  55                  60

Asn Thr Ile Phe Asp Ala Lys Arg Leu Ile Gly Arg Lys Phe Asp Asp
65                  70                  75                  80

Pro Ala Ile Gln Ala Asp Met Lys His Trp Pro Phe Asp Val Ile Ser
                85                  90                  95

Val Glu Gly Lys Pro Lys Ile Gln Val Glu Tyr Lys Gly Glu Thr Lys
            100                 105                 110

Asn Phe Phe Pro Glu Glu Ile Ser Ser Met Val Leu Thr Lys Met Lys
        115                 120                 125

Glu Thr Ala Glu Ala Tyr Leu Gly Lys Thr Val Ser Asn Ala Val Val
    130                 135                 140

Thr Val Pro Ala Tyr Phe Asn Asp Ser Gln Arg Gln Ala Thr Lys Asp
145                 150                 155                 160

Ala Gly Thr Ile Ser Gly Leu Asn Val Leu Arg Ile Ile Asn Glu Pro
                165                 170                 175

Thr Ala Ala Ala Ile Ala Tyr Gly Leu Asp Lys Lys Thr Ala Gly Glu
            180                 185                 190

Arg Asn Val Leu Ile Phe Asp Leu Gly Gly Gly Thr Phe Asp Val Ser
        195                 200                 205

Ile Leu Ser Ile Asp Asp Gly Ile Phe Glu Val Lys Ser Thr Ala Gly
    210                 215                 220

Asp Thr His Leu Gly Gly Glu Asp Phe Asp Asn Arg Leu Val Asn His
225                 230                 235                 240

Phe Ala Gln Glu Phe Lys Arg Lys His Lys Lys Asp Leu Ser Thr Asn
                245                 250                 255

Lys Arg Ala Leu Arg Arg Leu Arg Thr Ala Cys Glu Arg Ala Lys Arg
            260                 265                 270

Thr Leu Ser Ser Ser Thr Gln Ala Ser Ile Glu Ile Asp Ser Leu Phe
        275                 280                 285

Glu Gly Thr Asp Phe Tyr Thr Ser Ile Thr Arg Ala Arg Phe Glu Glu
    290                 295                 300

Leu Asn Ala Asp Leu Phe Arg Ser Thr Met Glu Pro Val Glu Lys Ala
305                 310                 315                 320

Ile Arg Asp Ala Lys Met Asp Lys Ala Ser Ile His Asp Ile Val Leu
                325                 330                 335

Val Gly Gly Ser Thr Arg Ile Pro Lys Val Gln Lys Leu Leu Gln Asp
            340                 345                 350

Phe Phe Asn Gly Lys Glu Leu Asn Lys Ser Ile Asn Pro Asp Glu Ala
        355                 360                 365

Val Ala Tyr Gly Ala Ala Val Gln Ala Ala Ile Leu His Gly Asp Lys
    370                 375                 380
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Ser Glu Glu Val Gln Asp Leu Leu Leu Leu Asp Val Thr Pro Leu Ser
385                 390                 395                 400

Leu Gly Ile Glu Thr Ala Gly Gly Val Met Ser Val Leu Ile Lys Arg
                405                 410                 415

Asn Thr Thr Ile Pro Thr Lys Gln Thr Gln Thr Phe Thr Thr Tyr Ser
            420                 425                 430

Asp Asn Gln Pro Gly Val Leu Ile Gln Val Phe Glu Gly Glu Arg Ala
        435                 440                 445

Met Thr Lys Asp Asn Asn Leu Leu Gly Lys Phe Glu Leu Ser Gly Ile
    450                 455                 460

Pro Pro Ala Pro Arg Gly Val Pro Gln Ile Glu Val Thr Phe Asp Ile
465                 470                 475                 480

Asp Ala Asn Gly Ile Leu Asn Val Thr Ala Leu Glu Lys Ser Thr Asn
                485                 490                 495

Lys Glu Asn Lys Ile Thr Ile Thr Asn Asp Lys Gly Arg Leu Ser Lys
            500                 505                 510

Glu Asp Ile Glu Arg Met Val Asn Glu Ala Glu Lys Tyr Arg Ser Glu
        515                 520                 525

Asp Glu Lys Gln Lys Glu Thr Ile Ser Ala Lys Asn Ala Leu Glu Ser
    530                 535                 540

Tyr Cys Phe Asn Met Lys Ala Thr Met Glu Asp Asp Lys Leu Lys Asp
545                 550                 555                 560

Lys Ile Thr Asp Ser Asp Lys Thr Leu Ile Met Asp Lys Cys Asn Asp
                565                 570                 575

Thr Ile Lys Trp Leu Asp Ala Asn Gln Leu Ala Glu Lys Glu Glu Tyr
            580                 585                 590

Glu His Arg Gln Lys Glu Leu Glu Ser Val Cys Asn Pro Ile Ile Thr
        595                 600                 605

Lys Leu Tyr Gln Ser Ala Gly Gly Ala Pro Gly Gly Met Pro Gly Phe
    610                 615                 620

Pro Gly Gly Ala Pro Gly Ala Gly Ala Gly Ala Ala Pro Gly Ala Gly
625                 630                 635                 640

Ser Gly Ser Gly Pro Thr Ile Glu Glu Val Asp
                645                 650


<210> SEQ ID NO 101
<211> LENGTH: 496
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 101

Met Ser Val Asn Arg Thr Ile Ser Ala His Gln Ala Ala Lys Glu His
1               5                   10                  15

Val Leu Ala Val Ser Arg Asp Phe Ile Ser Gln Pro Arg Leu Thr Tyr
            20                  25                  30

Lys Thr Val Ser Gly Val Asn Gly Pro Leu Val Ile Leu Asp Glu Val
        35                  40                  45

Lys Phe Pro Lys Phe Ala Glu Ile Val Gln Leu Arg Leu Asn Asp Gly
    50                  55                  60

Thr Val Arg Ser Gly Gln Val Leu Glu Val Ser Gly Ser Lys Ala Val
65                  70                  75                  80

Val Gln Val Phe Glu Gly Thr Ser Gly Ile Asp Ala Lys Asn Thr Val
                85                  90                  95
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Cys Glu Phe Thr Gly Asp Ile Leu Arg Thr Pro Val Ser Glu Asp Met
            100                 105                 110

Leu Gly Arg Val Phe Asn Gly Ser Gly Lys Pro Ile Asp Lys Gly Pro
        115                 120                 125

Pro Ile Leu Ala Glu Asp Phe Leu Asp Ile Gln Gly Gln Pro Ile Asn
    130                 135                 140

Pro Trp Ser Arg Ile Tyr Pro Glu Glu Met Ile Gln Thr Gly Ile Ser
145                 150                 155                 160

Ala Ile Asp Val Met Asn Ser Ile Ala Arg Gly Gln Lys Ile Pro Ile
                165                 170                 175

Phe Ser Ala Ala Gly Leu Pro His Asn Glu Ile Ala Ala Gln Ile Cys
            180                 185                 190

Arg Gln Ala Gly Leu Val Lys His Thr Gly Lys Ser Val Leu Asp Glu
        195                 200                 205

His Glu Asp Asn Phe Ala Ile Val Phe Ala Ala Met Gly Val Asn Met
    210                 215                 220

Glu Thr Ala Arg Phe Phe Lys Gln Asp Phe Glu Glu Asn Gly Ser Met
225                 230                 235                 240

Glu Asn Val Cys Leu Phe Leu Asn Leu Ala Asn Asp Pro Thr Ile Glu
                245                 250                 255

Arg Ile Ile Thr Pro Arg Leu Ala Leu Thr Ala Ala Glu Phe Leu Ala
            260                 265                 270

Tyr Gln Cys Glu Lys His Val Leu Val Ile Leu Thr Asp Met Ser Ser
        275                 280                 285

Tyr Ala Glu Ala Leu Arg Glu Val Ser Ala Ala Arg Glu Glu Val Pro
    290                 295                 300

Gly Arg Arg Gly Phe Pro Gly Tyr Met Tyr Thr Asp Leu Ala Thr Ile
305                 310                 315                 320

Tyr Glu Arg Ala Gly Arg Val Glu Gly Arg Asn Gly Ser Ile Thr Gln
                325                 330                 335

Ile Pro Ile Leu Thr Met Pro Asn Asp Asp Ile Thr His Pro Ile Pro
            340                 345                 350

Asp Leu Thr Gly Tyr Ile Thr Glu Gly Gln Ile Tyr Val Asp Arg Gln
        355                 360                 365

Leu His Asn Arg Gln Ile Tyr Pro Pro Val Asn Val Leu Pro Ser Leu
    370                 375                 380

Ser Arg Leu Met Lys Ser Ala Ile Gly Glu Gly Met Thr Arg Lys Asp
385                 390                 395                 400

His Ser Asp Val Ser Asn Gln Leu Tyr Ala Cys Tyr Ala Ile Gly Lys
                405                 410                 415

Asp Val Gln Ala Met Lys Ala Val Val Gly Glu Glu Ala Leu Thr Pro
            420                 425                 430

Asp Asp Leu Leu Tyr Leu Glu Phe Leu Thr Lys Phe Glu Lys Asn Phe
        435                 440                 445

Ile Ser Gln Gly Asn Tyr Glu Asn Arg Thr Val Phe Glu Ser Leu Asp
    450                 455                 460

Ile Gly Trp Gln Leu Leu Arg Ile Phe Pro Lys Glu Met Leu Lys Arg
465                 470                 475                 480

Ile Pro Ala Ser Ile Leu Ala Glu Phe Tyr Pro Arg Asp Ser Arg His
                485                 490                 495
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<210> SEQ ID NO 102
<211> LENGTH: 530
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 102

Met Pro Ala Asn Ile Ile Met Lys Ile Leu Ile Thr Ser Ile Leu Ile
1 5 10 15

Leu Lys Leu Ala Ile His Val Val Pro Gln His Leu Ile Ser Ser Gly
20 25 30

Ala Ser Ala Val Glu Ser Lys Pro Val Ser Ala Arg Pro Thr Tyr Glu
35 40 45

Asp Tyr Lys Arg Gln Arg Glu Asn Phe Leu Gln Ala Glu Glu Tyr His
50 55 60

Phe Leu Gly Ala Asn Val Thr Leu Asn Glu Asn Glu Gln Leu Val Asn
65 70 75 80

Lys Phe Leu Met Arg Leu Lys Leu Glu Glu Met Val Lys Gly Phe Asn
85 90 95

Asp Ser Tyr Asn Phe Ile Pro Ala Arg His Ile Phe Glu Val Leu Asp
100 105 110

Arg Phe Gly Gln Ser Lys Val Phe Lys Val Ile Gln Arg Leu Pro Lys
115 120 125

Gly Gly Val Leu His Ala His Asp Met Ala Leu Gly Ser Thr Asp Leu
130 135 140

Ile Val Asn Ala Thr Tyr Arg Glu Asn Leu Trp Gln Lys Gly Asn Phe
145 150 155 160

Gly Val Ser His Gly Pro Gln Phe Lys Phe Ser Lys Glu Lys Pro Gly
165 170 175

Lys Glu Trp Ser Leu Val Ser Glu Ile Arg Gln Trp Met Thr Asp Lys
180 185 190

Val Tyr Asp Ala Lys Val Gly Glu Ile Phe Ser Leu Tyr Asn Ala Asp
195 200 205

Pro Leu Asn Ala Tyr Lys Ser Leu Asp Asp Val Trp Ser Lys Phe Gln
210 215 220

Asn Leu Phe Gly Ser Leu Ala Pro Leu Ile Thr Phe Ala Pro Val Trp
225 230 235 240

Arg Gln Tyr Tyr His Asp Ser Leu Lys Gln Phe Tyr Asp Asp His Val
245 250 255

Gln Tyr Leu Glu Phe Arg Gly Val Leu Pro Asp Val Tyr Asp Leu Asp
260 265 270

Gly Lys Ile Tyr Ser Ala Glu Glu Ile Val Gln Met Tyr Tyr Glu Glu
275 280 285

Thr Glu Glu Phe Lys Ser Ser His Pro Glu Phe Ile Gly Ala Lys Phe
290 295 300

Ile Tyr Ala Pro Gly Arg Phe Ala Thr Asp Asp Glu Phe Leu Lys Ile
305 310 315 320

Ile Asp Thr Ala Lys Arg Leu His Lys Lys Phe Pro Thr Phe Leu Ala
325 330 335

Gly Phe Asp Leu Val Gly Gln Glu Asp Pro Gly Arg Ser Leu Leu Glu
340 345 350

Phe Ala Pro Ala Leu Leu Lys Leu Pro Ala Ser Ile Asn Phe Phe Phe
355 360 365

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His Ala Gly Glu Thr Asn Trp Tyr Gly Met Lys Thr Asp Gln Asn Leu
    370                 375                 380

Ile Asp Ala Val Leu Leu Gly Ser Lys Arg Ile Gly His Gly Phe Ala
385                 390                 395                 400

Val Leu Lys His Pro Lys Val Leu Lys Glu Ile Lys Arg Arg Gln Ile
                405                 410                 415

Cys Ile Glu Ile Asn Pro Ile Ser Asn Gln Val Leu Lys Leu Val Gln
            420                 425                 430

Asp Gln Arg Asn His Pro Ala Ala Leu Leu Phe Ser Asp Asn Tyr Pro
        435                 440                 445

Val Val Val Ser Ser Asp Asp Pro Ser Phe Trp Arg Ser Thr Pro Leu
    450                 455                 460

Ser His Asp Phe Tyr Val Ala Phe Thr Gly Ile Ala Ser Ala Lys Gln
465                 470                 475                 480

Asp Leu Arg Leu Leu Lys Gln Leu Ala Leu Asn Ser Ile Glu Tyr Ser
                485                 490                 495

Ala Met Asn Ser Glu Glu Lys Thr Ser Ala Lys Glu Lys Trp Ser Gln
            500                 505                 510

Ala Trp His Asp Gln Ile Ser Ala Leu Ala Thr Asp Ile Val Ala Gly
        515                 520                 525

Ser Val
    530


<210> SEQ ID NO 103
<211> LENGTH: 562
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 103

Met Ala Gly Arg Pro Gly Tyr Ser Glu Val Ile Phe Leu Tyr Val Val
1               5                   10                  15

Ser Val Ala Val Ile Ala Arg Ala Thr Asp Asn Met Pro Val Asn Lys
            20                  25                  30

Asp Val Ser Lys Leu Phe Pro Leu Thr Leu Ile His Ile Asn Asp Leu
        35                  40                  45

His Ala Arg Phe Glu Glu Thr Asn Met Lys Ser Asn Val Cys Thr Gln
    50                  55                  60

Lys Asp Gln Cys Ile Ala Gly Ile Ala Arg Val Tyr Gln Lys Ile Lys
65                  70                  75                  80

Asp Leu Leu Lys Glu Tyr Glu Ser Lys Asn Pro Ile Tyr Leu Asn Ala
                85                  90                  95

Gly Asp Asn Phe Gln Gly Thr Leu Trp Tyr Asn Leu Leu Arg Trp Asn
            100                 105                 110

Val Thr Ala Asp Phe Ile Lys Lys Leu Lys Pro Ala Ala Met Thr Leu
        115                 120                 125

Gly Asn His Glu Phe Asp His Thr Pro Lys Gly Leu Ala Pro Tyr Leu
    130                 135                 140

Ala Glu Leu Asn Lys Glu Gly Ile Pro Thr Ile Val Ala Asn Leu Val
145                 150                 155                 160

Met Asn Asn Asp Pro Asp Leu Lys Ser Ser Lys Ile Pro Lys Ser Ile
                165                 170                 175

Lys Leu Thr Val Gly Lys Arg Lys Ile Gly Ile Ile Gly Val Leu Tyr
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            180                 185                 190

Asp Lys Thr His Glu Ile Ala Gln Thr Gly Lys Val Thr Leu Ser Asn
        195                 200                 205

Ala Val Glu Ala Val Arg Arg Glu Ala Ala Ala Leu Lys Lys Asp Asn
    210                 215                 220

Ile Asp Ile Ile Val Val Leu Ser His Cys Ser Tyr Glu Glu Asp Lys
225                 230                 235                 240

Lys Ile Ala Ala Glu Ala Gly Asp Asp Ile Asp Val Ile Val Gly Ala
                245                 250                 255

His Ser His Ser Phe Leu Tyr Ser Pro Asp Ser Lys Gln Pro His Asp
            260                 265                 270

Pro Lys Asp Lys Val Glu Gly Pro Tyr Pro Thr Leu Val Glu Ser Lys
        275                 280                 285

Asn Lys Arg Lys Ile Pro Ile Val Gln Ala Lys Ser Phe Gly Lys Tyr
    290                 295                 300

Val Gly Arg Leu Thr Leu Tyr Phe Asp Glu Glu Gly Glu Val Lys Asn
305                 310                 315                 320

Trp Glu Gly Tyr Pro Val Phe Ile Asp His Lys Val Gln Gln Asp Pro
                325                 330                 335

Gln Ile Leu Lys Asp Leu Val Pro Trp Arg Ala Lys Val Glu Ala Ile
            340                 345                 350

Gly Ser Thr Val Val Gly Glu Thr Met Ile Glu Leu Asp Arg Asp Ser
        355                 360                 365

Cys Arg Asp Gln Glu Cys Thr Leu Gly Val Leu Tyr Ala Asp Gly Phe
    370                 375                 380

Ala Asp Gln Tyr Thr Asn Asp Thr Phe Arg Pro Phe Ala Ile Ile Gln
385                 390                 395                 400

Ala Gly Asn Phe Arg Asn Pro Ile Lys Val Gly Lys Ile Thr Asn Gly
                405                 410                 415

Asp Ile Ile Glu Ala Ala Pro Phe Gly Ser Thr Ala Asp Leu Ile Arg
            420                 425                 430

Leu Lys Gly Ala Asp Ile Trp Asp Val Ala Glu His Ser Phe Ala Leu
        435                 440                 445

Asp Asp Glu Gly Arg Thr Asn Cys Leu Gln Val Ser Gly Leu Arg Ile
    450                 455                 460

Val Ile Asp Ile Ser Lys Pro Val Arg Ser Arg Val Lys Lys Ile Glu
465                 470                 475                 480

Val Met Asp Tyr Thr Asn Pro Lys Ser Asp Lys Leu Lys Pro Leu Asp
                485                 490                 495

Lys Glu Ala Glu Tyr Tyr Ile Val Val Pro Ser Tyr Leu Ala Asp Gly
            500                 505                 510

Lys Asp Gly Phe Ser Ala Met Lys Arg Ala Thr Ala Arg Arg Thr Gly
        515                 520                 525

Pro Leu Asp Ser Asp Val Phe Lys Asn Tyr Val Glu Lys Ile Lys Lys
    530                 535                 540

Val Asp Asn Leu Lys Leu Gly Arg Val Ile Val Cys Lys Gly Ser Lys
545                 550                 555                 560

Cys Thr


<210> SEQ ID NO 104
<211> LENGTH: 572
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<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 104

Met Ile Asp Gln Cys Ala Cys Ser His Gln Leu Ser Ala Ala Leu Ser
1 5 10 15

Thr Glu Asp Met Leu Arg Thr Ser Ser Ile Val Phe Leu Thr Cys Cys
20 25 30

Leu Thr Phe Leu Ile Glu Gly Ser Ser Phe Lys Leu Lys Ile Ile His
35 40 45

Phe Asn Asp Ile His Ala Arg Phe Asp Glu Val Thr Asn Ser Ser Ser
50 55 60

Pro Cys Ser Gly Asn Gly Glu Thr Cys Val Ala Gly Ile Ala Arg Leu
65 70 75 80

Val Thr Thr Ile Glu Lys Leu Arg Lys Gln Asn Glu Asn His Leu Val
85 90 95

Leu Asn Ala Gly Asp Val Phe Gln Gly Thr Ile Trp Tyr Thr Leu Leu
100 105 110

Lys Trp Asn Val Ser Gln Gln Phe Met Asn Met Val Lys Ala Asp Ala
115 120 125

Met Thr Leu Gly Asn His Glu Phe Asp Asp Ser Phe Pro Val Leu Ile
130 135 140

Pro Phe Leu Glu Asn Thr Lys Asn Val Thr Pro Val Val Val Ser Asn
145 150 155 160

Leu Val Phe Pro Lys Gln Leu Ser Arg Asp Val Thr Lys Phe Arg Ser
165 170 175

Leu Ile Lys Glu Asp Pro Leu Val Leu Thr Val Gly Gly Gln Ser Ile
180 185 190

Gly Ile Ile Gly Val Ile Phe Asp Glu Thr Asp Lys Ile Gly Asn Ser
195 200 205

Asp Pro Leu Lys Phe Lys Ser Ser Ile Glu Thr Val Arg Ile Ala Ala
210 215 220

Lys Gln Leu Lys Ser Lys Gly Val Asn Ile Ile Ile Val Leu Ser His
225 230 235 240

Cys Gly Val Phe Asp Asp Lys Lys Ile Ala Glu Gln Ala Gly Glu Asp
245 250 255

Ile Asp Ile Ile Val Gly Gly His Thr His Thr Leu Leu Tyr Asn Gly
260 265 270

Asp Pro Pro Ser Lys His Ala Ala Leu Asp Lys Tyr Pro Ile Val Val
275 280 285

Glu Thr Gly Asn Asn His Lys Val Leu Ile Val Gln Ala Phe Cys His
290 295 300

Gly His Tyr Val Gly Asn Ile Asp Leu Thr Phe Asp Asp Glu Gly Glu
305 310 315 320

Ile Thr Ala Phe Glu Gly Gln Pro Ile Tyr Gln Glu Asn Arg Ile Glu
325 330 335

Lys Asn Ala Leu Val Glu Ala Arg Val Arg Glu Leu Arg Lys Asp Val
340 345 350

Glu Val Lys Ser Leu Val Lys Val Gly Glu Ser Lys Leu Glu Leu Ser
355 360 365

Asn Asp Cys Arg Leu Lys Asp Cys Thr Phe Gly Ser Val Leu Ala Asp
370 375 380

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Ala Tyr Val Trp His Phe Arg Ser Arg Ser Asn Ala Pro Met Ile Ala
385                 390                 395                 400

Met Ile His Pro Gly Asn Phe Arg Ile Ser Leu Ala Ala Gly Ala Ile
                405                 410                 415

Thr Arg Gly Gln Ile Leu Thr Ala Leu Pro Phe Asn Ser Asn Ala Asn
            420                 425                 430

Arg Val Thr Val Leu Gly Ser Thr Ile Lys Lys Ala Ile Glu Phe Gly
        435                 440                 445

Thr Ser Ile Asn Pro Arg Arg Cys Ser Phe Asn Ala Leu Gln Thr Ala
    450                 455                 460

Gly Ile Lys Ile Asp Val Asp Tyr Gly Lys Pro Val Gly Asn Arg Thr
465                 470                 475                 480

Val Ile Leu Leu Lys Thr Gly Gly Lys Tyr Lys Arg Leu Val Glu Ser
                485                 490                 495

Lys Lys Tyr Asp Ile Leu Val Asn Ser Tyr Val Phe Lys Gly Gly Asp
            500                 505                 510

Gly Phe Asp Met Phe Lys His Leu Ala Val Lys Gly Arg Ala Pro Phe
        515                 520                 525

Asp Ala Glu Leu Leu Glu Gln Tyr Ile Val Ala Arg Lys Gly Ile Gln
    530                 535                 540

Lys Ser Gly Leu Leu Gln Ser Arg Met Asn Val Ser His Val Glu Lys
545                 550                 555                 560

Ala Leu Ser Glu Val Lys Ser Cys Lys Gln Ser Arg
                565                 570


<210> SEQ ID NO 105
<211> LENGTH: 418
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 105

Met Cys Ser Thr Gly Phe Cys Leu Val Phe Phe Leu Ala Gln Val Val
1               5                   10                  15

Phe Gln Met Asn Tyr Ser Glu Gln Gln Thr Thr Val Val Met Glu Asn
            20                  25                  30

Gly Ala Ile Ser Glu Ser Glu Ile Asn Val Asp Ile Val Met Glu Gln
        35                  40                  45

Tyr Ile Leu Lys Phe Tyr Thr Lys Arg Phe Val Glu Gly Gln Asn Leu
    50                  55                  60

Val Val Ala Pro Leu Leu Thr Phe Arg Val Phe Met Ser Leu Tyr Lys
65                  70                  75                  80

Ala Met Asp Ala Ser Ala Lys Phe Asp Leu His Ser Leu Leu Gly Ile
                85                  90                  95

Gln Gln Asp Thr Ser Val Glu Lys Met Ser Glu Ile Glu Ala Phe Ala
            100                 105                 110

Asn Lys His Thr Leu Pro Val Asp Glu Lys Gln Ile Ser Val Glu Thr
        115                 120                 125

Arg Leu Tyr Tyr Asp Lys Ser Ile Gly Asn Ala Arg Ser Val Leu Thr
    130                 135                 140

Ala Lys Ser Leu Lys Pro Ile Gly Thr Ser Phe Ser Asp Lys Arg Ala
145                 150                 155                 160

Phe Cys Glu Lys Val Asn Ser Trp Ile Arg Asn Ala Pro Ile Lys Gly
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                165                 170                 175

Thr Asp Asn Leu Val Arg Asp Tyr Asp Leu Asn Asn Glu Thr Gln Ala
            180                 185                 190

Phe Val Ala Gly Ala Leu Ser Ile Tyr Trp Asn Thr Gln Leu Lys Ser
        195                 200                 205

Ser Thr Asp Gln Lys Gly Phe Gln Gly Glu Asn Val Lys Phe Leu Glu
    210                 215                 220

Gly Ser Ile Ser Ala Gly Tyr Ala Lys Leu Asp Asn Leu Lys Val Glu
225                 230                 235                 240

Val Val Glu Leu Ile Ser Asp Lys Val Asp Gly Val Lys Leu Trp Leu
                245                 250                 255

Ile Met Pro Asp Arg Ala Ser Ser Ile Lys Asp Phe Asn Asp Gln Leu
            260                 265                 270

Ser Val Glu Ser Ile Arg Gln Ile Glu Asn Gly Leu Thr Ala Gln Lys
        275                 280                 285

Val Asp Val Ser Leu Ala Leu Pro Met Val Thr Ile Glu Tyr Asn Ser
    290                 295                 300

Gln Glu Asp Ala Tyr Val Thr Glu Val Phe Glu Val Phe Ser Ser Leu
305                 310                 315                 320

Phe Thr Lys Pro Ser Val Lys Leu Val Asp Gly Lys Asp Asp Leu Tyr
                325                 330                 335

Val Ile Lys Asn Phe Leu Met Lys Cys Ile Leu Arg Phe Val Glu Ser
            340                 345                 350

Asp Ala Ser Ala Asp Ser Lys Ala Gln Ser Thr Gly Met Leu Val Lys
        355                 360                 365

Phe Asp Arg Pro Phe Val Met Met Met Leu Ser Lys Glu Gly Asn Val
    370                 375                 380

Pro Ile Leu Leu Ala Asn Tyr Phe Ser Pro Thr Asp Lys Leu Arg Ala
385                 390                 395                 400

Leu Glu Ala Lys Glu Arg Arg Leu Lys Ala Glu Ala Asn Glu His Leu
                405                 410                 415

Asp Leu


<210> SEQ ID NO 106
<211> LENGTH: 417
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 106

Met Asn Leu Trp Ile Ile Gly Phe Cys Ser Ile Tyr Phe Ala Cys Ser
1               5                   10                  15

Val Arg Ser Gln Phe Thr Ser Val Pro Val Ser Tyr Asp Ala Gln Asn
            20                  25                  30

Asp His Asn Glu Phe Ser Trp Asn Ala Phe Lys Lys Val Phe Thr Asp
        35                  40                  45

Tyr Lys Glu Asn Phe Val Met Ser Pro Tyr Ser Leu Arg Arg Leu Phe
    50                  55                  60

Ser Cys Phe Gln Gly Val Lys Leu Leu Thr Ser Ala Ser Gly Thr Asn
65                  70                  75                  80

Leu Gln Gln Glu Leu Ser Asn Val Leu Lys Ile Val Pro Asn Gln Gln
                85                  90                  95

Pro Ser Gly Gln Asp His Arg Pro Tyr Val Glu Gln Trp Val Arg Tyr
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            100                 105                 110

Ser Ser Ala Lys Tyr Leu Asn Arg Thr Ala Met Ala Val Ala Ile Gly
        115                 120                 125

Ser Glu Lys Val Ser Thr Val Tyr Glu Ser Ile Ile Asn Asn Cys Val
    130                 135                 140

Ile Tyr Thr Gly His Leu Gln Pro Ser Asn Ala Gln Arg Met Gly Gln
145                 150                 155                 160

Val Ile Asn Asp Ala Leu Lys Asn Ile Thr Asn Asn Ala Val Gln Ser
                165                 170                 175

Tyr Leu Thr Asp Thr Asp Ile Asn Pro Asn Trp Lys Phe Phe Ala Ile
            180                 185                 190

Asp Ser Trp Gln Phe Glu Gly Leu Trp Lys Phe Lys Phe Gln Glu Glu
        195                 200                 205

Phe Ser Ala Thr Cys Tyr Phe Tyr Ala Ser Arg Glu Lys Lys Gly Leu
    210                 215                 220

Thr Lys Phe Leu Tyr Leu Glu Glu Met Leu Lys Tyr Gly Asn Phe Pro
225                 230                 235                 240

Glu Trp Asn Val Gln Ala Val Glu Leu Pro Tyr His Asp Gln Ser Pro
                245                 250                 255

Leu Ser Cys Leu Leu Met Met Pro Leu Asp Gly Asn Tyr Glu Ser Leu
            260                 265                 270

Ile His Ser Met Asn Gln Ser Arg Phe Lys Glu Val Leu Ser Lys Leu
        275                 280                 285

Asn Glu Ile Lys Thr Thr Val Arg Ile Pro Gln Phe Gly Leu Gln Thr
    290                 295                 300

Thr Val Pro Gly Arg Gln Leu Leu Glu Ser Met Gly Met Lys Val Pro
305                 310                 315                 320

Phe Asn Gln Gly Val Phe Lys Val Phe Glu Gln Gly Gln Asp Val Ala
                325                 330                 335

Leu Gly Glu Ile Val Gln Lys Met Glu Met Ser Ile Ala Ala Asp Gly
            340                 345                 350

Glu Lys Gln Ala Gln Ser Phe Val Asp Lys Arg Gln Asp Lys Gln Phe
        355                 360                 365

Thr Ala His Gln Pro Phe Leu Phe Val Val Tyr Asp Arg Asn Glu Leu
    370                 375                 380

Val Pro Ile Leu Val Gly Phe Tyr Leu Lys Thr Pro Pro Glu Ala Ala
385                 390                 395                 400

Met Gly Leu Glu Asp Lys Gln Lys Cys Asp Asp Pro Pro Val Gly Tyr
                405                 410                 415

Gln


<210> SEQ ID NO 107
<211> LENGTH: 291
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 107

Met Asn Arg Gln Leu Trp Ile Ile Ile Phe Ala Ile Leu Cys Val Ala
1               5                   10                  15

Gln Ala Glu Glu Asp Asn Pro Thr Thr Glu Lys Met Glu Glu Leu Gly
            20                  25                  30

Ile Ala Thr Ile Asn Asn Phe Thr Arg Glu Phe Tyr Ser Tyr Val Glu
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        35                  40                  45

Ala Val Ser Gln Val Leu Ala Asp Leu Glu Leu Thr Thr Thr Ala Ser
    50                  55                  60

Ile Thr Gln Ile Lys His Arg Ile Lys His Leu Leu Gln Glu Lys Cys
65                  70                  75                  80

Asn Leu Cys Ser Ala Lys Ala Glu Gly Pro Ala Leu Asp Gln Gly Tyr
                85                  90                  95

Val Thr Thr Ser Asn Gly Ser Val Ile Pro Val Ser Tyr Glu Gln Thr
            100                 105                 110

Arg Phe Gly Gly Gly Trp Ile Val Leu Met Gln Arg Tyr Asp Gly Thr
        115                 120                 125

Val Arg Phe Asn Arg Ser Trp Ala Glu Tyr Arg Asp Gly Phe Gly Met
    130                 135                 140

Val Gly His Glu Phe Trp Leu Gly Leu Glu Arg Ile His Gln Met Thr
145                 150                 155                 160

Lys Asp Ala Glu Tyr Glu Leu Met Ile Glu Met Gln Asp Phe Glu Gly
                165                 170                 175

Asn Tyr Lys Tyr Ala Gly Tyr Asp Ala Phe Ala Val Gly Pro Glu Glu
            180                 185                 190

Glu Arg Tyr Pro Leu Ala Lys Val Gly Lys Phe Asn Lys Thr Ala Tyr
        195                 200                 205

Val Asp Ser Phe Gly Lys His Arg Gly Tyr Gly Phe Ser Thr Tyr Asp
    210                 215                 220

Asn Asp Asp Asn Gly Cys Ser Asn Gln Tyr Gly Arg Gly Gly Trp Trp
225                 230                 235                 240

Tyr Tyr Arg Lys Ser Cys Phe Gly Ala Ser Leu Thr Gly Ile Trp Gln
                245                 250                 255

Asn Lys Gln Asp Trp Lys Ser Ile Ser Trp Val Trp Phe Ser Thr Glu
            260                 265                 270

Lys Lys Gln Val Pro Leu Lys Phe Ala Arg Met Met Met Arg Leu Lys
        275                 280                 285

Thr Ala Glu
    290


<210> SEQ ID NO 108
<211> LENGTH: 290
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 108

Met Ile Leu Gln Phe Trp Phe Val Thr Phe Ser Val Leu Phe Ala Ala
1               5                   10                  15

Arg Ala Asp Glu Asn His Ser Ile Leu Ile Lys Leu Asn Asp Leu Asp
            20                  25                  30

His Arg Phe Thr Gln Met Phe Ser Gln Gln Phe Tyr Arg His Thr Arg
        35                  40                  45

Glu Val Thr Asp Arg Val Ser Ala Leu Lys Ala Ser Ile Asp Thr Asn
    50                  55                  60

Leu Leu Glu Leu Asp Gln Gln Ile Gln Gln Ala Leu Asp Gly Ile Gln
65                  70                  75                  80

Ser Asn Glu Ser Ser Ser Ser Ser Thr Ser Ala Thr Lys Ser Ser Gly Leu
                85                  90                  95
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```
Thr Thr Ile Pro Ile Gly Ser Glu Pro Arg Val Pro Ala Leu Tyr Glu
            100                 105                 110

Arg Glu Arg Tyr Gly Gly Asp Trp Leu Val Val Met His Arg Tyr Asp
        115                 120                 125

Gly Ser Val Lys Phe Asp Arg Thr Trp Ala Glu Tyr Arg Asp Gly Phe
    130                 135                 140

Gly Met Val Gly Gln Glu Phe Trp Tyr Gly Leu Glu Arg Leu His Gln
145                 150                 155                 160

Leu Thr Lys Glu Lys Ser Tyr Glu Leu Met Val Glu Met Glu Asp Phe
                165                 170                 175

Asn Gly Asn Leu Lys Tyr Ala Trp Tyr Asp Lys Phe Val Val Gly Pro
            180                 185                 190

Glu Glu Gln Arg Tyr Ala Leu Val Glu Leu Gly Thr Phe Asn Gly Thr
        195                 200                 205

Thr Asp Gly Asp Ser Leu Lys Pro His Lys Gly Ser Gly Phe Ser Thr
    210                 215                 220

Tyr Asp Asn Asp Asp Phe Gly Cys Ser Asn Lys Tyr Ala Lys Gly Gly
225                 230                 235                 240

Trp Trp Tyr Tyr Ser Gly Lys Cys Tyr Gly Ser Ser Leu Thr Gly Ile
                245                 250                 255

Trp Lys Asn Glu Leu Ala Tyr Ser Ser Ile Val Trp Val Lys Phe Ser
            260                 265                 270

Asp Val Ser Asn Thr Pro Leu Lys Leu Val Arg Met Met Ile Arg Pro
        275                 280                 285

Lys Asn
    290


<210> SEQ ID NO 109
<211> LENGTH: 312
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 109

Met Ser Pro Ser Asn Lys Ile Leu Val Leu Leu Leu Phe Pro Ile Leu
1               5                   10                  15

Leu Val Ser Ser His Pro Ile Pro Ala Glu Asp Pro Ala Lys Gln Cys
            20                  25                  30

Asn Leu Ser Glu Asp Asp Leu Thr Lys Leu Lys Ala Ala Ile Ser Gly
        35                  40                  45

Ala Ser Ser Ala Lys Ala Ala Asn Glu Asp Ile Leu Pro Asn Thr Thr
    50                  55                  60

Leu Ala Ala Cys Pro Met Leu Lys Asn Phe Thr Glu Met Leu Lys Thr
65                  70                  75                  80

Val Ala Thr Asp Met Glu Val Leu Lys Thr Gln Gly Val Ser Asn Met
                85                  90                  95

Glu Val Gln Leu Leu Arg Glu Ser Phe Glu Glu Lys Leu Asn Asp Leu
            100                 105                 110

Ala Lys Asn Lys Asp Ile Phe Glu Arg Gln Ala Asn Gln Asp Thr Ser
        115                 120                 125

Lys Ala Glu Gly Glu Met Val Glu Lys Ile Asn Lys Leu Gln Leu Glu
    130                 135                 140

Met Ala Lys Leu Gln Glu Glu Ile Glu Glu Gln Thr Lys Gln Met Tyr
145                 150                 155                 160
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```
Val Asp Met Ile Glu Tyr Ile Phe Glu Arg Leu Lys Met Asn Asp Thr
                165                 170                 175

Glu Ala Ile Asp Ser Tyr Ala Gln Ile Val Met Lys Thr Lys Met His
            180                 185                 190

Glu Leu Ile Met Lys Leu Lys Thr Asp Arg Leu Val Leu Trp Glu Met
        195                 200                 205

Val Lys Tyr Val Glu Gly Lys Lys Asn Lys Trp Val Gly Arg Lys Val
    210                 215                 220

Leu Asn Thr Ile Leu Asp Gln Val Asn Lys Leu Lys Leu Tyr Lys Pro
225                 230                 235                 240

Glu Glu Val Glu Ile Gly Lys Asn Ser Leu Val Val Val Trp Cys Trp
                245                 250                 255

Lys Phe Asn Ser Glu Thr Val Tyr Gly Thr Thr Asp Glu Asp Gln Lys
            260                 265                 270

Ser Phe His Leu Ala Lys Leu Phe Phe Pro Lys Glu Lys Gly Cys Lys
        275                 280                 285

Glu Cys Ala Asn Val Lys Ser Arg Thr Met Cys Asn Asn Asp Tyr Pro
    290                 295                 300

Lys Val Met Val Lys Ala Phe Gly
305                 310


<210> SEQ ID NO 110
<211> LENGTH: 321
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 110

Met Lys Leu Pro Leu Leu Leu Ala Ile Val Thr Thr Phe Ser Val Val
1               5                   10                  15

Ala Ser Thr Gly Pro Phe Asp Pro Glu Glu Met Leu Phe Thr Phe Thr
            20                  25                  30

Arg Cys Met Glu Asp Asn Leu Glu Asp Gly Pro Asn Arg Leu Pro Met
        35                  40                  45

Leu Ala Lys Trp Lys Glu Trp Ile Asn Glu Pro Val Asp Ser Pro Ala
    50                  55                  60

Thr Gln Cys Phe Gly Lys Cys Val Leu Val Arg Thr Gly Leu Tyr Asp
65                  70                  75                  80

Pro Val Ala Gln Lys Phe Asp Ala Ser Val Ile Gln Glu Gln Phe Lys
                85                  90                  95

Ala Tyr Pro Ser Leu Gly Glu Lys Ser Lys Val Glu Ala Tyr Ala Asn
            100                 105                 110

Ala Val Gln Gln Leu Pro Ser Thr Asn Asn Asp Cys Ala Ala Val Phe
        115                 120                 125

Lys Ala Tyr Asp Pro Val His Lys Ala His Lys Asp Thr Ser Lys Asn
    130                 135                 140

Leu Phe His Gly Asn Lys Glu Leu Thr Lys Gly Leu Tyr Glu Lys Leu
145                 150                 155                 160

Gly Lys Asp Ile Arg Gln Lys Lys Gln Ser Tyr Phe Glu Phe Cys Glu
                165                 170                 175

Asn Lys Tyr Tyr Pro Ala Gly Ser Asp Lys Arg Gln Gln Leu Cys Lys
            180                 185                 190

Ile Arg Gln Tyr Thr Val Leu Asp Asp Ala Leu Phe Lys Glu His Thr
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        195                 200                 205

Asp Cys Val Met Lys Gly Ile Arg Tyr Ile Thr Lys Asn Asn Glu Leu
    210                 215                 220

Asp Ala Glu Glu Val Lys Arg Asp Phe Met Gln Val Asn Lys Asp Thr
225                 230                 235                 240

Lys Ala Leu Glu Lys Val Leu Asn Asp Cys Lys Ser Lys Glu Pro Ser
                245                 250                 255

Asn Ala Gly Glu Lys Ser Trp His Tyr Tyr Lys Cys Leu Val Glu Ser
            260                 265                 270

Ser Val Lys Asp Asp Phe Lys Glu Ala Phe Asp Tyr Arg Glu Val Arg
        275                 280                 285

Ser Gln Ile Tyr Ala Phe Asn Leu Pro Lys Lys Gln Val Tyr Ser Lys
    290                 295                 300

Pro Ala Val Gln Ser Gln Val Met Glu Ile Asp Gly Lys Gln Cys Pro
305                 310                 315                 320

Gln


<210> SEQ ID NO 111
<211> LENGTH: 332
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 111

Met His Ser Pro Lys Ser Phe Leu Leu Leu Ala Val Val Phe Val Ala
1               5                   10                  15

Leu Arg Val Thr Ala Ala Pro Leu Trp Asn Ala Lys Asn Pro Glu Gln
            20                  25                  30

Leu Gln Tyr Ile Ala Ala Arg Cys Met Glu Glu Trp Ser Pro Lys Ala
        35                  40                  45

Lys Asp Pro Lys Ala Ala Leu Lys Asn Trp Met Glu Trp Lys Leu Gln
    50                  55                  60

Pro Ser Asn Glu Glu Ala Thr Gln Cys Tyr Thr Lys Cys Met Leu Glu
65                  70                  75                  80

Asn Ile Gly Tyr Tyr Glu Pro Gly Glu Lys Arg Leu Lys Gly Val Arg
                85                  90                  95

Val Met Gln Gln Trp Glu Thr Phe Asn Arg Tyr Gln Ser Ala Asp Arg
            100                 105                 110

Asn Lys Val His Asp Leu Thr Asp Thr Phe Asp Phe Ile Lys Pro Leu
        115                 120                 125

Lys Ser Ser Ser Cys Ser Asp Val Phe Asn Ala Tyr Lys Asp Val His
    130                 135                 140

Ala Lys His Leu Glu Thr Ile Lys Ala Ile Leu Phe Cys Asp Gly Lys
145                 150                 155                 160

Ser Ala Glu Lys Tyr Tyr Lys Asp Lys Gly Lys Asn Val Lys Gln Lys
                165                 170                 175

Gly Glu Ser Ile Phe Val His Cys Glu Glu Ile His Tyr Pro Val Gly
            180                 185                 190

Ser Pro Gln Arg Asn Glu Leu Cys Lys Val Arg Lys Tyr Glu Leu Gly
        195                 200                 205

Thr Gly Lys Pro Phe Glu Asn Leu Met Glu Cys Ile Phe Lys Gly Val
    210                 215                 220

Arg Tyr Phe Asn Asp Lys Asn Glu Leu Asn Ile Asp Glu Ile Ala Arg
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225                 230                 235                 240

Asp Phe Thr Gln Val Gly Lys Lys Pro Asp Ala Val Lys Ala Ala Met
                245                 250                 255

Glu Asn Cys Lys Ser Lys Thr Lys Glu Thr Asp Pro Gly Lys Lys Ala
            260                 265                 270

Val Glu Tyr Tyr Lys Cys Leu Leu Ala Asp Ser Lys Val Lys Lys Asp
        275                 280                 285

Phe Met Glu Ala Phe Asp Tyr Arg Glu Ile Arg Ser Lys Asp Tyr Tyr
    290                 295                 300

Ala Gln Ile Thr Gly Lys Leu Lys Pro Tyr Ser Ala Ser Asp Val Arg
305                 310                 315                 320

Lys Glu Val Asn Asp Ile Asp Ser Asn Lys Cys Val
                325                 330


<210> SEQ ID NO 112
<211> LENGTH: 568
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 112

Met Lys Leu Lys Val Tyr Ile Cys Gln Val Ile Phe Ser Phe Leu Ala
1               5                   10                  15

Val Ser Val Phe Cys Glu Glu Asn Cys Asn Ile Pro Glu Ser Glu Leu
            20                  25                  30

Ser Lys Ile Asp His Val Leu Arg His Met Glu Lys Pro Ile Tyr Ser
        35                  40                  45

Glu Glu Gln Phe Ala Ser Asp Asn Glu Glu Cys Thr Asn Leu Leu Asn
    50                  55                  60

Gly Ile His Ala Gln Leu Arg Arg Leu Thr Gln Arg Tyr Lys Leu Met
65                  70                  75                  80

Asn Lys Gly Tyr Val Lys Val Glu Glu Tyr Gln Arg Met Ala Asp Asp
                85                  90                  95

Tyr Glu Lys Gln Leu Lys Thr Leu Asn Asp Glu Leu Val Glu Leu Gln
            100                 105                 110

Gln His Thr Ser Glu Lys Ala Ser Ala Thr Ile Ala Lys Leu Lys Glu
        115                 120                 125

Asp Ile Lys Lys Leu Asp Glu Glu Val Gly Thr Leu His Glu Lys Leu
    130                 135                 140

Lys Gly Ile Lys Gln Asp Phe Glu Lys Val Lys Arg Asp Leu Cys Val
145                 150                 155                 160

Thr Tyr Leu Asn Ser Asn Gln Met Ser Lys Ala Lys Ala Lys Leu Lys
                165                 170                 175

Glu Met Ala Ser Thr Tyr Leu Ile Glu Ile Val Gln Gln Gln Leu Asn
            180                 185                 190

Lys Ser Asn Ala Asn Ile Met Pro Met Leu Glu Phe Ser Ala Ala Ile
        195                 200                 205

Pro Asp Leu Asp Asp Met Gly Glu Ala Tyr Lys Glu Ile Tyr Lys Phe
    210                 215                 220

Leu Glu Glu Gln Lys Arg Leu Glu Gly Glu Asp Ser Val Leu Leu Glu
225                 230                 235                 240

Ala Thr Val Leu Lys Met Asn Ala Ser Leu Lys Glu Gly Ser Asn Ile
                245                 250                 255
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Thr Asp Glu Arg Arg Thr Gln Ile Glu Gly Leu Leu Lys Asp Leu Ala
            260                 265                 270

Thr Lys Ser Thr Ile Val Phe Ser Thr Trp Thr Lys Glu Leu Lys Lys
        275                 280                 285

Ile Asn Asp Ala Val Val Ile Lys Asn Ala Leu Asp His Met Phe Val
    290                 295                 300

Ser Gln Met Lys Val Phe Gly Ala Leu Val Gly Asp Thr Ser Asp Phe
305                 310                 315                 320

Gly Ser Ile Arg Asn Phe Val Lys Leu Thr Val Val Cys Asn Asn Tyr
                325                 330                 335

Tyr Lys Val Ala Ala Tyr Lys Glu Leu Ile Asp Arg Lys Ile Gly Asn
            340                 345                 350

Ala Leu Gly Thr Ile Met Phe Asp Leu Leu Thr Leu Glu Val Asn Glu
        355                 360                 365

Met Lys Phe Asp Pro His Val Pro Asp Glu Ile Pro Lys Leu Phe Glu
    370                 375                 380

Ala Thr Leu Ser Ser Leu Pro Asn Ser Leu Thr Glu Leu Arg Thr Cys
385                 390                 395                 400

Leu Gly Lys Val Gln Ile Tyr Asn Lys Lys Thr Asn Lys Cys Val Val
                405                 410                 415

Ala Thr Gly Asn Asp Phe Asp Val His Lys Asp Lys Leu Gly Asp Phe
            420                 425                 430

Tyr Arg Val Val Val Ala Asp Tyr Gly Cys Thr Ser Phe Arg Leu Glu
        435                 440                 445

Ala Ser Gly Asp Lys Ala Ser Val Arg Ile Val Thr Pro Ser Gly Asn
    450                 455                 460

Pro Met Ser Asn Val Asn Leu His Leu Glu Gly Asn Ser Leu His Asn
465                 470                 475                 480

Tyr Val Ala Thr Pro Lys Ser Asn Lys Pro Asp Arg Thr Pro Ser Ser
                485                 490                 495

Ser Asp Glu Trp Ile Leu Asp Ala Asn Tyr Asn Asn Asp Thr Ile Lys
            500                 505                 510

Ile Glu Ser Gln Phe Ser Asp Tyr Lys Thr Lys Lys Thr Glu Val Asp
        515                 520                 525

His Leu Leu Val Arg Asp Ile Asn His Leu Pro His Val Leu Val Ala
    530                 535                 540

Arg Tyr Gly Phe Met Gly Leu Lys Asn Ser Asp Ala Lys Asp Thr Ile
545                 550                 555                 560

Glu Trp Asn Leu Lys Cys Gly Ser
                565


<210> SEQ ID NO 113
<211> LENGTH: 316
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 113

Met Glu Thr Ser Leu Pro Ile Thr Val Val Phe Leu Ile Val Leu Ile
1               5                   10                  15

Thr Gly Ala Gln Thr Lys Pro Thr Gln Gly Ser Cys Thr Leu Thr Asp
            20                  25                  30

Glu Asp Ile Ser Asp Ile Lys Ser Ala Val Gln Lys Ala Ser Lys Ala
        35                  40                  45
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Ala Val Asn Asp Ile Val Leu Asp Pro Thr Leu Ile Asp Lys Cys Pro
    50                  55                  60

Met Leu Glu Lys Ile Thr Ala Ser Leu Lys Ser Val Ala Thr Glu Ile
65                  70                  75                  80

Val Gln Met Arg Asp Ser Ala Ile Ser Thr Asp Gln Val Asp Gln Leu
                85                  90                  95

Lys Gln Asn Phe Glu Asp Gln Val Asn Gln Ile Val Lys Ser Arg Asp
            100                 105                 110

Ile Phe Glu Lys Gln Ser Gly Thr Gln Ala Thr Lys Glu His Gly Glu
        115                 120                 125

Met Leu Glu Arg Met Thr Ala Leu Gln Val Lys Val Thr Glu Leu Glu
    130                 135                 140

Gln Gln Ile Ala Lys Gln Thr Ala Ser Met Tyr Glu Asp Met Ala Glu
145                 150                 155                 160

Leu Ile Phe Gln Arg Leu Gln Met Asn Ser Thr Glu Ser Val Arg Ser
                165                 170                 175

Tyr Thr Lys His Met Met Glu Glu Lys Leu Glu Glu Leu Met Asn Lys
            180                 185                 190

Leu Glu Thr Asn Tyr Arg Ile Tyr Leu Gly Ala Leu Arg Phe Leu Asn
        195                 200                 205

His Met Asn Asp Gln Glu Leu Ile Gly Lys Val Phe Asp Gly Ile Leu
    210                 215                 220

Lys Arg Leu Gly Asp Met Lys Ala Asp Ser Asp Asp Val Lys Glu Asn
225                 230                 235                 240

Gly Arg Asn Leu Leu Val Asn Leu Leu Cys Trp Thr Val Asn Asn Asp
                245                 250                 255

Phe Leu Gly Lys Lys Tyr Lys Glu Arg Gln Val Asp Leu Tyr Arg Met
            260                 265                 270

Ala Leu Lys Phe Tyr Pro Lys Thr Tyr Glu Lys Ala Ala Asn Glu Ala
        275                 280                 285

Asp Val Arg Ser Arg Gln Phe Cys Glu Glu Asn Phe Pro Ala Asn Leu
    290                 295                 300

Ile Thr Trp Phe Ala Val Ser Trp Asn Asp Arg Gly
305                 310                 315


<210> SEQ ID NO 114
<211> LENGTH: 215
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 114

Met Lys Tyr Leu Leu Thr Phe Leu Met Ala Leu Ser Leu Val Asn Leu
1               5                   10                  15

Met Leu Thr Arg Pro Thr Pro Glu Asp Asp Gly Gly Thr Ser Glu Glu
            20                  25                  30

Pro Gln Thr Gln Glu Thr Thr Gly Ser Asp Glu Lys Asn Gly Ala Ser
        35                  40                  45

Glu Glu Pro Asn Ala Asp Asp Ala Ser Lys Pro Asp Asp Val Glu Glu
    50                  55                  60

Lys Gly Asp Asp Asp Thr Ala Lys Lys Glu Asp Asp Gly Glu Ser Lys
65                  70                  75                  80

Asp Gly Glu Gly Ser Glu Lys Ser Asp Lys Glu Lys Gly Glu Pro Lys
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               85                  90                  95

Asn Asp Pro Arg Glu Thr Tyr Asn Lys Val Ile Glu Gln Leu Asp Gln
            100                 105                 110

Ile Lys Val Asp Asn Val Glu Asp Gly His Glu Arg Ser Glu Leu Ala
        115                 120                 125

Ala Asp Ile Gln Arg Tyr Leu Arg Asn Pro Ile Val Asp Val Ile Gly
    130                 135                 140

Ser Ala Gly Asp Phe Ser Lys Ile Ala Lys Cys Phe Lys Ser Met Val
145                 150                 155                 160

Gly Asp Ala Lys Lys Ala Ile Glu Glu Asp Val Lys Gly Phe Lys Glu
                165                 170                 175

Cys Thr Ala Lys Lys Asp Ser Asn Ala Tyr Gln Cys Ser Gln Asp Arg
            180                 185                 190

Ser Thr Val Gln Asp Lys Ile Ala Lys Met Ser Ser Lys Ile Ala Ser
        195                 200                 205

Cys Val Ala Ser Asn Arg Ser
    210                 215


<210> SEQ ID NO 115
<211> LENGTH: 183
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 115

Met His Ser Leu Lys Ser Ser Pro Leu Leu Ala Ala Val Phe Leu Ala
1               5                   10                  15

Leu His Val Thr Gly Ala Pro Phe Trp Asn Ala Lys Asn Pro Asp Glu
            20                  25                  30

Leu Gln Ser Ile Ala Ala Arg Cys Met Asp Glu Trp Ser Pro Lys Ala
        35                  40                  45

Lys Asp Pro Lys Ala Ala Leu Lys Asn Trp Lys Glu Trp Arg Leu Gln
    50                  55                  60

Pro Ser Asn Asp Glu Ala Thr Lys Cys Tyr Thr Lys Cys Met Leu Glu
65                  70                  75                  80

Asn Ile Gly Phe Tyr Glu Pro Ala Glu Lys Arg Leu Lys Gly Val Arg
                85                  90                  95

Ile Met Gln Gln Trp Glu Thr Phe Ser Arg Tyr Gln Ser Ala Asp Arg
            100                 105                 110

Glu Lys Val His Asp Leu Thr Asp Thr Phe Asn Phe Ile Arg Pro Leu
        115                 120                 125

Lys Ser Ser Ser Cys Thr Asp Val Phe Asn Ala Tyr Lys Asp Val His
    130                 135                 140

Ala Arg His Leu Glu Thr Ile Lys Ala Ile Leu Phe Cys Asp Gly Lys
145                 150                 155                 160

Ser Ala Glu Lys Tyr Tyr Lys Asp Lys Gly Lys Thr Ser Lys Gln Lys
                165                 170                 175

Lys Val Leu Cys Thr Gly Ser
            180


<210> SEQ ID NO 116
<211> LENGTH: 322
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti
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<400> SEQUENCE: 116

Met Lys Thr Ser Leu Pro Ile Val Val Leu Leu Thr Ala Val Ile Ser
1 5 10 15

Gly Val His Pro Asn Pro Thr Pro Lys Ser Cys Thr Val Ser Glu Glu
20 25 30

Asp Leu Thr Thr Ile Arg Asn Ala Ile Gln Lys Ala Ser Arg Ala Ser
35 40 45

Leu Asp Asp Val Asn Leu Asp Glu Asp Leu Ile Ala Lys Cys Pro Leu
50 55 60

Leu Lys Thr Ile Thr Ala Ser Leu Lys Ser Val Ala Ser Glu Ile Ala
65 70 75 80

Thr Leu Lys Asp Thr Gly Ile Ser Glu Glu Gln Val Asp Glu Leu Lys
85 90 95

Gln Ser Tyr Glu Gln Gln Val Asn Glu Ile Val Lys Ser Arg Asp Ile
100 105 110

Phe Glu Lys Gln Ser Gly Gly Asp Val Met Lys Glu Gln Gly Ala Met
115 120 125

Ile Asn Arg Met Thr Glu Leu Gln Val Gln Val Ala Gln Leu Gln Gln
130 135 140

Gln Ile Gly Glu Gln Thr Ser Arg Met Tyr Asp Asp Met Ala Glu Leu
145 150 155 160

Ile Phe Gln Arg Leu Ala Met Asn Ser Thr Asp Ser Ile Arg Asn Tyr
165 170 175

Thr Ala His Met Met Glu Gln Lys Leu His Thr Leu Met Thr Lys Leu
180 185 190

Glu Thr Asn Tyr Arg Ile Phe Leu Gly Ala Leu Arg Tyr Leu Asp His
195 200 205

Leu Gly Asp Gln Pro Leu Ile Asp Lys Val Phe Asp Gly Ile Leu Lys
210 215 220

Arg Leu Asp Glu Met Ser Leu Glu Thr Asn Lys Glu Arg Glu Asn Gly
225 230 235 240

Lys Tyr Val Leu Val Asn Leu Leu Cys Trp Thr Val Asn Asn Arg Phe
245 250 255

Leu Thr Glu Lys Tyr Arg Lys Lys Gln Leu Glu Leu Phe Arg Ile Ala
260 265 270

Leu Lys Phe Tyr Pro Lys Thr Gly Asn Lys Glu Ala Asn Glu Ala Asp
275 280 285

Ile Arg Gly Arg Gln Phe Cys Asp Ala Asn Phe Pro Val Asn Val Ile
290 295 300

Thr Trp Phe Ala Val Ser Arg Ala Ala Glu Gly Trp Gly Leu Arg Gly
305 310 315 320

Thr Leu

<210> SEQ ID NO 117
<211> LENGTH: 614
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 117

Met Ser Thr Leu Lys Lys Ile Ser Asp Glu Asp Arg Glu Ser Lys Phe
1 5 10 15

Gly Tyr Val Phe Ala Val Ser Gly Pro Val Val Thr Ala Glu Arg Met

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            20                  25                  30

Ser Gly Ser Ala Met Tyr Glu Leu Val Arg Val Gly Tyr Tyr Glu Leu
        35                  40                  45

Val Gly Glu Ile Ile Arg Leu Glu Gly Asp Met Ala Thr Ile Gln Val
    50                  55                  60

Tyr Glu Glu Thr Ser Gly Val Thr Val Gly Asp Pro Val Leu Arg Thr
65                  70                  75                  80

Gly Lys Pro Leu Ser Val Glu Leu Gly Pro Gly Ile Met Gly Ser Ile
                85                  90                  95

Phe Asp Gly Ile Gln Arg Pro Leu Lys Asp Ile Asn Glu Leu Thr Ser
            100                 105                 110

Ser Ile Tyr Ile Pro Lys Gly Val Asn Ile Pro Cys Leu Ser Arg Thr
        115                 120                 125

Gln Ser Trp Gly Phe Asn Pro Leu Asn Val Lys Val Gly Ser His Ile
    130                 135                 140

Thr Gly Gly Asp Leu Tyr Gly Leu Val His Glu Asn Thr Leu Val Lys
145                 150                 155                 160

His Lys Leu Leu Val Pro Pro Arg Ala Lys Gly Thr Val Arg Tyr Ile
                165                 170                 175

Ala Pro Pro Gly Asn Tyr Thr Val Asp Asp Ile Ile Leu Glu Thr Glu
            180                 185                 190

Phe Asp Gly Glu Ile Asn Lys Trp Ser Met Leu Gln Val Trp Pro Val
        195                 200                 205

Arg Gln Pro Arg Pro Val Thr Glu Lys Leu Pro Ala Asn His Pro Leu
    210                 215                 220

Leu Thr Gly Gln Arg Val Leu Asp Ser Leu Phe Pro Cys Val Gln Gly
225                 230                 235                 240

Gly Thr Thr Ala Ile Pro Gly Ala Phe Gly Cys Gly Lys Thr Val Ile
                245                 250                 255

Ser Gln Ala Leu Ser Lys Tyr Ser Asn Ser Asp Val Ile Ile Tyr Val
            260                 265                 270

Gly Cys Gly Glu Arg Gly Asn Glu Met Ser Glu Val Leu Arg Asp Phe
        275                 280                 285

Pro Glu Leu Ser Val Glu Ile Asp Gly Val Thr Glu Ser Ile Met Lys
    290                 295                 300

Arg Thr Ala Leu Val Ala Asn Thr Ser Asn Met Pro Val Ala Ala Arg
305                 310                 315                 320

Glu Ala Ser Ile Tyr Thr Gly Ile Thr Leu Ser Glu Tyr Phe Arg Asp
                325                 330                 335

Met Gly Tyr Asn Val Ser Met Met Ala Asp Ser Thr Ser Arg Trp Ala
            340                 345                 350

Glu Ala Leu Arg Glu Ile Ser Gly Arg Leu Ala Glu Met Pro Ala Asp
        355                 360                 365

Ser Gly Tyr Pro Ala Tyr Leu Gly Ala Arg Leu Ala Ser Phe Tyr Glu
    370                 375                 380

Arg Ala Gly Arg Val Lys Cys Leu Gly Asn Pro Glu Arg Glu Gly Ser
385                 390                 395                 400

Val Ser Ile Val Gly Ala Val Ser Pro Pro Gly Gly Asp Phe Ser Asp
                405                 410                 415

Pro Val Thr Ser Ala Thr Leu Gly Ile Val Gln Val Phe Trp Gly Leu
            420                 425                 430
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Asp Lys Lys Leu Ala Gln Arg Lys His Phe Pro Ser Ile Asn Trp Leu
        435                 440                 445

Ile Ser Tyr Ser Lys Tyr Met Arg Ala Leu Asp Asp Phe Tyr Asp Lys
    450                 455                 460

Asn Phe Gln Glu Phe Val Pro Leu Arg Thr Lys Val Lys Glu Ile Leu
465                 470                 475                 480

Gln Glu Glu Glu Asp Leu Ser Glu Ile Val Gln Leu Val Gly Lys Ala
                485                 490                 495

Ser Leu Ala Glu Thr Asp Lys Ile Thr Leu Glu Val Ala Lys Leu Leu
            500                 505                 510

Lys Asp Asp Phe Leu Gln Gln Asn Ser Tyr Ser Ala Tyr Asp Arg Phe
        515                 520                 525

Cys Pro Phe Tyr Lys Thr Val Gly Met Leu Arg Asn Met Ile Gly Phe
    530                 535                 540

Tyr Asp Met Ala Arg His Ala Val Glu Thr Thr Ala Gln Ser Glu Asn
545                 550                 555                 560

Lys Ile Thr Trp Asn Val Ile Arg Asp Ser Met Gly Asn Ile Leu Tyr
                565                 570                 575

Gln Leu Ser Ser Met Lys Phe Lys Asp Pro Val Lys Asp Gly Glu Ala
            580                 585                 590

Lys Ile Lys Ala Asp Phe Asp Gln Leu Tyr Glu Asp Leu Gln Gln Ala
        595                 600                 605

Phe Arg Asn Leu Glu Asp
    610


<210> SEQ ID NO 118
<211> LENGTH: 564
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 118

Met Ala Gly Lys Pro Gly Ile Gln Leu Phe Val Ile Phe Ile Leu Leu
1               5                   10                  15

Ser Ser Phe Ala Ala Val Val Trp Thr Thr Asp Asn Met Pro Ala Asp
            20                  25                  30

Lys Asp Val Ser Lys Leu Phe Pro Leu Thr Leu Ile His Ile Asn Asp
        35                  40                  45

Leu His Ala Arg Phe Asp Glu Thr Asn Met Lys Ser Asn Ala Cys Thr
    50                  55                  60

Ala Lys Asp Gln Cys Ile Ala Gly Ile Ala Arg Val Tyr Gln Lys Ile
65                  70                  75                  80

Gln Asp Leu Leu Lys Glu Tyr Lys Ser Lys Asn Ala Ile Tyr Leu Asn
                85                  90                  95

Ala Gly Asp Asn Phe Gln Gly Thr Leu Trp Tyr Asn Leu Leu Arg Trp
            100                 105                 110

Gln Val Thr Ala Asp Phe Ile Thr Lys Leu Lys Pro Thr Ala Met Thr
        115                 120                 125

Leu Gly Asn His Glu Phe Asp His Thr Pro Lys Gly Leu Ala Pro Tyr
    130                 135                 140

Leu Ala Glu Leu Asp Lys Ala Gly Ile Pro Thr Leu Val Ala Asn Leu
145                 150                 155                 160

Val Met Asn Asp Asp Pro Asp Leu Lys Ser Ser Lys Ile Gln Lys Ser
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                165                 170                 175

Ile Lys Val Thr Val Gly Gly Lys Thr Ile Gly Ile Ile Gly Val Leu
            180                 185                 190

Tyr Asp Lys Thr His Glu Ile Ala Gln Thr Gly Lys Val Thr Leu Ser
        195                 200                 205

Asn Ala Val Glu Thr Val Lys Arg Glu Ala Ala Ala Leu Lys Lys Asp
    210                 215                 220

Lys Val Asp Ile Ile Val Val Leu Ser His Cys Ser Tyr Asp Glu Asp
225                 230                 235                 240

Lys Lys Ile Ala Lys Glu Ala Gly Gln Asp Ile Asp Val Ile Val Gly
                245                 250                 255

Ala His Ser His Ser Phe Leu Tyr Ser Lys Glu Ser Asn Lys Pro Tyr
            260                 265                 270

Asp Gln Lys Asp Lys Ile Glu Gly Pro Tyr Pro Thr Ile Val Glu Ser
        275                 280                 285

Asn Asn Lys Arg Lys Ile Pro Ile Val Gln Ala Lys Ser Phe Gly Lys
    290                 295                 300

Tyr Val Gly Arg Leu Thr Leu Tyr Phe Asp Asn Glu Gly Glu Val Lys
305                 310                 315                 320

His Trp Glu Gly Tyr Pro Glu Phe Ile Asp Asn Lys Val Lys Gln Asp
                325                 330                 335

Pro Lys Ile Leu Glu Ala Leu Ile Pro Trp Arg Lys Lys Val Gln Glu
            340                 345                 350

Ile Gly Ser Thr Lys Val Gly Glu Thr Thr Ile Glu Leu Asp Arg Asp
        355                 360                 365

Ser Cys Arg Asp Lys Glu Cys Thr Leu Gly Val Leu Tyr Ala Asp Ala
    370                 375                 380

Phe Ala Asp His Tyr Thr Asn Ser Ser Phe Arg Pro Phe Ala Ile Ile
385                 390                 395                 400

Gln Ala Gly Asn Phe Arg Asn Pro Ile Lys Val Gly Lys Ile Thr Asn
                405                 410                 415

Gly Asp Ile Ile Glu Ala Ala Pro Phe Gly Ser Thr Ala Asp Leu Ile
            420                 425                 430

Arg Leu Lys Gly Asp Ser Leu Trp Ala Val Ala Glu His Ser Phe Ala
        435                 440                 445

Leu Asp Asp Glu Asn Arg Thr Asn Cys Leu Gln Val Ser Gly Leu Arg
    450                 455                 460

Ile Val Ile Asp Pro Ser Lys Lys Ile Gly Ser Arg Val Val Lys Ile
465                 470                 475                 480

Asp Val Met Asp Asn Arg Asn Pro Lys Ser Glu Asp Leu Lys Pro Leu
                485                 490                 495

Asp Lys Asn Ala Glu Tyr Phe Ile Ala Leu Pro Ser Tyr Leu Ala Asp
            500                 505                 510

Gly Lys Asp Gly Phe Ser Ala Met Lys Lys Ala Thr Ala Arg Trp Thr
        515                 520                 525

Gly Pro Leu Asp Ser Asp Val Phe Lys Ser Tyr Val Glu Lys Ile Lys
    530                 535                 540

Lys Val Asp Lys Leu Lys Trp Gly Arg Val Ile Val Cys Lys Ala Gly
545                 550                 555                 560

Ser Pro Cys Thr
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<210> SEQ ID NO 119
<211> LENGTH: 567
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 119

Met Lys Trp Ser Val Tyr Ile Ala Leu Leu Val Phe Ala Phe Leu Thr
1 5 10 15

Ser Pro Val Phe Ser Glu Glu Asn Cys Asn Ile Pro Glu Ser Glu Leu
20 25 30

Ser Lys Ile Asp Asp Val Leu Arg His Met Glu Lys Pro Ile Tyr Ser
35 40 45

Glu Asp His Tyr Thr Ser Asn Asn Glu Glu Cys Thr Asn Leu Leu Asn
50 55 60

Gly Ile His Ala Gln Leu Arg Arg Leu Thr Gln Arg Tyr Lys Leu Met
65 70 75 80

Asn Lys Gly Tyr Val Lys Val Glu Glu Tyr Lys Arg Met Ala Glu Asp
85 90 95

Tyr Glu Asn Gln Leu Lys Thr Leu Asn Ala Glu Leu Leu Glu Leu Gln
100 105 110

Glu His Thr Ser Asp Lys Ala Asn Ala Ala Ile Ala Lys Leu Lys Glu
115 120 125

Asp Ile Lys Lys Leu Asp Glu Asp Val Asp Thr Leu His Asn Lys Leu
130 135 140

Lys Gly Ile Lys Gln Asp Phe Glu Lys Val Lys Arg Asp Leu Cys Leu
145 150 155 160

Thr Tyr Leu Asn Ser Asn Gln Met Ser Asn Ala Lys Ala Lys Val Lys
165 170 175

Glu Met Ala Ser Thr Tyr Leu Ile Glu Ile Ile Gln Gln Arg Leu Asn
180 185 190

Thr Lys Tyr Ala Asn Ile Ile Pro Met Leu Asp Phe Ser Thr Ala Ile
195 200 205

Pro Asp Leu Asp Asp Arg Gly Glu Ala Tyr Lys Glu Ile Tyr Lys Phe
210 215 220

Ile Glu Thr His Glu Arg Leu Asp Gly Glu Asp Ala Val Leu Leu Glu
225 230 235 240

Ala Ser Leu Leu Lys Met Asn Ala Thr Leu Lys Glu Gly Ser Asn Ile
245 250 255

Thr Asp Glu Arg Arg Thr Glu Ile Glu Lys Met Leu Lys Glu Leu Ala
260 265 270

Glu Lys Ser Ala Val Val Phe Lys Thr Trp Ser Thr Glu Leu Lys Gly
275 280 285

Ile Glu Asp Thr Ile Ile Lys Tyr Ala Leu Asp His Leu Phe Val Asn
290 295 300

Gln Met Lys Val Phe Gly Gly Ile Val Gly Asp Thr Phe Glu Phe Ala
305 310 315 320

Pro Ile Arg His Leu Leu Lys Leu Leu Val Val Cys Asn Asn Tyr Tyr
325 330 335

Lys Val Ala Ala Tyr Lys Glu Leu Ile Asp Arg Lys Ile Gly Asn Val
340 345 350

Leu Gly Thr Ile Met Phe Asp Leu Thr Thr Leu Glu Ala Asn Glu Met
355 360 365

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Ser Phe Asp Leu His Val Pro Asp Glu Ile Pro Lys Leu Phe Asn Ala
    370                 375                 380

Thr Leu Gly Ser Leu Pro Asn Ser Leu Thr Gln Leu Leu Pro Cys Leu
385                 390                 395                 400

Asn Lys Val His Val Tyr Asn Ala Lys Thr Asn Met Cys Ile Val Ala
                405                 410                 415

Pro Glu Asp Arg Phe Asp Val Gln Gln Glu Lys Leu Thr Asp Phe His
            420                 425                 430

Arg Val Val Leu Ala Lys Tyr Gly Cys Thr Ala Phe Arg Leu Glu Ser
        435                 440                 445

Ser Pro Asn Lys Ala Ser Val Lys Phe Val Lys Pro Ser Gly Asn Ala
    450                 455                 460

Leu Ser Ser Ile Asn Leu Gln Leu Glu Asn Asp Gln Trp His Ser His
465                 470                 475                 480

Val Gly Thr Pro Thr Ala Asn Lys Pro Asp Arg Lys Pro Ser Ser Ser
                485                 490                 495

Asp Glu Trp Ile Leu Asp Ala Asn Tyr Val Asn Asp Thr Val Lys Ile
            500                 505                 510

Gln Ser Glu Phe Asn Glu Tyr Lys Ala Ser Gln Ala Glu Val Asp His
        515                 520                 525

Leu Leu Val Met Asp Val Lys Tyr Leu Pro His Val Val Val Gly Arg
    530                 535                 540

Tyr Gly Val Arg Gly Leu Lys Arg Ser Ser Ala Lys Asp Thr Ile Glu
545                 550                 555                 560

Trp Tyr Leu Lys Cys Ala Ser
                565


<210> SEQ ID NO 120
<211> LENGTH: 256
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 120

Met Ala Phe Asn Gly Ile Ala Leu Leu Ile Thr Ala Thr Ile Phe Ile
1               5                   10                  15

Gly Ser Cys Tyr Ala Asn Tyr Cys Asp Ser Ser Leu Cys Arg Gln Gly
            20                  25                  30

Pro His Val Ala Cys Asn Ala Pro Gln Gln Phe Gly Pro Ala Cys Gly
        35                  40                  45

Asn Asn Arg Lys Phe Val Pro Met Asp Ser Lys Leu Lys Thr Ile Ile
    50                  55                  60

Leu Asn Thr His Asn Lys Leu Arg Ala Glu Ile Ala Asn Gly Met His
65                  70                  75                  80

Gly Phe Pro Gln Ala Ala Arg Met Pro Thr Leu Val Trp Asp Asp Glu
                85                  90                  95

Leu Ala His Ile Ala Ser Phe Asn Ala Arg Lys Cys Ile Phe Ala His
            100                 105                 110

Asp Lys Cys Arg Asn Thr Arg Gln Phe Lys Phe Ser Gly Gln Asn Leu
        115                 120                 125

Ala Ile Thr Thr Phe Tyr Gly Phe Asn Phe Gln Ala Gly Asp Arg Ala
    130                 135                 140

Glu Asn Phe Thr Gln Glu Trp Phe Asn Glu His Lys Asp Cys Pro Lys
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145                 150                 155                 160

Ser Tyr Val Asp Ala Tyr Pro Ser Ser His Arg Gly Pro Gln Ile Gly
                165                 170                 175

His Phe Thr Gln Leu Val Asn Asp Arg Thr Trp Lys Val Gly Cys Ser
            180                 185                 190

Met Met His Tyr Ile Thr Asn Gly Lys Met Ile Asn Tyr Tyr Leu Val
        195                 200                 205

Cys Asn Tyr Thr Met Thr Asn Met Ile Gly Glu Pro Ile Tyr Thr Lys
    210                 215                 220

Gly Arg Thr Gly Ser Lys Cys Glu Thr Gly Gln Asn Pro Gln Phe Lys
225                 230                 235                 240

Gly Leu Cys Ser Pro Arg Glu Lys Val Lys Ser Glu Ser Tyr Asn Gly
                245                 250                 255


<210> SEQ ID NO 121
<211> LENGTH: 422
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 121

Met Cys Ser Thr Gly Leu Cys Leu Val Phe Phe Ile Ala Gln Ala Val
1               5                   10                  15

Phe Leu Met Asn Tyr Ser Glu Gln Gln Thr Thr Val Val Met Glu Asn
            20                  25                  30

Gly Ala Ile Ser Glu Lys Glu Thr Asn Val Asp Glu Val Met Thr Gln
        35                  40                  45

Phe Ile Met Lys Phe Tyr Thr Lys Arg Phe Val Glu Gly Gln Asn Leu
    50                  55                  60

Val Val Ala Pro Leu Leu Ile Phe Arg Val Phe Met Ser Met Tyr Gly
65                  70                  75                  80

Glu Met Asp Ala Ser Ala Lys Phe Asp Leu His Ser Leu Val Gly Ile
                85                  90                  95

Pro Gln Glu Ala Ser Ala Glu Lys Met Ser Glu Phe Glu Ala Phe Ala
            100                 105                 110

Asn Lys Tyr Ala Leu Pro Val Gly Val Gln Arg Asn Leu Val Glu Thr
        115                 120                 125

Arg Leu Tyr Tyr Asp Lys Ser Ile Gly Lys Ile Arg Ser Ser Leu Glu
    130                 135                 140

Ala Lys Ser Leu Lys Pro Phe Pro Thr Asn Phe Ala Asp Lys Gln Thr
145                 150                 155                 160

Phe Cys Asn Glu Val Asn Thr Trp Ile Arg Asn Thr Pro Ile Asn Gly
                165                 170                 175

Thr Asp Asp Leu Val His Asp Tyr Tyr Leu Asn Asn Glu Thr Ala Ala
            180                 185                 190

Phe Val Ala Gly Ala Leu Ser Ile Asp Trp Asn Met Gln Leu Lys Thr
        195                 200                 205

Ser Ser Asp Val Lys Ala Phe Glu Gly Glu Asn Val Lys Phe Leu Glu
    210                 215                 220

Gly Ser Ile Ser Thr Arg Tyr Ala Lys Leu Asp Asn Leu Lys Val Glu
225                 230                 235                 240

Val Val Glu Met Val Thr Asp Asn Leu Ser Gly Val Lys Leu Trp Leu
                245                 250                 255
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Ile Met Pro Asp Glu Ala Ser Ser Ile Lys Lys Phe Asn Asp Gln Leu
            260                 265                 270

Ser Ile Ala Ser Ile Arg Gln Ile Glu Lys Gly Leu Thr Ala Leu Gln
        275                 280                 285

Lys Glu Asp Val Ala Leu Thr Val Pro Met Val Thr Ile Glu Tyr Asn
    290                 295                 300

Ser Gln Glu Asp Ala Tyr Val Thr Glu Val Phe Glu Val Phe Ser Ser
305                 310                 315                 320

Leu Phe Ser Lys Pro Ala Val Lys Pro Trp Phe Arg Val Ser Val Lys
                325                 330                 335

Asp Asp Leu Tyr Ala Val Lys Asn Phe Leu Met Lys Cys Ile Leu Arg
            340                 345                 350

Phe Val Gly Ser Asp Ala Pro Ala Asp Ser Lys Gly Gln Ser Thr Glu
        355                 360                 365

Lys Ala Val Ser Phe Asn Arg Pro Phe Val Met Met Ile Leu Ser Lys
    370                 375                 380

Glu Ser Asn Val Pro Ile Leu Leu Ala Asn Tyr Phe Ser Pro Lys Asp
385                 390                 395                 400

Lys Leu Arg Ala Leu Glu Ala Lys Glu Arg His Leu Arg Met Lys Ala
                405                 410                 415

Lys Glu His Leu Asp Leu
            420


<210> SEQ ID NO 122
<211> LENGTH: 533
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 122

Met Lys Ile Leu Leu Ala Val Val Phe Val Leu Asn Leu Thr Asn Leu
1               5                   10                  15

Ala Val Pro Gln His Leu Ile Thr Ser Ser Pro Ser Leu Pro Glu Ser
            20                  25                  30

Lys Pro Val Gly Arg Arg Pro Thr Tyr Glu Glu Tyr Lys Gln Gln Arg
        35                  40                  45

Glu Ser Phe Leu Gln Thr Glu Asp His His Leu Leu Gly Ala Asn Val
    50                  55                  60

Thr Leu Thr Glu Asn Glu Gln Leu Val Asn Lys Phe Ile Met Gln Met
65                  70                  75                  80

Lys Leu Asp Glu Met Glu Lys Gly Phe Asn Asp Ser Tyr Asn Phe Ile
                85                  90                  95

Pro Ala Arg His Ile Phe Glu Val Leu Asp Arg Phe Gly Gln Ser Lys
            100                 105                 110

Val Phe Asn Val Ile Arg Arg Leu Pro Lys Gly Gly Val Leu His Ala
        115                 120                 125

His Asp Met Ala Leu Gly Ser Thr Asp Leu Ile Val Asn Ala Thr Tyr
    130                 135                 140

Leu Glu Asn Leu Trp Gln Lys Gly Asn Phe Gly Leu Asn His Gly Pro
145                 150                 155                 160

Glu Phe Lys Phe Ser Arg Glu Arg Pro Gly Lys Glu Trp Ser Leu Val
                165                 170                 175

Ser Glu Ile Arg Gln Trp Met Thr Asn Glu Val Tyr Asp Ala Lys Val
            180                 185                 190
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Ala Glu Val Phe Ser Leu Tyr Asn Ala Asp Pro Leu Asn Ala Tyr Lys
        195                 200                 205

Ser Leu Asp Asn Val Trp Ser Lys Phe Gln Asn Leu Phe Ala Cys Leu
    210                 215                 220

Ala Pro Leu Ile Thr Phe Ala Pro Val Trp Arg Gln Tyr Tyr His Asp
225                 230                 235                 240

Ser Leu Lys Gln Phe Tyr Asp Asp His Val Gln Tyr Leu Glu Phe Arg
                245                 250                 255

Gly Val Leu Pro Glu Val Tyr Asp Leu Asp Gly Lys Val Tyr Ser Ala
            260                 265                 270

Glu Glu Ile Val Gln Leu Tyr Tyr Glu Glu Thr Glu Gln Phe Lys Ala
        275                 280                 285

Lys Tyr Pro Asp Phe Ile Gly Val Lys Phe Ile Tyr Ala Pro Gly Arg
    290                 295                 300

Tyr Ala Ser Asp Glu Glu Phe Gln Lys Leu Leu Asp Thr Thr Asn Arg
305                 310                 315                 320

Leu His Lys Lys Phe Pro Asn Phe Leu Ala Gly Phe Asp Leu Val Gly
                325                 330                 335

Gln Glu Asp Pro Gly Arg Ser Leu Phe Glu Phe Ala Pro Ala Leu Leu
            340                 345                 350

Lys Leu Pro Ala Ser Ile Asn Phe Phe Phe His Ala Gly Glu Thr Asn
        355                 360                 365

Trp Tyr Gly Met Lys Thr Asp Gln Asn Leu Val Asp Ala Val Leu Leu
    370                 375                 380

Gly Thr Lys Arg Ile Gly His Gly Phe Ala Val Leu Lys His Pro Lys
385                 390                 395                 400

Val Leu Lys Glu Ile Lys Arg Arg Gln Ile Cys Ile Glu Ile Asn Pro
                405                 410                 415

Ile Ser Asn Gln Val Leu Lys Leu Val Gln Asp Gln Arg Asn His Pro
            420                 425                 430

Ala Ala Leu Leu Phe Ser Asp Asn Tyr Pro Val Val Val Ser Ser Asp
        435                 440                 445

Asp Pro Ser Phe Gly Arg Ser Thr Pro Leu Ser His Asp Phe Tyr Val
    450                 455                 460

Ala Phe Thr Gly Ile Ala Ser Ala Lys Gln Asp Trp Arg Trp Leu Lys
465                 470                 475                 480

Gln Leu Ala Leu Asn Ser Ile Glu Tyr Ser Ala Met Asn Ser Glu Glu
                485                 490                 495

Lys Thr Val Ala Lys Glu Lys Trp Asn Gln Ala Trp Asp His Gln Phe
            500                 505                 510

Ser Arg Leu Ala Val Asp Phe Val Ala Gly Lys Ile Leu Glu Asn Trp
        515                 520                 525

Ile Met Lys Ile Val
    530


<210> SEQ ID NO 123
<211> LENGTH: 389
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 123

Met Gln Pro Arg Ile Leu His Leu Thr Val Leu Ala Thr Ile Ile Gly
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-continued

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1               5                   10                  15

Val Ala Leu Thr Ala Asn Val Pro Ser Thr Pro Gly Arg Lys Leu Asn
            20                  25                  30

Ile Pro Ala Phe Ser Asn Ala Gly Lys Thr Lys Gly Ile Glu Ile Trp
        35                  40                  45

Arg Ile Glu Asn Phe Gln Pro Val Ala Val Pro Lys Ala Glu Tyr Gly
    50                  55                  60

Lys Phe Tyr Thr Gly Asp Ser Tyr Leu Val Leu Asn Thr Asn Glu Asp
65                  70                  75                  80

Lys Asn Lys Lys Lys Ser Tyr Asp Val His Phe Trp Leu Gly Leu Lys
                85                  90                  95

Thr Thr Gln Asp Glu Ala Gly Ser Ala Ala Ile Leu Thr Val Gln Leu
            100                 105                 110

Asp Asp Leu Leu Gly Gly Gly Pro Val Gln His Arg Glu Val Glu Gly
        115                 120                 125

Ser Glu Ser Asp Leu Phe Leu Ser Tyr Phe Lys Gly Gly Ile Arg Tyr
    130                 135                 140

Leu Glu Gly Gly Val Ala Ser Gly Phe Lys His Val Gln Thr Asn Ala
145                 150                 155                 160

Ala His Pro Lys Arg Leu Phe His Val Lys Gly Ala Lys Asn Ile Arg
                165                 170                 175

Leu Arg Gln Val Glu Leu Ala Val Ser Ala Met Asn Lys Gly Asp Cys
            180                 185                 190

Phe Ile Leu Asp Ser Asp Arg Asp Val Phe Val Trp Val Gly Pro Lys
        195                 200                 205

Ala Asn Arg Val Glu Lys Leu Lys Ala Ile Asn Val Ala Asn Asp Ile
    210                 215                 220

Arg Asp Arg Asp His Asn Gly Arg Ala Thr Val His Ile Val Asp Glu
225                 230                 235                 240

Phe Ser Thr Leu Ser Asp Gln Glu Ser Phe Phe Lys Ser Leu Gly Ser
                245                 250                 255

Gly Ser Pro Ser Thr Val Pro Asp Gln Ser Thr Ala Lys Glu Asp Ala
            260                 265                 270

Ala Phe Glu Lys Ala Asp Ala Ala Arg Val Glu Leu Tyr Lys Val Thr
        275                 280                 285

Asp Ser Lys Ala Gly Lys Leu Ala Val Glu Pro Ile Thr Gln Lys Pro
    290                 295                 300

Leu Lys Gln Glu Met Leu Lys Pro Asp Asp Ala Phe Ile Leu Asp Thr
305                 310                 315                 320

Gly Ser Gly Leu Tyr Val Trp Ile Gly Lys Ser Ala Thr Gln Gln Glu
                325                 330                 335

Lys Thr Gln Ser Leu Val Lys Ala Gln Glu Phe Ile Lys Asn Lys Lys
            340                 345                 350

Tyr Pro Ala Trp Thr Pro Val Glu Arg Ile Val Gln Asn Ala Glu Thr
        355                 360                 365

Ala Pro Phe Lys His Phe Phe Gln Thr Trp Arg Asp Ala Gly Ser Thr
    370                 375                 380

Gly Ser Arg Leu Val
385
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<210> SEQ ID NO 124

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<211> LENGTH: 259
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 124

Met Lys Ser Ile Val Ser Ile Thr Ile Thr Val Leu Ala Ile Ile Cys
1 5 10 15

Glu Gly Gln Ala Thr Asn Tyr Cys Asp Pro Ser Leu Cys Ala Arg Gly
20 25 30

Thr Pro His Ile Ala Cys Asn Gly Leu Ser Thr Leu Ser Arg Thr Cys
35 40 45

Gly Ala Gly Ser Phe Glu Val Ala Leu Asn Arg Ala Asp Gln Gln Leu
50 55 60

Ile Val Asp Leu His Asn Lys Leu Arg Ser Lys Val Ala Met Gly Gln
65 70 75 80

Gln Lys Asn Ser Ala Gly Gln Arg Phe Gln Gln Ala Cys Arg Met Ala
85 90 95

Thr Leu Gln Trp Asp Pro Glu Leu Ala His Ile Ala Ala Thr Asn Ala
100 105 110

Arg Arg Cys Val Tyr Gly His Asp Thr Cys Arg Asn Thr Ala Ser Met
115 120 125

Lys Phe Ala Gly Gln Asn Ile Ala Ile Lys Tyr Tyr Tyr Gly Met Thr
130 135 140

Phe Thr Asn Glu Gln Leu Leu Thr Gly Phe Ile Asn Ser Trp Phe Ser
145 150 155 160

Glu Phe Lys Asp Ala Thr Pro Gln Gln Ile Ala Arg Tyr Pro Ala Asn
165 170 175

Tyr Arg Gly Pro Ala Ile Gly His Phe Thr Gln Ile Val Ser Asp Arg
180 185 190

Thr Ser Arg Ile Gly Cys Ser Met Val Ser Tyr Asn Lys Asn Gly Phe
195 200 205

Ile Asn Lys Leu Phe Val Cys Asn Tyr Gly Leu Thr Asn Ile Ile Asn
210 215 220

Gln Pro Val Tyr Val Ala Gly Asn Val Cys Ser Gly Cys Thr Thr Gly
225 230 235 240

Cys Asn Lys Val Phe Pro Gly Leu Cys Asn Thr Ala Glu Arg Val Ser
245 250 255

Asn Asn Pro

<210> SEQ ID NO 125
<211> LENGTH: 566
<212> TYPE: PRT
<213> ORGANISM: Aedes aegypti

<400> SEQUENCE: 125

Met Lys Val Tyr Ile Cys Gln Val Ile Phe Ser Phe Leu Ala Val Ser
1 5 10 15

Val Phe Cys Glu Glu Asn Cys Asn Ile Pro Glu Ser Glu Leu Ser Lys
20 25 30

Ile Asp His Val Leu Arg His Met Glu Lys Pro Ile Tyr Ser Glu Glu
35 40 45

Gln Phe Ala Ser Asp Asn Glu Glu Cys Thr Asn Leu Leu Asn Gly Ile
50 55 60

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His Ala Gln Leu Arg Arg Leu Thr Gln Arg Tyr Lys Leu Met Asn Lys
65                  70                  75                  80

Gly Tyr Val Lys Val Glu Glu Tyr Gln Arg Met Ala Asp Asn Tyr Glu
                85                  90                  95

Lys Gln Leu Lys Thr Leu Asn Asp Glu Leu Val Glu Leu Gln Gln His
            100                 105                 110

Thr Ser Glu Lys Ala Ser Ala Thr Ile Ala Lys Leu Lys Glu Asp Ile
        115                 120                 125

Lys Lys Leu Asp Glu Glu Val Gly Thr Leu His Glu Lys Leu Lys Gly
    130                 135                 140

Ile Lys Gln Asp Phe Glu Lys Val Lys Arg Asp Leu Cys Val Thr Tyr
145                 150                 155                 160

Leu Asn Ser Asn Gln Met Ser Lys Ala Lys Ala Lys Leu Lys Glu Met
                165                 170                 175

Ala Ser Thr Tyr Leu Ile Glu Ile Val Gln Gln Gln Leu Asn Lys Ser
            180                 185                 190

Asn Ala Asn Ile Met Pro Met Leu Glu Phe Ser Ala Ala Ile Pro Asp
        195                 200                 205

Leu Asp Asp Met Gly Glu Ala Tyr Lys Glu Ile Tyr Lys Phe Leu Glu
    210                 215                 220

Glu Gln Lys Arg Leu Glu Gly Glu Asp Ser Val Leu Leu Glu Ala Thr
225                 230                 235                 240

Val Leu Lys Met Asn Ala Ser Leu Lys Glu Gly Ser Asn Ile Thr Asp
                245                 250                 255

Glu Arg Arg Thr Gln Ile Glu Gly Leu Leu Lys Asp Leu Ala Thr Lys
            260                 265                 270

Ser Thr Ile Val Phe Ser Thr Trp Thr Lys Glu Leu Lys Lys Ile Asn
        275                 280                 285

Asp Ala Val Val Ile Lys Asn Ala Leu Asp His Met Phe Val Ser Gln
    290                 295                 300

Met Lys Val Phe Gly Ala Leu Val Gly Asp Thr Ser Asp Phe Gly Ser
305                 310                 315                 320

Ile Arg Asn Phe Val Lys Leu Thr Ile Val Cys Asn Asn Tyr Tyr Lys
                325                 330                 335

Val Ala Ala Tyr Lys Glu Leu Ile Asp Arg Lys Ile Gly Asn Ala Leu
            340                 345                 350

Gly Thr Ile Met Phe Asp Leu Leu Thr Leu Glu Val Asn Glu Met Lys
        355                 360                 365

Phe Asp Pro His Val Pro Asp Glu Ile Pro Lys Leu Phe Glu Ala Thr
    370                 375                 380

Leu Ser Ser Leu Pro Asn Ser Leu Thr Glu Leu Arg Thr Cys Leu Gly
385                 390                 395                 400

Lys Val Gln Ile Tyr Asn Lys Lys Thr Asn Lys Cys Val Val Ala Thr
                405                 410                 415

Gly Asn Asp Phe Asp Val His Lys Asp Lys Leu Gly Asp Phe Tyr Arg
            420                 425                 430

Val Val Val Ala Asp Tyr Gly Cys Thr Ser Phe Arg Leu Glu Ala Ser
        435                 440                 445

Gly Asp Lys Ala Ser Val Arg Ile Val Thr Pro Ser Gly Asn Pro Met
    450                 455                 460

Ser Asn Val Asn Leu His Leu Glu Gly Asn Ser Leu His Asn Tyr Val
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465                 470                 475                 480

Ala Thr Pro Lys Ser Asn Lys Pro Asp Arg Thr Pro Ser Ser Ser Asp
                485                 490                 495

Glu Trp Ile Leu Asp Ala Asn Tyr Asn Asn Asp Thr Ile Lys Ile Glu
            500                 505                 510

Ser Gln Phe Ser Asp Tyr Lys Thr Lys Lys Thr Glu Val Asp His Leu
        515                 520                 525

Leu Val Arg Asp Ile Asn His Leu Pro His Val Leu Val Ala Arg Tyr
    530                 535                 540

Gly Phe Met Gly Leu Lys Asn Ser Asp Ala Lys Asp Thr Ile Glu Trp
545                 550                 555                 560

Asn Leu Lys Cys Gly Ser
                565
```

<210> SEQ ID NO 126
<211> LENGTH: 42
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer

<400> SEQUENCE: 126

taatacgact cactataggg gatggacaga tgtctcttcg tg 42

<210> SEQ ID NO 127
<211> LENGTH: 40
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer

<400> SEQUENCE: 127

taatacgact cactataggg ccaaatccaa tccatcgaaa 40

<210> SEQ ID NO 128
<211> LENGTH: 38
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer

<400> SEQUENCE: 128

taatacgact cactataggg gtgagcaagg gcgaggag 38

<210> SEQ ID NO 129
<211> LENGTH: 44
<212> TYPE: DNA
<213> ORGANISM: Artificial sequence
<220> FEATURE:
<223> OTHER INFORMATION: PCR primer

<400> SEQUENCE: 129

taatacgact cactataggg catgatatag acgttgtggc tgtt 44

1. A composition comprising two or more polypeptides, wherein said two or more polypeptides are selected from the group consisting of LOC5573204, LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

2. A composition comprising a nucleic acid molecule or two or more nucleic acid molecules encoding two or more polypeptides, wherein said two or more polypeptides are selected from the group consisting of LOC5573204, LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

3.-**9**. (canceled)

10. The composition of claim **2**, wherein the two or more polypeptides comprise (i) LOC5573204 Bacteria-Responsive Protein 1 (AgBR1) or a fragment, derivative or variant thereof and (ii) LOC5578631 Neutrophil Stimulating Factor 1 (NetSt1) or a fragment, derivative or variant thereof.

11. The composition of claim **10**, wherein the LOC5573204 polypeptide comprises the sequence SEQ ID NO: 1.

12.-**13**. (canceled)

14. The composition of claim **10**, wherein the LOC5573204 polypeptide fragment comprises the sequence selected from SEQ ID NOS: 6-13.

15.-**20**. (canceled)

21. The composition of claim **10**, wherein the LOC5578631 polypeptide comprises the sequence SEQ ID NO: 3.

22.-**23**. (canceled)

24. The composition of claim **10**, wherein the LOC5578631 polypeptide fragment comprises the sequence selected from SEQ ID NOS: 22-29.

25.-**54**. (canceled)

55. The composition of claim **2**, further comprising a carrier or excipient.

56. The composition of claim **2**, further comprising an adjuvant.

57. (canceled)

58. A method of preventing or treating a disease in a subject in need thereof, wherein the disease is associated with a mosquito-borne infectious agent, said method comprising administering to said subject an effective amount of the composition of claim **2**.

59. The method of claim **58**, wherein the mosquito is *Aedes aegypti*.

60. The method of claim **58**, wherein the mosquito-borne infectious agent is a mosquito-borne virus.

61. The method of claim **60**, wherein the mosquito-borne virus is a flavivirus.

62. (canceled)

63. The method of claim **61**, wherein the flavivirus is Zika virus.

64. The method of claim **61**, wherein the flavivirus is West Nile virus.

65. The method of claim **60**, wherein the mosquito-borne virus is an alphavirus.

66. (canceled)

67. The method of claim **58**, wherein the subject is human.

68. A method of preventing or treating a disease in a subject in need thereof, wherein the disease is associated with a mosquito-borne infectious agent, said method comprising administering to said subject an effective amount of the composition of claim **1**.

69. A method of preventing or treating a disease in a subject in need thereof, wherein the disease is associated with a mosquito-borne infectious agent, said method comprising administering to said subject an effective amount of two or more polypeptides, wherein said two or more polypeptides are selected from the group consisting of LOC5573204, LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

70. A method of preventing or treating a disease in a subject in need thereof, wherein the disease is associated with a mosquito-borne infectious agent, said method comprising administering to said subject an effective amount of two or more nucleic acid molecules encoding polypeptides selected from the group consisting of LOC5573204, LOC5578630, LOC5578631, LOC5567956, LOC5580038, LOC5566287, LOC5567958, LOC5568702, LOC110675548, and fragments, derivatives or variants thereof.

* * * * *