



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification⁵ : A61K 37/02, 39/395	A3	(11) International Publication Number: WO 94/04180 (43) International Publication Date: 3 March 1994 (03.03.94)
(21) International Application Number: PCT/US93/07646 (22) International Filing Date: 18 August 1993 (18.08.93) (30) Priority data: 07/932,900 20 August 1992 (20.08.92) US 07/933,419 21 August 1992 (21.08.92) US 07/933,462 21 August 1992 (21.08.92) US 07/933,950 21 August 1992 (21.08.92) US (71) Applicant: SCHERING CORPORATION [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033 (US). (72) Inventors: COFFMAN, Robert ; 239 Echo Lane, Portola Valley, CA 94025 (US). DE VRIES, Jan, E. ; 763 Sunshine Drive, Los Altos, CA 94022 (US). DE WAAL MALEFYT, Rene ; 891 Muender Avenue, Sunnyvale, CA 94086 (US). POWRIE, Fiona ; 541 Del Medio Avenue, #204, Mountain View, CA 94040 (US). RENNICK, Donna ; 601 Almond Avenue, Los Altos, CA 94022 (US).	(74) Agents: DULAK, Norman, C. et al. ; Schering-Plough Corporation, One Giralda Farms, M3W, Madison, NJ 07940-1000 (US). (81) Designated States: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i> (88) Date of publication of the international search report: 09 June 1994 (09.06.94)	
(54) Title: NOVEL USES OF IL-4 AND/OR IL-10, AND ANTIBODIES AGAINST THE SAME		
(57) Abstract Compositions and methods are provided for the use of IL-4 and/or IL-10, or antibodies against IL-4 and IL-10, for the treatment of a number of diseases. In one embodiment, IL-10 is used to inhibit IL-2 production by neoplastic lymphocytes, or IL-2-dependent neoplastic cell proliferation. In another embodiment, IL-10 is used to treat inflammatory bowel disease. In still another embodiment, antibodies against IL-4 and IL-10 are used to increase levels of IFN- γ . In still another embodiment, a combination of IL-4 and IL-10 is used to potentiate IL-10-mediated inhibition of cytokine production by T cells. In still another embodiment IL-10, alone or in combination with IL-4, is used to inhibit delayed type hypersensitivity reactions. This invention further provides pharmaceutical compositions comprising a physiologically acceptable carrier and a combination of IL-4 and IL-10, or a combination of antibodies against IL-4 and IL-10.		

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 93/07646

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 A61K37/02 A61K39/395

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 5 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)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
O, X	JOURNAL OF CELLULAR BIOCHEMISTRY, SUPPL. 0, (16 PART C) 21 February 1992, NEW YORK, N.Y., US page 74 C. FLUCKIGER ET AL. 'BIOLOGIC EFFECTS OF IL-10 ON CHRONIC LYMPHOCYTIC LEUKEMIA CELLS' & KEYSTONE SYMPOSIUM ON HEMATOPOIESIS, TAMARRON, COLORADO, US, FEBRUARY 27 - MARCH 5, 1992 see abstract M 211 ---	1,3,4,6, 7,9,11
A	WO,A,92 12725 (SCHERING CORPORATION) 6 August 1992 see claims --- -/--	1,3,4,6, 7,9,11

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	"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	

Date of the actual completion of the international search 13 April 1994	Date of mailing of the international search report 04. 05. 94
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 Ryckebosch, A

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 International Application No
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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	EP,A,0 405 980 (SCHERING CORPORATION) 2 January 1991	1,3,4,6, 7,9,11
Y	see page 2, line 13 - line 15; claims 17,26,28 see page 2, line 48 - line 54 see page 3, line 14 - line 18 see page 8, line 21 - line 24 see page 16, line 36 - line 38 ---	1,3,4,6, 7,9,11
Y	IMMUNOLOGY vol. 72, no. 2 , February 1991 , OXFORD, GB pages 161 - 166 C. BELLO-FERNANDEZ ET AL. 'IL-4 ACTS AS A HOMEOSTATIC REGULATOR OF IL-2-INDUCED TNF AND IFN-GAMMA.' see page 164, right column, line 1 - line 6 ---	1,3,4,6, 7,9,11
X	JOURNAL OF IMMUNOLOGY. vol. 145, no. 9 , 1 November 1990 , BALTIMORE US pages 2938 - 2945 T.R. MOSMANN ET AL. 'ISOLATION OF MONOCLONAL ANTIBODIES SPECIFIC FOR IL-4, IL-5, IL-6, AND A NEW Th2-SPECIFIC CYTOKINE (IL-10), CYTOKINE SYNTHESIS INHIBITORY FACTOR, BY USING A SOLID PHASE RADIOIMMUNOADSORBENT ASSAY.' see page 2938, right column, line 8 - line 13 ---	1,3,4,6, 7,9,11
A	INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY vol. 99, no. 1 , 17 July 1992 , BASEL, CH pages 8 - 15 H. SPITS ET AL. 'FUNCTIONAL CHARACTERIZATION OF HUMAN IL-10.' see the whole document ---	1,3,4,6, 7,9,11
A	JOURNAL OF CLINICAL IMMUNOLOGY vol. 12, no. 4 , July 1992 , NEW YORK, N.Y., US pages 239 - 247 M. HOWARD ET AL. 'BIOLOGICAL PROPERTIES OF INTERLEUKIN 10.' see the whole document ---	1,3,4,6, 7,9,11
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INTERNATIONAL SEARCH REPORT

 Internat Application No
 PCT/US 93/07646

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
O,P, X	CHEMICAL ABSTRACTS, vol. 119, no. 23, 6 December 1993, Columbus, Ohio, US; abstract no. 247336s, D. RENNICK ET AL 'INTERLEUKIN 10 AND THE INFLAMMATORY RESPONSE.' page 737 ; see abstract & PROG. IMMUNOL., PROC. INT. CONGR. IMMUNOL., 8TH, BUDAPEST, AUG. 23-28, 1992 vol. VIII , 1993 pages 355 - 360 ---	1,3,4,6, 7,9,11
O,P, X	GASTROENTEROLOGY vol. 104, no. 4 SP , April 1993 , NEW YORK, N.Y., US page A751 G.E. MULLIN ET AL. 'ABNORMAL IL-10 mRNA PRODUCTION IN THE INTESTINAL MUCOSAL LESIONS OF INFLAMMATORY BOWEL DISEASE.' & 94TH. ANNUAL MEETING OF THE AMERICAN GASTROENTEROLOGICAL ASSOC., BOSTON, US, MAY 15-21, 1993 see abstract -----	1,3,4,6, 7,9,11

INTERNATIONAL SEARCH REPORT

national application No.

PCT/US 93/07646

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:
Remark : Although claims 7,8,11(partially) are directed to a method of treatment of the human/animal body the search has been carried out and based on the alleged effects of the compound/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:

see PCT/ISA/206 mailed on 11.01.94

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 93/07646

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A-9212725	06-08-92	AU-A- 1261792 EP-A- 0567576	27-08-92 03-11-93
EP-A-0405980	02-01-91	AU-B- 635058 AU-A- 6077090 CA-A- 2062763 CN-A- 1051393 EP-A- 0567450 JP-T- 4502560 WO-A- 9100349 US-A- 5231012	11-03-93 17-01-91 29-12-90 15-05-91 03-11-93 14-05-92 10-01-91 27-07-93