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(54) Title: DISRUPTION OF SONIC HEDGEHOG-SURF4 INTERACTION FOR CANCER TREATMENT

(57) Abstract: Provided are compositions and methods that block the interaction between Sonic hedgehog (Shh) and Surf4 protein 4 (SURF4), particularly for use in treating subjects with cancer or at risk of suffering from cancer. The subject methods block the interaction between SURF4 and Shh, either by mutating residue E50, D53, D56, or any combination thereof of SURF4 or mutating the CW motif (amino acid residues 32-38) on human Shh. Also provided is a composition comprising a polypeptide that contains the CW motif at the position of 32-38 on human Shh, a polypeptide that contains the first luminal loop (residues 49-60) of human SURF4, or small chemical molecules that block the interaction between SURF4 and Shh and administering said composition to a subject, particularly in subjects with cancer or at risk of suffering from cancer.



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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER

C07K7/06(2006.01)i; C07K7/08(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC: C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

VEN,CNABS, PubMed, DWPI, CNTXT, WOTXT, USTXT, EPTXT, JPTXT, CNKI, Web of Science, baidu, Patents, NCBI Genbank, EBI, STNext: SEQ ID NOs: 6-8,10, cancer, Surfeit locus protein 4, SURF4, Sonic hedgehog, Shh, signaling, block, interact, glycosaminoglycan, GAG, heparin sulfate proteoglycans, HSPG, heparin, chondroitin sulfate proteoglycans, CSPG

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FARSHI, P. et al. "Dual Roles of the Cardin-Weintraub Motif in Multimeric Sonic Hedgehog" <i>THE JOURNAL OF BIOLOGICAL CHEMISTRY</i> , Vol. 286, No. 26, 01 July 2011 (2011-07-01), pages 23608–23619	1-6, 15-18
X	XP_011517246.1. "surfeit locus protein 4 isoform X1 [Homo sapiens]" <i>GenPept</i> , 22 November 2021 (2021-11-22), ORIGIN	1-6
A	WO 2005005601 A2 (THE REGENTS OF THE UNIVERSITY OF MICHIGAN et al.) 20 January 2005 (2005-01-20) the whole document	1-18
A	WO 2010032061 A1 (MEDIMMUNE LLC) 25 March 2010 (2010-03-25) the whole document	1-18
A	WO 2012031008 A2 (THE GENERAL HOSPITAL CORPORATION et al.) 08 March 2012 (2012-03-08) the whole document	1-18

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:

“A” document defining the general state of the art which is not considered to be of particular relevance

“D” document cited by the applicant in the international application

“E” earlier application or patent but published on or after the international filing date

“L” document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

“O” document referring to an oral disclosure, use, exhibition or other means

“P” document published prior to the international filing date but later than the priority date claimed

“T” later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

“X” document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

“Y” document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

“&” document member of the same patent family

Date of the actual completion of the international search

22 September 2023

Date of mailing of the international search report

08 October 2023

Name and mailing address of the ISA/CN

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C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2011117328 A1 (NETRIS PHARMA) 29 September 2011 (2011-09-29) the whole document	1-18
A	CHAN, J. A. et al. "Proteoglycan interactions with Sonic Hedgehog specify mitogenic responses" <i>NATURE NEUROSCIENCE</i> , Vol. 12, No. 4, 15 March 2009 (2009-03-15), pages 409-417	1-18

INTERNATIONAL SEARCH REPORT

International application No.

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Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of a sequence listing:
 - a. forming part of the international application as filed.
 - b. furnished subsequent to the international filing date for the purposes of international search (Rule 13ter.1(a)),
 accompanied by a statement to the effect that the sequence listing does not go beyond the disclosure in the international application as filed.
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been established to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence listing.
3. Additional comments:

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **7-18**
because they relate to subject matter not required to be searched by this Authority, namely:

Claims 7-18 relate to a method of treating a cancer in a subject, and therefore do not warrant an international search according to the criteria set out in PCT Rule 39.1(iv). However, the search has been carried out and based on the use of the antibody for manufacturing of a medicament for the treatment of disease.
2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

PCT/IB2023/000075

Patent document cited in search report			Publication date (day/month/year)	Patent family member(s)			Publication date (day/month/year)
WO	2005005601	A2	20 January 2005	EP	2003196	A2	17 December 2008
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				US	8207306	B2	26 June 2012
				KR	20110059755	A	03 June 2011
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WO	2012031008	A2	08 March 2012	US	2020399714	A1	24 December 2020
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				WO	2012031008	A3	01 November 2012
				US	2014045915	A1	13 February 2014
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WO	2011117328	A1	29 September 2011	EP	2407173	A1	18 January 2012
				US	2013089548	A1	11 April 2013
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				EP	2550010	A1	30 January 2013
				AU	2011231579	A1	18 October 2012