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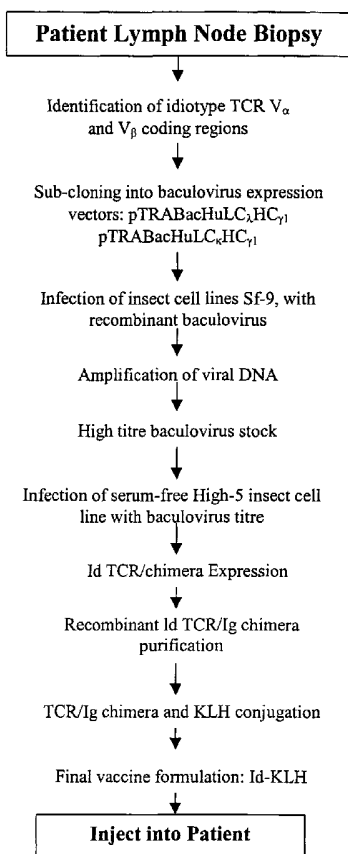
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- (74) Agents: **GUISE, Jeffrey, W.** et al.; Brobeck, Phleger & Harrison LLP, 12390 El Camino Real, San Diego, CA 92130 (US).
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(54) Title: METHOD AND COMPOSITION FOR ALTERING A T CELL MEDIATED PATHOLOGY



(57) Abstract: The present invention provides a method for altering a T cell mediated pathology in a patient. This method comprises administering a composition comprising at least one and/or two chimeric proteins. Each chimeric protein comprises at least a portion of either the V_α or V_β region of a TCR from particular T cells from a patient having a T cell mediated pathology, and an immunoglobulin constant region. The genes encoding V_α and/or V_β regions and the genes encoding immunoglobulin constant regions are isolated and inserted into an expression vector. The chimeric proteins are produced by introducing the expression vectors into insect cell lines. The chimeric proteins are purified using antibody affinity columns, and then chemically conjugated to an immunogenic carrier, keyhole-limpet hemocyanin (KLH). Since the conjugates comprises chimeric proteins made specifically from particular T cells from a patient having T cell mediated pathology, when it is administered to such a patient, with or without a cytokine, such as granulocyte-macrophage-CSF, or a chemokine, it can induce immune responses to alter such a T cell mediated pathology.



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patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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INTERNATIONAL SEARCH REPORT

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A. CLASSIFICATION OF SUBJECT MATTER IPC 7 A61P37/00 A61P35/00 A61K39/395 A61K39/385 C12N15/866 //C12N5/10,C07K16/00,G01N33/68,(A61K39/395,38:19)				
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 A61K				
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, MEDLINE, BIOSIS, EMBASE, CHEM ABS Data, CANCERLIT				
C. DOCUMENTS CONSIDERED TO BE RELEVANT				
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.		
X	WO 99 18129 A (SUNOL MOLECULAR CORP) 15 April 1999 (1999-04-15) page 4	1-56		
E	WO 01 93913 A (SUNOL MOLECULAR CORP) 13 December 2001 (2001-12-13) example 13	1-56		
X	JESSON M I ET AL: "THE IMMUNE RESPONSE TO SOLUBLE D10 TCR: ANALYSIS OF ANTIBODY AND T CELL RESPONSES" INTERNATIONAL IMMUNOLOGY, OXFORD UNIVERSITY PRESS, GB, vol. 1, no. 10, January 1998 (1998-01), pages 27-35, XP001098180 ISSN: 0953-8178 page 28	1-56		
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<input checked="" type="checkbox"/> Further documents are listed in the continuation of box C.				
<input checked="" type="checkbox"/> Patent family members are listed in annex.				
° Special categories of cited documents :				
<table style="width: 100%; border: none;"> <tr> <td style="width: 50%; border: none; vertical-align: top;"> *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 </td> <td style="width: 50%; border: none; vertical-align: top;"> *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 </td> </tr> </table>			*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. *&* document member of the same patent family
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. *&* document member of the same patent family			
Date of the actual completion of the international search	Date of mailing of the international search report			
28 August 2002	05/09/2002			
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Wagner, R			

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 01/25203

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	JESSON M ET AL: "IMMUNOGENICITY OF RECOMBINANT, SOLUBLE CELL RECEPTORS IN SYNGENEIC MICE" INTERNATIONAL CONGRESS OF IMMUNOLOGY ABSTRACTS, BUDAPEST, HU, 1995, page 442 XP002002802 abstract ---	1-56
X	MCKEEVER U ET AL: "IMMUNIZATION WITH SOLUBLE BDC 2.5 T CELL RECEPTOR-IMMUNOGLOBULIN CHIMERIC PROTEIN: ANTIBODY SPECIFICITY AND PROTECTION OF NONOBESSE DIABETIC MICE AGAINST ADOPTIVE TRANSFER OF DIABETES BY MATERNAL IMMUNIZATION" JOURNAL OF EXPERIMENTAL MEDICINE, TOKYO, JP, vol. 5, no. 184, 1 November 1996 (1996-11-01), pages 1755-1768, XP001095349 ISSN: 0022-1007 page 1755 -page 1758 ---	1-56
A	WONG C P ET AL: "RECOMBINANT ADENOVIRUS VACCINE ENCODING A CHIMERIC T-CELL ANTIGEN RECEPTOR INDUCES PROTECTIVE IMMUNITY AGAINST A T-CELL LYMPHOMA" CANCER RESEARCH, AMERICAN ASSOCIATION FOR CANCER RESEARCH, BALTIMORE, MD, US, vol. 10, no. 60, 15 May 2000 (2000-05-15), pages 2689-2695, XP001093915 ISSN: 0008-5472 abstract ---	1-56
A	GASCOIGNE N ET AL: "Secretion of a chimeric T-cell receptor-immunoglobulin protein" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 84, no. 9, May 1987 (1987-05), pages 2936-2940, XP002149784 ISSN: 0027-8424 abstract ---	1-56
A	WO 00 31239 A (ESHAR ZELIG ;YEDA RES & DEV (IL); BOLHUIS REINDER L H (NL); WILLE) 2 June 2000 (2000-06-02) the whole document ---	1-56

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/25203

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>VANDENBARK A A ET AL: "T CELL RECEPTOR PEPTIDES IN TREATMENT OF AUTOIMMUNE DISEASE: RATIONALE AND POTENTIAL" JOURNAL OF NEUROSCIENCE RESEARCH, WILEY-LISS, US, vol. 43, no. 4, 15 February 1996 (1996-02-15), pages 391-402, XP000612005 ISSN: 0360-4012 the whole document -----</p>	1-56

INTERNATIONAL SEARCH REPORT

International application No.
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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.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-35 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.
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).

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.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/25203

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
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