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Declaration under Rule 4.17:

— *of inventorship (Rule 4.17(iv)) for US only*

Published:

— *with international search report*
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26 August 2004

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: IMMUNOGENIC EPITOPES FOR FIBROBLAST GROWTH FACTOR 5 (FGF-5) PRESENTED BY HLA-A3 AND HLA-A2

(57) Abstract: The present disclosure relates to peptides for use in immunotherapy of tumors. The peptides disclosed herein are derived from the amino acid sequence of a renal cell carcinoma-associated antigen, fibroblast growth factor-5 (FGF-5). In one example, the peptide is an HLA-A3 epitope (such as NTYASPRFK). In another example, the peptide is an HLA-A2 epitope (such as MLSVLEIFAV). Methods are provided for using such peptides, and variants or fusions thereof, to stimulate an immune response in a subject. The peptides disclosed herein can be formulated into pharmaceutical composition for administration to a subject.



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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/37065

A. CLASSIFICATION OF SUBJECT MATTER		
IPC(7) : A61K 38/00 US CL : 514/17		
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. : 514/17		
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) Please See Continuation Sheet		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 01/25271 A2 (THE GOVERNMENT OF THE UNITED STATES OF AMERICA, AS REPRESENTED BY THE SECRETARY, DEPARTMENT OF HEALTH AND HUMAN SERVICES) 12 April 2001 (12.04.2001), entire document (FGF-5).	1-10, 23-24, and 26-27
A	US 2002/0031805 A1 (CONKLIN) 14 March 2002 (14.03.2002), entire document (FGF Homologs).	1-10,23-24, and 26-27
<input type="checkbox"/> Further documents are listed in the continuation of Box C. <input type="checkbox"/> 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 "E" earlier application or patent 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		Date of mailing of the international search report
08 March 2004 (08.03.2004)		28 JUN 2004
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230		Authorized officer Maury Audet Telephone No. 703-308-1123

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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.

- I. Claims 1-10, 23-24, and 26-27, drawn to a purified immunogenic peptide comprising an uncountable number of substitutions/lengths/% identities, etc. of SEQ ID NOS: 1, 3-7, 9, 17 (i.e. a peptide of 8-500 amino acids) or a pharmaceutical composition containing such.
- II. Claims 19-20, 23, and 25-27, drawn to an isolated nucleic acid encoding any of defined or undefined peptides of Group I or a pharmaceutical composition containing such.
- III. Claim 21, drawn to a vector comprising any of the defined or undefined nucleic acids of Group III.
- IV. Claim 22, drawn to a host cell transformed with the vector of Group III.
- V. Claims, 28-40, drawn to a method eliciting an immune response in a subject, comprising administering a peptide of SEQ ID NO: 17 (a 6-mer) that is at least 8 residues long, a sequence having at least 80% homology to SEQ ID NO: 7 (a 10-mer), or both.
- VI. Claims 41-45, drawn to a method of treating an FGF-5 expressing tumor in a subject, comprising administering a peptide of SEQ ID NO: 17 (a 6-mer) that is at least 8 residues long, a sequence having at least 80% homology to SEQ ID NO: 7 (a 10-mer), or both.
- VII. Claim 46, drawn to a method of generating antibodies specific for an FGF-5 antigen, comprising introducing into the subject a peptide of SEQ ID NO: 17 (a 6-mer) that is at least 8 residues long, a sequence having at least 80% homology to SEQ ID NO: 7 (a 10-mer).
- VIII. Claim 47, drawn to the use of a peptide comprising any of SEQ ID NOS: 1-7, or 9, to treat an FGF-5 expressing tumor.
- IX. Claim 48, drawn to the use of a peptide comprising any of SEQ ID NOS: 1-7, or 9, to elicit an immune response.

The inventions listed as Groups I-IV 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:

An international and a national stage application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention"). Where a group of inventions is claimed in an application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art. An international or a national stage application containing claims to different categories of invention will be considered to have unity of invention if the claims are drawn only to one of the following combinations of categories: (1) a product and a process specially adapted for the manufacture of said product; or (2) a product and a process of use of said product; or (3) a product, a process specially adapted for the manufacture of the said product, and a use of the said product; or (4) a process and an apparatus or means specifically designed for carrying out the said process; or (5) a product, a process specially adapted for the manufacture of the said product, and an apparatus or means specifically designed for carrying out the said process. If multiple products, processes of manufacture or uses are claimed, the first invention of the category first mentioned in the claims of the application and the first recited invention of each of the other categories related thereto will be considered as the main invention in the claims, see PCT Article 17(3)(a) and 1.476(c).

The alleged special technical feature is a peptide that comprises Tyr-Ala-A3-A4-Arg-Phe. However, the invention is broadly drawn to any peptide with the above, having from 8-500 amino acids. Since the core of the above only a dipeptide residue (at 2 different locations), there is no substantial core that is capable of being searched for all the possible peptides, including the short SEQ ID NOS: claimed. Thus, due to the range of peptide structures/SEQ ID NOS: capable of use in Groups I-IX, each one represents a separate and distinct structure (invention), each subject to their own respective search. Thus, there is no special technical feature among Groups I-IV. Groups I-IV lack unity.

Inventions I-IX are drawn to compounds, compositions, and/or methods that are related in that they contain at least the dipeptides Tyr-Ala and Arg-Phe. However, because each invention is of different chemical and/or peptide and/or pharmaceutical substitutions and/or method steps/results, each invention differs in structure (chemically, physically, or pharmacologically) and in function; or alternatively in steps/results. Therefore, a separate and distinct search is required for each invention and each invention and compound is patentably distinct one from the other.

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The first named invention is Group I (claims 1-10, 23-24, and 26-27), drawn to a purified immunogenic peptide of SEQ ID NO: 1 (9-mer) (the 1st distinctly claimed compound with Tyr-Ala and Arg-Phe, wherein the peptide is at least eight amino acids in length (calim 1)). [Note: Should any additional inventions be paid for to be searched (see also below), which would include any other distinct compounds as drawn to Group I, Applicant must specifically identify the compound SEQ ID NO: or compound structure to be searched and what invention (Group) it is drawn to]. On March 11, 2004, Sheree Rybak, Attorney for Applicant, elected to pay for one additional invention, Group I as drawn to SEQ ID NO: 7.

Pursuant to PCT practice, Applicant was orally advised of the right to pay additional fees for the search of additional inventions (\$210.00 for each additional invention). Applicant was also orally advised that there is no right to protest for any group not paid for and that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/IPEA/210).

Continuation of B. FIELDS SEARCHED Item 3:

EAST (USPTO Internal Patents/Publications); STIC-USPTO Internal search of FGF compounds in structure DB's (i.e. Registry, CAPLUS, etc.); STIC-USPTO Internal Search of SEQ ID NOS: 1 and 7 on relevant DB's (did not search pending DB's). SEQ ID NOS: 1 and 7 were found to be free of the art in the DB's searched.

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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:

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.: 1-10, 23-24, and 26-27 as drawn to SEQ ID NOS: 1 and 7.
- Remark on Protest The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.