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[Continued on next page]

(54) Title: HE4 BASED THERAPY FOR MALIGNANT DISEASE

(57) Abstract: The invention provides compositions and methods for utilizing human epididymal secretory protein E4 (HE4) in the prevention and treatment of cancer and other human diseases.

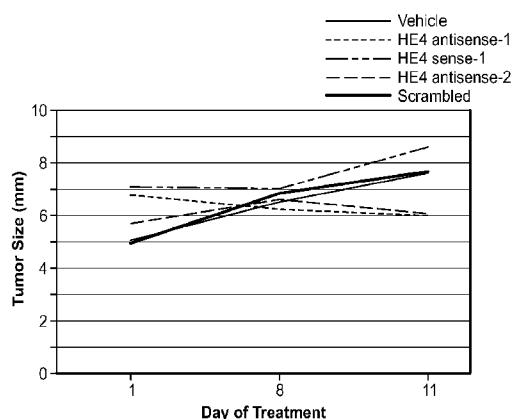


FIG. 27A

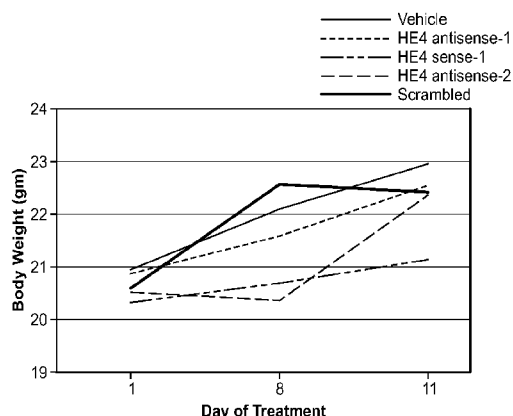


FIG. 27B



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(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, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

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Published:

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— with sequence listing part of description (Rule 5.2(a))

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31 January 2013

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 2012/041080

A. CLASSIFICATION OF SUBJECT MATTER		<i>A61K 38/17 (2006.01)</i> <i>A61K 38/22 (2006.01)</i> <i>A61K 39/395 (2006.01)</i> <i>A61P 35/00 (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) A61K 38/17, 38/22, 39/395, A61P 35/00																							
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) CIPO, DEPATISnet, DWPI, EAPATIS, EMBL, EPO-Internal, Esp@ce, Esp@cenet, Google, KIPRIS, PAJ, PabMed, RUPTO, SCIEDIRECT, SIPO, USPTO, WIPO, ВИНІТИ (VINITI)																							
C. DOCUMENTS CONSIDERED TO BE RELEVANT																							
Category*	Citation of document, with indication, where appropriate, of the relevant passages		Relevant to claim No.																				
X	YU-HUNG HUANG et al. Nanoparticle-Delivered Suicide Gene therapy Effectively Reduces Ovarian Tumor Burden in Mice. Cancer Res., 2009 August 1, Vol.69, No.15, pp. 6184-6191		1-5, 10, 11, 15-20																				
Y			6-9, 12, 13, 21-24																				
Y	US 5552390 A (THE BOARD OF REGENTS OF THE UNIVERSITY OF NEBRASKA) 03.09.1996, abstract, claims		7, 21-30																				
Y	RONNY DRAPKIN et al. Human Epididymis Protein 4 (HE4) Is a Secreted Glycoprotein that Is Overexpressed by Serous and Endometrioid Ovarian Carcinomas. Cancer Res, 2005, March 15, Vol. 65, No:6, pp. 2162-2169		6, 8, 9, 28-30																				
Y	ELZBIETA GOCER et al. Vitamin D and differentiation in cancer, Crit Rev Clin Lab Sci., 2009, 46(4), pp.1-31		12,13																				
☒ Further documents are listed in the continuation of Box C. ☐ See patent family annex.																							
* Special categories of cited documents: <table border="0"> <tr> <td>"A"</td> <td>document defining the general state of the art which is not considered to be of particular relevance</td> <td>"T"</td> <td>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</td> </tr> <tr> <td>"E"</td> <td>earlier document but published on or after the international filing date</td> <td>"X"</td> <td>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</td> </tr> <tr> <td>"L"</td> <td>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)</td> <td>"Y"</td> <td>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</td> </tr> <tr> <td>"O"</td> <td>document referring to an oral disclosure, use, exhibition or other means</td> <td>"&"</td> <td>document member of the same patent family</td> </tr> <tr> <td>"P"</td> <td>document published prior to the international filing date but later than the priority date claimed</td> <td></td> <td></td> </tr> </table>				"A"	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	"E"	earlier document 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)	"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	"O"	document referring to an oral disclosure, use, exhibition or other means	"&"	document member of the same patent family	"P"	document published prior to the international filing date but later than the priority date claimed		
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"P"	document published prior to the international filing date but later than the priority date claimed																						
Date of the actual completion of the international search		Date of mailing of the international search report																					
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Name and mailing address of the ISA/ FIPS Russia, 123995, Moscow, G-59, GSP-5, Berezhkovskaya nab., 30-1		Authorized officer O. Fedonova																					
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 2012/041080

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.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 14
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: **claim 14 does not contain the technical features of the claimed process.**
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).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

According to Rule 13 of the Regulations under the PCT the claimed inventions does not meet the requirement of unity of invention, therefore independent claims 1, 15-17, 20, 26 - 29 form several groups of inventions, which are not so linked as to form a single general inventive concept.

The special technical feature of independent claims 1, 15, 16, 17 and 20 is modulating the level of human epididymal secretory protein E4 (HE4).

The special technical feature of independent claims 26 and 27 is an oligonucleotide with a nucleic acid sequence selected from the group consisting of SEQ ID NO: 2 and SEQ ID NO:4.

The special technical feature of independent claims 28 and 29 is an HE4-specific antibody or antigen binding fragment thereof.

Consequently, in the independent claims 1, 15-17, 20, 26 - 29 the special technical feature is absent.

Hence, claims comprise 3 groups of inventions, namely:

- 1 group includes inventions of claims 1-13,15-25
- 2 group includes inventions of claims 26 and 27
- 3 group includes inventions of claims 28 and 29-30

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 2012/041080

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X Y	US 2007/0286865 A1 (RICHARD MOORE et al.) 13.12.2007, claims	20 25-30