



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 35/74, 38/16, 39/395, 48/00	A3	(11) International Publication Number: WO 00/15175 (43) International Publication Date: 23 March 2000 (23.03.00)
(21) International Application Number: PCT/SE99/01560 (22) International Filing Date: 8 September 1999 (08.09.99) (30) Priority Data: 9803098-4 10 September 1998 (10.09.98) SE 60/135,798 24 May 1999 (24.05.99) US (71)(72) Applicants and Inventors: ARENCIBIA, Ignacio [CU/SE]; Historiegränd 20A, 102, S-907 34 Umeå (SE). SUNDQVIST, Karl-Gösta [SE/SE]; Skäluddsvägen 16, S-178 32 Ekerö (SE).		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, VZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian 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), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> (88) Date of publication of the international search report: 13 July 2000 (13.07.00)
(54) Title: USE AS AN ACTIVE SUBSTANCE OF MOLECULES BINDING TO BETA-1-INTEGRIN WITH THE CAPACITY TO KILL CELLS (57) Abstract <p>The present invention relates to the use as an active substance of molecules binding to β_1-integrins and with the capacity to kill cells having β_1-integrins for production of pharmaceuticals for treatment of conditions dependent on cells having β_1-integrins such as cancer and conditions dependent on T lymphocytes and fibrotic conditions. Especially the invention relates to the use of Invasin (Inv) from Yersinia (Yer) species, subfragments, variants, and peptides thereof, microorganisms producing invasin and invasin like substances and antibodies binding β_1-integrins and with the capacity to kill cells having β_1-integrins.</p>		

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 99/01560

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 35/74, A61K 38/16, A61K 39/395, A61K 48/00

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)

IPC7: A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE,DK,FI,NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, 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.
X	WO 9613250 A1 (AMGEM INC.), 9 May 1996 (09.05.96), page 4, line 20 - line 34; page 6, line 20 - line 26; page 9, line 3 - line 24, page 12, line 8 - line 18; page 13, line 4 - line 31; page 15, line 24 - line 26; page 19, line 8-16 --	1-4,6,8-10
X	Science, Volume 267, February 1995, Nancy Boudreau et al, "Suppression of ICE and Apoptosis in Mammary Epithelial Cells by E xtracellular Matrix", page 891 - page 893, see abstract --	1-2,4-6,8

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

* Special categories of cited documents:

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"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

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Date of the actual completion of the international search

14 March 2000

Date of mailing of the international search report

28-03-2000

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE 99/01560

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	Dialog Information Services, File 155, MEDLINE, MEDLINE accession no. 08950105, Mitra RS et al: Apoptosis in keratinocytes is not dependent on induction of differentiation"; & Lab Invest Jan 1997, 76 (1) p99-107, ISSN 0023-6837, see abstract --	1-2,4-6,8
P,X	US 5846536 A (MINA J. BISSELL ET AL), 8 December 1998 (08.12.98), see abstract; column 16, lines 3-7 -- -----	1-2,4-6,8

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 99/01560

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:

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:

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 next 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.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

Unity of invention is lacking

According to PCT Rules 13.1 and 13.2, an international application shall relate to one invention only or a group of inventions linked by one or more of the same corresponding "special technical features", i.e. features that define a contribution which each of the inventions makes over the prior art.

In Your application the following inventions have been found:

1. Use as an active substance of a molecule binding to beta-1-integrin, such as the invasin protein from *Yersinia*, possibly coupled to an antibody. This invention also discloses a pharmaceutical composition comprising the active substance and methods of killing T-lymphocytes and tumor cells. The special technical feature of this invention is the use of invasin. This invention is disclosed in claims 1-4, 6 and 8-10.
2. Use as an active substance of a monoclonal antibody or a hybrid antibody binding to and killing cells with beta-1-integrins. The special technical feature of this invention is the use of a monoclonal or hybrid antibody with the ability to kill cells having beta-1-integrin. This invention is disclosed in claims 1 and 5.
3. Use in gene therapy of a molecule binding to beta-1-integrin wherein the invasin gene sequence is used. The special technical feature of this invention is the use of the invasin gene sequence. This invention is disclosed in claims 1 and 7.

The three inventions are not linked by any common "special technical feature". Thus, the inventions lack unity. The first and second inventions have been searched.

INTERNATIONAL SEARCH REPORT

Information on patent family members

02/12/99

International application No.

PCT/SE 99/01560

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9613250 A1	09/05/96	AU 4010395 A	23/05/96
US 5846536 A	08/12/98	NONE	