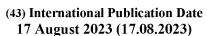
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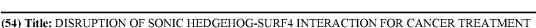
- (71) Applicant: THE HONG KONG UNIVERSITY OF SCIENCE AND TECHNOLOGY [CN/CN]; Clear Water Bay, Kowloon, Hong Kong (CN).
- (72) Inventors: GUO, Yusong; c/o The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong (CN). TANG, Xiao; c/o The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong (CN). WANG, Tingxuan; c/o The Hong Kong University of Science and Technology, Clear Water Bay, Kowloon, Hong Kong (CN).
- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE,

SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))
- with sequence listing part of description (Rule 5.2(a))
- (88) Date of publication of the international search report: 16 November 2023 (16.11.2023)





(57) **Abstract:** Provided are compositions and methods that block the interaction between Sonic hedgehog (Shh) and Surfeit locus 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.

International application No.

PCT/IB2023/000075

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, Patentics, 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

✓ Further documents are listed in the continuation of Box C.

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" THE JOURNAL OF BIOLOGICAL CHEMISTRY, 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]" GenPept, 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

* "A"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance	"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
"D" "E"	document cited by the applicant in the international application earlier application or patent but published on or after the international filing date	"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
"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) document referring to an oral disclosure, use, exhibition or other	"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
"P"	document published prior to the international filing date but later than the priority date claimed	"&"	document member of the same patent family
	the priority date elained		
Date	of the actual completion of the international search	Date	of mailing of the international search report
	22 September 2023		08 October 2023
Name	e and mailing address of the ISA/CN	Auth	norized officer
A 6	CHINA NATIONAL INTELLECTUAL PROPERTY LIDMINISTRATION , Xitucheng Rd., Jimen Bridge, Haidian District, Beijing 00088, China		XI,Jing
		Tele	phone No. (+86) 010-53961974

✓ See patent family annex.

International application No.

DOC	UMENTS CONSIDERED TO BE RELEVANT		
ategory*	Citation of document, with indication, where appropriate, of the releva	nt 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 responses" NATURE NEUROSCIENCE, Vol. 12, No. 4, 15 March 2009 (2009-03-15), pages 409-417	nitogenic	1-18
	pages 409-417		

International application No.

Box No. I	Nucleotide and/or amino acid sequence(s) (Continuation of item 1.c of the first sheet)
carried out	rd to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was on the basis of a sequence listing: orming part of the international application as filed. urnished 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.
	n regard to any nucleotide and/or amino acid sequence disclosed in the international application, this report has been blished to the extent that a meaningful search could be carried out without a WIPO Standard ST.26 compliant sequence ag.
3. Additional	comments:

International application No.

Box No. I	Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)
This inter	rnational 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.

	ent document in search report		Publication date (day/month/year)	Pate	nt family member	r(s)	Publication date (day/month/year)
WO	2005005601	A2	20 January 2005	EP	2003196	A2	17 December 2008
				EP	2003196	A3	07 January 2009
				EP	1639090	A2	29 March 2006
				EP	1639090	A4	16 April 2008
				WO	2005005601	A8	07 April 2005
				WO	2005005601	A3	27 April 2006
				AU	2008202471	A 1	26 June 2008
				AU	2008202471	B2	05 July 2012
				KR	20060031809	A	13 April 2006
				US	2008292546	A 1	27 November 2008
				US	2012315216	A 1	13 December 2012
				JP	2007516693	A	28 June 2007
				US	2013244256	A 1	19 September 2013
				AU	2004256425	A 1	20 January 2005
				CA	2528669	A 1	20 January 2005
				EP	2481814	A2	01 August 2012
				EP	2481814	A 3	10 October 2012
				US	2006019256	A1	26 January 2006
WO	2010032061	A1	25 March 2010	BRPI	0918739	A2	26 September 2017
				EP	2344535	A 1	20 July 2011
				AU	2009294416	A 1	25 March 2010
				AU	2009294416	B2	22 May 2014
				JP	2012502967	A	02 February 2012
				US	2012328625	A 1	27 December 2012
				US	8569459	B2	29 October 2013
				MX	2011002838	A	29 July 2011
				CA	2734330	A 1	25 March 2010
				US	2010196388	A 1	05 August 2010
				US	8207306	B2	26 June 2012
				KR	20110059755	A	03 June 2011
WO	2012031008	A2	08 March 2012	US	2020399714	A1	24 December 2020
				US	2016153053	A 1	02 June 2016
				US	10793914	B2	06 October 2020
				WO	2012031008	A 3	01 November 2012
				US	2014045915	A 1	13 February 2014
WO	2011117328	A1	29 September 2011	EP	2407173	A1	18 January 2012
			_,,	US	2013089548	A1	11 April 2013
				CA	2793750	A1	29 September 2011
				EP	2550010	A1	30 January 2013
				AU	2011231579	A1	18 October 2012