



(11) **EP 4 317 950 A3**

(12) **EUROPEAN PATENT APPLICATION**

(88) Date of publication A3:
17.04.2024 Bulletin 2024/16

(43) Date of publication A2:
07.02.2024 Bulletin 2024/06

(21) Application number: **23215659.6**

(22) Date of filing: **17.03.2020**

(51) International Patent Classification (IPC):
C12N 5/071 ^(2010.01) **C12N 9/22** ^(2006.01)
C12N 15/11 ^(2006.01) **G01N 33/68** ^(2006.01)
G01N 21/64 ^(2006.01)

(52) Cooperative Patent Classification (CPC):
G01N 33/6896; C12N 5/0686; C12N 9/22;
C12N 15/11; C12N 2310/20; C12N 2510/00;
G01N 2021/6441

(84) Designated Contracting States:
AL AT BE BG CH CY CZ DE DK EE ES FI FR GB
GR HR HU IE IS IT LI LT LU LV MC MK MT NL NO
PL PT RO RS SE SI SK SM TR

(30) Priority: **18.03.2019 US 201962820086 P**

(62) Document number(s) of the earlier application(s) in
accordance with Art. 76 EPC:
20718950.7 / 3 768 826

(71) Applicant: **Regeneron Pharmaceuticals, Inc.**
Tarrytown, NY 10591 (US)

(72) Inventors:
• **PRISSETTE, Marine**
Tarrytown, NY 10591 (US)
• **KOSS, Matthew**
Tarrytown, NY 10591 (US)
• **FURY, Wen**
Tarrytown, NY 10591 (US)
• **ZAMBROWICZ, Brian**
Tarrytown, NY 10591 (US)

(74) Representative: **Mewburn Ellis LLP**
Aurora Building
Counterslip
Bristol BS1 6BX (GB)

(54) **CRISPR/CAS SCREENING PLATFORM TO IDENTIFY GENETIC MODIFIERS OF TAU SEEDING OR AGGREGATION**

(57) Cas-protein-ready tau biosensor cells, CRISPR/Cas synergistic activation mediator (SAM)-ready tau biosensor cells, and methods of making and using such cells to screen for genetic modifiers of

tau seeding or aggregation are provided. Reagents and methods for sensitizing such cells to tau seeding activity or tau aggregation or for causing tau aggregation are also provided.

EP 4 317 950 A3



EUROPEAN SEARCH REPORT

Application Number

EP 23 21 5659

5

10

15

20

25

30

35

40

45

50

55

1

EPO FORM 1503 03.82 (P04C01)

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	D.L. NATHANIEL ET AL: "Elucidating Cellular Trafficking Pathways Controlling Prion-like Spread of Tau Aggregation Using CRISPR interference Screens.", ABSTRACTS: PORTER PRESENTATIONS / CELL BIOLOGY 2016 / ASCB ANNUAL MEETING, 3 December 2016 (2016-12-03), - 7 December 2016 (2016-12-07), page P887, XP055695205, * the whole document *	1-31	INV. C12N5/071 C12N9/22 C12N15/11 G01N33/68 ADD. G01N21/64
Y	Anonymous: "Identification of genetic regulators for intracellular aggregation by genome-wide CRISPR screening", / 16 January 2018 (2018-01-16), XP055694949, Retrieved from the Internet: URL:https://kaken.nii.ac.jp/en/report/KAKE NHI-PROJECT-16K15229/16K152292016jisseki/ [retrieved on 2020-05-13] * the whole document *	1-31	
Y	Anonymous: "ascb annual meeting. abstracts: oral proceedings", Mol Biol Cell. 2016 Dec 15; 27(25), 15 December 2016 (2016-12-15), XP055695180, Retrieved from the Internet: URL:file:///C:/Users/SO51107/Downloads/sup p_27.25.3947_2016ASCBMeeting-OralAbstracts %20(2).pdf [retrieved on 2020-05-14] * the whole document *	1-31	TECHNICAL FIELDS SEARCHED (IPC) C12N G01N
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 6 March 2024	Examiner Offermann, Stefanie
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	



EUROPEAN SEARCH REPORT

Application Number

EP 23 21 5659

5

10

15

20

25

30

35

40

45

50

55

1

EPO FORM 1503 03.82 (P04C01)

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
Y	B. B. HOLMES ET AL: "Proteopathic tau seeding predicts tauopathy in vivo", PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES, vol. 111, no. 41, 14 October 2014 (2014-10-14), pages E4376-E4385, XP055456307, ISSN: 0027-8424, DOI: 10.1073/pnas.1411649111 * the whole document *	1-31	
Y	MARTIN KAMPMANN: "CRISPRi and CRISPRa Screens in Mammalian Cells for Precision Biology and Medicine", ACS CHEMICAL BIOLOGY, vol. 13, no. 2, 24 October 2017 (2017-10-24), pages 406-416, XP055694953, ISSN: 1554-8929, DOI: 10.1021/acschembio.7b00657 * the whole document * * figure 2 *	1-31	TECHNICAL FIELDS SEARCHED (IPC)
Y	SILVANA KONERMANN ET AL: "Genome-scale transcriptional activation by an engineered CRISPR-Cas9 complex", NATURE, vol. 517, no. 7536, 1 January 2015 (2015-01-01), pages 583-588, XP055585957, London ISSN: 0028-0836, DOI: 10.1038/nature14136 * the whole document * * figure 1b *	1-31	
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 6 March 2024	Examiner Offermann, Stefanie
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	



EUROPEAN SEARCH REPORT

Application Number

EP 23 21 5659

5

10

15

20

25

30

35

40

45

50

55

1

EPO FORM 1503 03.82 (P04C01)

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
T	JOHN J. CHEN ET AL: "Compromised function of the ESCRT pathway promotes endolysosomal escape of tau seeds and propagation of tau aggregation", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 294, no. 50, 2 October 2019 (2019-10-02), pages 18952-18966, XP055694877, US ISSN: 0021-9258, DOI: 10.1074/jbc.RA119.009432 -----		
T	"The 96th Annual Meeting of The Physiological Society of Japan", JOURNAL OF PHYSIOLOGICAL SCIENCES, SPRINGER JAPAN KK, JP, vol. 69, no. 1, 20 June 2019 (2019-06-20), pages 1-314, XP036820069, ISSN: 1880-6546, DOI: 10.1007/S12576-019-00673-W [retrieved on 2019-06-20] -----		TECHNICAL FIELDS SEARCHED (IPC)
T	YUNG WEN CHIU ET AL: "Identification of calcium and integrin-binding protein 1 as a novel regulator of production of amyloid [beta] peptide using CRISPR/Cas9-based screening system", THE FASEB JOURNAL, 19 April 2020 (2020-04-19), XP055694940, US ISSN: 0892-6638, DOI: 10.1096/fj.201902966RR -----		
The present search report has been drawn up for all claims			
Place of search Munich		Date of completion of the search 6 March 2024	Examiner Offermann, Stefanie
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	