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ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: ANTIBODIES AND CYCLIC PEPTIDES WHICH BIND CEA (CARCINOEMBRYONIC ANTIGEN) AND THEIR
USE AS CANCER THERAPEUTICS

(57) Abstract: The present invention relates to differentiation and tumorigenicity. The present invention more particularly relates to ligands which target CEA and CEACAM6 such that the adhesion, differentiation-inhibitory activities and tumorigenic effects of Ig superfamily members, CEA and CEACAM6, can be reduced or blocked. More particularly, the present invention relates to CEA-binding agents which reverse CEA-mediated tumorigenic effects by declustering CEA and CEACAM6. In one embodiment the invention relates to methods of reducing, preventing or reversing a CEA-mediated tumorigenic effect comprising a use of a CEA-mediated tumorigenic effect reducing CEA-declustering agent. In one embodiment, the invention relates to compositions and use thereof for reversing CEA-mediated tumorigenic effects on human cancer cells and uses thereof. In particular, the application relates to a monovalent CEA binding agent which interferes with a CEA interaction responsible for a CEA-mediated tumorigenic effects, thereby minimizing or reversing same.



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INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07K14/705 C07K16/30 C07K16/28

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 7 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 practical, search terms used)

EPO-Internal, WPI Data, PAJ

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 584 368 A (SUNTORY LTD) 2 March 1994 (1994-03-02) page 3, line 20 - line 42 claims; examples ---	1-7, 9-12, 14-19
X	WO 98/25971 A (CELLTECH THERAPEUTICS LTD ;CHAPMAN ANDREW PAUL (GB); KING DAVID JO) 18 June 1998 (1998-06-18) page 1, line 1 - line 12 page 3, line 25 -page 4, line 5 page 11, line 22 - line 31 page 13, line 14 - line 25 claims 1,10; example 1 --- -/--	1-4, 9-12, 14-19

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document 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.
- *G* document member of the same patent family

Date of the actual completion of the international search

7 May 2004

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07/06/2004

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INTERNATIONAL SEARCH REPORT

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PEDLEY R B ET AL: "THE POTENTIAL FOR ENHANCED TUMOUR LOCALISATION BY POLY(ETHYLENE GLYCOL) MODIFICATION OF ANTI-CEA ANTIBODY" BRITISH JOURNAL OF CANCER, LONDON, GB, vol. 70, 1994, pages 1126-1130, XP000575990 ISSN: 0007-0920 page 1126 -page 1130 ---	1-4, 9-12, 14-19
X	WO 01/74849 A (LADNER ROBERT CHARLES ;DYAX CORP (US); RONDON ISAAC JESUS (US)) 11 October 2001 (2001-10-11) page 2, line 18 -page 3, line 6 page 10, line 20 - line 34 page 19, line 1 - line 12 page 25, line 11 -page 26, line 16 examples ---	1-5, 14-19
X	US 5 872 215 A (ALLEN DEBORAH JULIE ET AL) 16 February 1999 (1999-02-16) column 1, line 10 - line 14 column 4, line 17 - line 62 column 6, line 17 - line 20 column 9, line 14 - line 49 column 16, line 36 - line 60 claims 1,27; examples 6,9,10 ---	1-7, 10-12, 14-19
Y	US 2002/052479 A1 (ARMOUR KATHRYN ET AL) 2 May 2002 (2002-05-02) page 1, paragraph 1 page 3, paragraph 23 - paragraph 28 page 4, paragraph 48 page 5, paragraph 60 claims; examples ---	1-19
Y	WO 99/41370 A (SCREATON ROBERT A ;STANNERS CLIFFORD P (CA); TAHERI MARYAM (CA); U) 19 August 1999 (1999-08-19) cited in the application page 3, line 10 -page 4, line 2 page 5, line 18 -page 7, line 24 page 14, line 32 -page 15, line 16 page 16, line 8 - line 24 claims; examples --- -/--	1-19

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 03/01533

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	TAHERI M. ET. AL.: "Identification of precise subdomains in carcinoembryonic antigen required for intracellular adhesion" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 275, no. 35, September 2001 (2001-09), pages 26935-26943, XP002277780 cited in the application page 26935 -page 26943 ---	1-19
A	KUROKI M ET AL: "BIOCHEMICAL CHARACTERIZATION OF 25 DISTINCT CARCINOEMBRYONIC ANTIGEN (CEA) EPITOPES RECOGNIZED BY 57 MONOCLONAL ANTIBODIES AND CATEGORIZED INTO SEVEN GROUPS IN TERMS OF DOMAIN STRUCTURE OF THE CEA MOLECULE" HYBRIDOMA, LIEBERT, NEW YORK, NY, US, vol. 11, no. 4, 1992, pages 391-407, XP000606978 ISSN: 0272-457X page 391 -page 407 ---	1-19
X,P	WO 02/076389 A (BAJENOVA OLGA ;UNIV BOSTON (US); THOMAS PETER (US)) 3 October 2002 (2002-10-03) page 2, paragraph 7 -page 3, paragraph 14 page 6, paragraph 27 -page 7, paragraph 31 page 8, paragraph 35 -page 9, paragraph 39 claims; examples -----	1-4,11

INTERNATIONAL SEARCH REPORT

International application No.
PCT/CA 03/01533

Box I Observations where certain claims were found unsearchable (Continuation of item 1 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.: 11-13, 15, 17-18
because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. ☒ Claims Nos.: 1-5, 9-12, 14-19
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:
see FURTHER INFORMATION sheet PCT/ISA/210
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 II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

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

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 an additional fee, this Authority did not invite payment of any additional fee.
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.
- ☐ No protest accompanied the payment of additional search fees.

Continuation of Box I.1

Although claims 11-13, 15, 17-18 are directed to a method of treatment of the human body, the search has been carried out and based on the alleged effects of the composition.

Continuation of Box I.1

Claims Nos.: 11-13, 15, 17-18

Rule 39.1(iv) PCT - Method for treatment of the human or animal body by therapy

Continuation of Box I.2

Claims Nos.: 1-5, 9-12, 14-19

Present claims 1-5, 9-12 & 14-19 relate to an extremely large number of possible compounds and methods. In fact, the claims contain so many options that a lack of clarity within the meaning of Article 6 PCT arises to such an extent as to render a meaningful search of the claims impossible. Consequently, the search has been carried out for those parts of the application which do appear to be clear, namely monovalent fragments of antibodies against CEA and the cyclized peptides of claim 6 and 13.

Present claims 1-5, 9-12 & 14-19 relate to a products and methods defined by reference to a desirable characteristic or property, namely:

The ability of a molecule to bind CEA (claims 1-5, 9, 15, 16, 19)

The ability of an assay to identify said molecules (claims 10-12, 14, 17, 18)

The claims cover all products and methods having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT for only a very limited number of such products and methods. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible.

Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the products and methods by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to monovalent fragments of antibodies against CEA and the cyclized peptides of Claim 6 and 13.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international

search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 03/01533

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