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- (71) Applicant (for all designated States except US): **THE CORPORATION OF MERCER UNIVERSITY** [US/US]; Office of General Counsel, 1400 Coleman Avenue, Macon, GA 31207-0001 (US).
- (72) Inventor; and
- (75) Inventor/Applicant (for US only): **D'SOUZA, Martin, J.** [US/US]; 710 Creek Wind Court, Duluth, GA 30097 (US).
- (74) Agent: **BERNSTEIN, Jason, A.**; Powell, Goldstein, Frazer & Murphy LLP, 16th Floor, 191 Peachtree Street, NE, Atlanta, GA 30303-1736 (US).
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(54) Title: METHOD OF MANUFACTURING ALBUMIN MICROSPHERES COMPRISING ANTISENSE OLIGONUCLEOTIDES (OLIGOMERS) TO NF-KB

(57) Abstract: A method of forming microspheres of a bioactive material, such as an antisense digonucleotide to NF-KB by nebulizing a solubilized form of a material to be encapsulated and an encapsulating material, such as albumin, in a stirred chilled solvent system comprising a vegetable oil, mineral oil and/or a lower alcohol such that the formed microspheres demonstrate intracellular bioactivity when taken up by macrophages.

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 03/26912

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K9/16 C12N15/11 A61K48/00

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)
IPC 7 A61K C12N

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, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 5 069 936 A (YEN RICHARD C K) 3 December 1991 (1991-12-03) claims 1-22 column 9, line 31 -column 12, line 15 examples 4,5,14	1
Y	US 2002/006912 A1 (NERENBERG MICHAEL I ET AL) 17 January 2002 (2002-01-17) claims 1,13,34 paragraphs '0034!, '0037!-'0039! example 3	1
Y	WO 98 44908 A (UNIV LELAND STANFORD JUNIOR) 15 October 1998 (1998-10-15) claims 6-9,11 page 4, line 6 -page 4, line 25 page 7, line 17 -page 7, line 31 page 16, line 1 -page 17, line 3	1
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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
- "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

24 February 2004

Date of mailing of the international search report

03/03/2004

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

Schifferer, H

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 03/26912

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 97 47325 A (MEYER ZUM BUESCHENFELDE K H ;NEURATH MARKUS F (DE); KAROLINSKA INN) 18 December 1997 (1997-12-18) claims 1,8,9,11,14,15 page 8, line 17 -page 9, line 20 example 4	1
A,P	US 2003/105037 A1 (MONIA BRETT P ET AL) 5 June 2003 (2003-06-05) paragraphs '0062!-'0070!	1

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1 (in part)

Present claim 1 relates to a compound defined by reference to a desirable characteristic or property, namely

to an antisense oligonucleotides (oligomers) to NF-kB.

The claims cover all products having this characteristic or property, whereas the application provides support within the meaning of Article 6 PCT and/or disclosure within the meaning of Article 5 PCT for only a very limited number of such products. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Independent of the above reasoning, the claims also lack clarity (Article 6 PCT). An attempt is made to define the product by reference to a result to be achieved. Again, this lack of clarity in the present case is such as to render a meaningful search over the whole of the claimed scope impossible. Consequently, the search has been carried out for those parts of the claims which appear to be clear, supported and disclosed, namely those parts relating to

the terms "antisense oligonucleotide", "antisense oligomer", "antisense RNA", "antisense mRNA", "antisense DNA", "antisense oligo ribonucleotide"

and

the terms "NF-kB", "NF-kappaB".

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 03/26912

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.: 1 (in part)
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:
see FURTHER INFORMATION sheet PCT/ISA/210

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 03/26912

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