(54) Title: CANCER-ASSOCIATED EPITOPE

(57) Abstract: The present invention provides a cancer-associated epitope comprised of two polypeptides, where the first polypeptide is from cytokeratin K8 and the second polypeptide is from cytokeratin K18. The cancer-associated epitope becomes exposed during malignant transformation, particularly during malignant transformation of colon, breast, ovarian, renal, lung and testicular tissues. Exposure of the cancer-associated epitope is by cleavage and removal of N-terminal peptides from cytokeratins K8 and K18. The invention also provides for the cancer-associated epitope can be as high as about 10 M-1 in cancer tissues, more than 100-fold higher than for cytokeratin K8/K18 complexes in normal tissues. The invention provides cancer-associated epitopes, binding entities, antibodies and methods of using such epitopes, binding entities and antibodies for detection and treatment of cancer.
INTERNATIONAL SEARCH REPORT

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07K 5/00
US CL : 530/350

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)
U.S. : 530/350

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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

<table>
<thead>
<tr>
<th>Category</th>
<th>Citation of document, with indication, where appropriate, of the relevant passages</th>
<th>Relevant to claim No.</th>
</tr>
</thead>
</table>

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

Date of the actual completion of the international search: 01 August 2003 (01-08-2003)

Date of mailing of the international search report: 10 SEP 2003

Name and mailing address of the ISA/US
Mail Stop PCT, Attn: ISA/US Commissioner for Patents
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Alexandria, Virginia 22313-1450
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Authorized officer: Shelia J Huff
Telephone No. 703-308-1235

Form PCT/ISA/210 (second sheet) (July 1998)
BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1-7 and 65-67, drawn to isolated cancer-associated epitope and method for identifying mutant binding entity.

Group II, claim(s) 8-39, drawn to binding entity and kit and comprising said binding entity.

Group III, claim(s) 40-43 and 69, drawn to a composition comprising an inhibitor.

Group IV, claim(s) 44-54, drawn to methods of detecting adenocarcinoma using the binding entity of Group III attached to a detectable label.

Group V, claim(s) 55-64 and 68, drawn to methods of treating or preventing cancer using the binding entity of Group III.

In addition, with Group I, applicant will have SEQ ID NO. 7 examined without paying additional fees.

In addition, if applicant pays for Group II, they will get Group II as they read on SEQ ID NO. 7. If applicant wants any more peptides or peptides encoded by nucleic acid, they need to pay additional fees.

In addition, if applicant pays for Group IV, they will get Group IV as they read on SEQ ID NO. 7. If applicant wants any more peptides or peptides encoded by nucleic acid, they need to pay additional fees.

In addition, if applicant pays for Group V, they will get Group V as they read on SEQ ID NO. 7. If applicant wants any more peptides or peptides encoded by nucleic acid, they need to pay additional fees.

The inventions listed as Groups I-V do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Each of the products of Groups I-III differ structurally and functionally and thus lack the same of corresponding special technical feature. Each of the methods of Groups IV and V require the use of different products. The product required in Group IV is the binding entity attached to a detectable label whereas the product of Group V requires a conjugate.

According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(B)(1) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common structure, which is a significant structural element. Although SEQ ID NOS. 7-35 and 47-49 share a common structure of a single amino acid, the compounds are not regarded as being of similar nature because the shared common structure is not a significant structural element. A common structure of a single amino acid is not a significant structural element because the amino acid is found in every peptide or protein.

According to PCT Rule 13.2 and to the guidelines in Section (f)(i)(B)(1) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group must have a common structure, which is a significant structural element. Although SEQ ID NOS. 36-39 share a common structure of a single nucleic acid, the compounds are not regarded as being of similar nature because the shared common structure is not a significant structural element. A common structure of a single nucleic acid is not a significant structural element because the nucleic acid is found in every nucleic acid sequence.

The number of inventions has been determined as follows: Each of Groups I, II, IV and V has 39 additional sequences (in addition to SEQ ID No. 7). 39 X 4 results in 156 inventions. Thus 156 + the original 5 groups results in 161 inventions.

If no additional fees are paid, Group I, claims 1-7 and 65-67 with respect to SEQ ID NO 7 will be searched
INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

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

1. □ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. □ Claim 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. □ Claim 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:
Please See Continuation Sheet

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.: 1-7 and 65-67 (SEQ ID No. 7)

Remark on Protest □ The additional search fees were accompanied by the applicant’s protest.
□ No protest accompanied the payment of additional search fees.

Form PCT/ISA/210 (continuation of first sheet(1)) (July 1998)