



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification ⁵ : A61K 47/48, C12N 15/62, 15/11 C07K 15/00</p>	<p>A3</p>	<p>(11) International Publication Number: WO 92/22332</p> <p>(43) International Publication Date: 23 December 1992 (23.12.92)</p>
<p>(21) International Application Number: PCT/US92/05085</p> <p>(22) International Filing Date: 17 June 1992 (17.06.92)</p> <p>(30) Priority data: 716,062 17 June 1991 (17.06.91) US</p> <p>(71) Applicant: THE REGENTS OF THE UNIVERSITY OF CALIFORNIA [US/US]; 300 Lakeside Drive, 22nd Floor, Oakland, CA 94612-3550 (US).</p> <p>(72) Inventors: PARDRIDGE, William, M. ; 1180 Tellem Drive, Pacific Palisades, CA 90272 (US). BOADO, Ruben, J. ; 29481 Trailway Lane, Agoura Hills, CA 91301 (US).</p>	<p>(74) Agents: OLDENKAMP, David, J. et al.; Poms, Smith, Lande & Rose, 2121 Avenue of the Stars, Suite 1400, Los Angeles, CA 90067 (US).</p> <p>(81) Designated States: AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE (European patent), DK (European patent), ES (European patent), FI, FR (European patent), GA (OAPI patent), GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL (European patent), NO, PL, RO, RU, SD, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent).</p> <p>Published <i>With international search report. Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i></p> <p>(68) Date of publication of the international search report: 4 February 1993 (04.02.93)</p>	
<p>(54) Title: DRUG DELIVERY OF ANTISENSE OLIGONUCLEOTIDES AND PEPTIDES TO TISSUES IN VIVO AND TO CELLS USING AVIDIN-BIOTIN TECHNOLOGY</p>		
<p>(57) Abstract</p> <p>A composition for delivering an agent to cells <i>in vitro</i> or to tissues or organs <i>in vivo</i>. The composition comprises either avidin or an avidin fusion protein bonded to a biotinylated agent to form an avidin-biotin-agent complex. A method is further provided for delivering an agent to cells using the avidin-biotin-agent complex which involves administering the complex to an individual subject. The avidin-biotin-agent complex is used in therapeutic and diagnostic methods.</p>		

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INTERNATIONAL SEARCH REPORT

PCT/US 92/05085

International Application No

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶		
According to International Patent Classification (IPC) or to both National Classification and IPC		
Int.Cl. 5 A61K47/48;	C12N15/62;	C12N15/11; C07K15/00
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
Int.Cl. 5	A61K ; C07H ; C07K ; C12N	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹		
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X	EP,A,0 251 494 (THE BOARD OF TRUSTEES OF THE LELAND STANFORD JUNIOR UNIVERSITY) 7 January 1988	1-7, 13-15, 19-30
Y	see the whole document ---	1-31
Y	WO,A,9 012 096 (PURDUE RESEARCH FOUNDATION) 18 October 1990 see page 7 - page 14 ---	1-7, 13-31
Y	WO,A,8 705 026 (THE TRUSTEES OF COLUMBIA UNIVERSITY IN THE CITY OF NEW YORK) 27 August 1987 cited in the application see page 1 - page 16 ---	1-31
Y	WO,A,8 602 077 (MEADE ET AL) 10 April 1986 see page 1 - page 8 ---	1-31
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<p>⁹ Special categories of cited documents :¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"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)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> <p>"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</p> <p>"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"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.</p> <p>"A" document member of the same patent family</p>		
IV. CERTIFICATION		
Date of the Actual Completion of the International Search 26 NOVEMBER 1992		Date of Mailing of this International Search Report 07. 12. 92
International Searching Authority EUROPEAN PATENT OFFICE		Signature of Authorized Officer SITCH W.D.C. <i>W.D.C. Sitch</i>

III. DOCUMENTS CONSIDERED TO BE RELEVANT (CONTINUED FROM THE SECOND SHEET)		
Category °	Citation of Document, with indication, where appropriate, of the relevant passages	Relevant to Claim No.
X	JOURNAL OF NUCLEAR MEDICINE vol. 28, 1987, NEW YORK, USA pages 1294 - 1302 HNATOWICH ET AL 'INVESTIGATIONS OF AVIDIN AND BIOTIN FOR IMAGING APPLICATIONS' cited in the application see the whole document ---	1-3, 5-7, 13-15, 19-30
X	FILE SERVER STN KARLSRUHE, FILE BIOSIS ABSTRACT NO. 91:317080 & BIOL. ABSTRACTS 92:27595 & MOL. CELL. ENDOCRINOL., VOL. 77(1-3)MAY 1991 PAGES 123-132 see abstract ---	1-5, 14, 15, 19, 21-29
Y	US, A, 4 772 691 (HERMAN) 20 September 1988 see the whole document ---	32
Y	EP, A, 0 431 523 (ENZO BIOCHEM, INC.) 12 June 1991 see the whole document -----	32

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 92/05085

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 19-23 , 26-28 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:

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.

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. US 9205085
SA 61825**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information. 26/11/92

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A-0251494	07-01-88	US-A- 4863713 JP-A- 63005033	05-09-89 11-01-88
WO-A-9012096	18-10-90	US-A- 5108921 AU-A- 5356490 AU-A- 5437590 CA-A- 2013580 CA-A- 2013582 EP-A- 0466816 WO-A- 9012095	28-04-92 05-11-90 05-11-90 03-10-90 03-10-90 22-01-92 18-10-90
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WO-A-8602077	10-04-86	DE-A- 3583940 EP-A,B 0198015 JP-T- 62500700	02-10-91 22-10-86 26-03-87
US-A-4772691	20-09-88	None	
EP-A-0431523	12-06-91	CA-A- 2029273 JP-A- 3190895	05-06-91 20-08-91