



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/US89/01453</p> <p>(22) International Filing Date: 7 April 1989 (07.04.89)</p> <p>(30) Priority data:</p> <table border="0"> <tr> <td>179,406</td> <td>8 April 1988 (08.04.88)</td> <td>US</td> </tr> <tr> <td>232,630</td> <td>15 August 1988 (15.08.88)</td> <td>US</td> </tr> <tr> <td>315,342</td> <td>23 February 1989 (23.02.89)</td> <td>US</td> </tr> </table> <p>(60) Parent Applications or Grants (63) Related by Continuation</p> <table border="0"> <tr> <td>US</td> <td>179,406 (CIP)</td> </tr> <tr> <td>Filed on</td> <td>8 April 1988 (08.04.88)</td> </tr> <tr> <td>US</td> <td>232,630 (CIP)</td> </tr> <tr> <td>Filed on</td> <td>15 August 1988 (15.08.88)</td> </tr> <tr> <td>US</td> <td>315,342 (CIP)</td> </tr> <tr> <td>Filed on</td> <td>23 February 1989 (23.02.89)</td> </tr> </table> <p>(71) Applicant (for all designated States except US): CREATIVE BIOMOLECULES, INC. [US/US]; 35 South Street, Hopkinton, MA 01748 (US).</p> <p>(72) Inventors; and (75) Inventors/Applicants (for US only): KUBERASAMPATH, Thangavel [IN/US]; 6 Spring Street, Medway, MA 02053 (US). OPPERMANN, Hermann [US/US]; 25 Summer Hill Road, Medway, MA 02053 (US). RUEGER, David, C. [US/US];</p>	179,406	8 April 1988 (08.04.88)	US	232,630	15 August 1988 (15.08.88)	US	315,342	23 February 1989 (23.02.89)	US	US	179,406 (CIP)	Filed on	8 April 1988 (08.04.88)	US	232,630 (CIP)	Filed on	15 August 1988 (15.08.88)	US	315,342 (CIP)	Filed on	23 February 1989 (23.02.89)	<p>150 Edgemere Road, Apt. 4, West Roxbury, MA 02132 (US). OZKAYNAK, Engin [TR/US]; 44 Purdue Drive, Milford, MA 01757 (US).</p> <p>(74) Agent: PITCHER, Edmund, R.; Lahive & Cockfield, 60 State Street, Boston, MA 02109 (US).</p> <p>(81) Designated States: AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CF (OAPI patent), CG (OAPI patent), CH (European patent), CM (OAPI patent), DE (European patent), DK, FI, FR (European patent), GA (OAPI patent), GB (European patent), HU, IT (European patent), JP, KP, KR, LK, LU (European patent), MC, MG, ML (OAPI patent), MR (OAPI patent), MW, NL (European patent), NO, RO, SD, SE (European patent), SN (OAPI patent), SU, TD (OAPI patent), TG (OAPI patent), US.</p> <p>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></p> <p>(88) Date of publication of the international search report: 8 February 1990 (08.02.90)</p>
179,406	8 April 1988 (08.04.88)	US																				
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<p>(54) Title: OSTEOGENIC DEVICES</p> <p>(57) Abstract</p> <p>Disclosed are 1) osteogenic devices comprising a matrix containing osteogenic protein and methods of inducing endochondral bone growth in mammals using the devices; 2) amino acid sequence data, amino acid composition, solubility properties, structural features, homologies and various other data characterizing osteogenic proteins, and 3) methods of producing osteogenic proteins using recombinant DNA technology.</p>																						

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INTERNATIONAL SEARCH REPORT

International Application No. PCT/US 89/01453

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		
IPC ⁴ : C 07 K 13/00, A 61 L 27/00, C 12 N 15/00, A 61 K 35/32, C 12 P 21/02		
II. FIELDS SEARCHED		
Minimum Documentation Searched ⁷		
Classification System	Classification Symbols	
IPC ⁴	C 07 K, C 12 N, A 61 K, A 61 L, C 12 P	
Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched ⁸		
III. DOCUMENTS CONSIDERED TO BE RELEVANT ⁹		
Category ⁹	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³
X, Y	WO, A, 88/00205 (GENETICS INSTITUTE) 14 January 1988 see pages 1-12, 15-17, 22-24, 49; pages 61-73, claims 1-23 --	1-16, 25, 26, 28, 32, 33
Y	The Journal of Cell Biology, volume 97. December 1983, The Rockefeller University Press, S.M. Seyedin et al.: "In vitro induction of cartilage-specific macromolecules by a bone extract", pages 1950-1953 see the whole article, especially page 1952, right-hand column --	1-16, 25, 26, 28, 32, 33
Y	EP, A, 0182483 (COLLAGEN CORP.) 28 May 1986 see the whole document, especially page 6, first paragraph; page 7, lines 10-18 --	1-16, 25, 26, 28, 32, 33
	--	./.
<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	Date of Mailing of this International Search Report	
13th November 1989	10. 01. 90	
International Searching Authority	Signature of Authorized Officer	
EUROPEAN PATENT OFFICE	T.K. WILLIS	

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
Y	WO, A, 85/05274 (R.F. OLIVERS) 5 December 1985 see the whole document --	8
Y	Analytical Biochemistry, volume 146, 1985, Academic press, Inc., C.A. Olson et al.: "Deglycosylation of chondroitin sulfate proteoglycan by hydrogen fluoride in pyridine", pages 232-237 see "Discussion" on page 236 --	8
A	Trends in Biochem. Sci. (TIBS), volume 9, 1984, Elsevier Science Publishers B.V., (Amsterdam, NL), E. Simpson: "Growth factors which affect bone", pages 527-530 see the whole article --	1-19,23-33
A	EP, A, 0148155 (DOW CHEMICAL CO.) 10 July 1985 cited in the application --	
A	WO, A, 86/00526 (A.I. CAPLAN) 30 January 1986 --	
A	US, A, 4394370 (S.R. JEFFERIES) 19 July 1983 --	
A	US, A, 4563489 (M.R. URIST) 7 January 1986 --	
A	S.P. Colowick et al.: "Methods in Enzymology", volume 146, Peptide Growth Factors, part A, edited by David Barnes et al., Academic Press Inc., M.R. Urist et al.: "Preparation and bioassay of bone morphogenetic protein and polypeptide fragments", pages 294- 312 --	
A	EP, A, 0169016 (COLLAGEN CORP.) 22 January 1986 -----	

FURTHER INFORMATION CONTINUED FROM THE SECOND SHEET

V. OBSERVATIONS WHERE CERTAIN CLAIMS WERE FOUND UNSEARCHABLE ¹

This International search report has not been established in respect of certain claims under Article 17(2) (a) for the following reasons:

1. Claim numbers because they relate to subject matter not required to be searched by this Authority, namely:

** Claim numbers 20-22:
See PCT Rule 39.1(iv)
Methods for treatment of the human or animal body
by surgery or therapy, as well as diagnostic methods.

2. Claim numbers 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:

** Claim numbers 1-16, 19, 32, 33
See Article 6 PCT, 17(2)(a)(ii) PCT

./.

3. Claim numbers because they are dependent claims and are not drafted in accordance with the second and third sentences of PCT Rule 6.4(a).

VI. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING ²

This International Searching Authority found multiple inventions in this International application as follows:

Please see Form PCT/ISA/206 dated 14-8-89

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims of the international application.

2. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims of the international application for which fees were paid, specifically claims:

3. 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 claim numbers:

4. As all searchable claims could be searched without effort justifying an additional fee, the International Searching Authority did not invite payment of any additional fee.

Remark on Protest

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

FURTHER INFORMATION CONTINUED FROM PCT/ISA/210 (supplemental sheet (2))

The present application is admittedly NOT the first to describe the phenomenon of bone inducing proteins, or devices containing them. It is therefore necessarily drafted to the individual compounds (on well-known devices).

In claims 1-16, however, proteins (on a device) are claimed, which are only defined by their biological activity and/or their molecular weight, which is clearly not sufficient for a full characterization of individual compounds. Despite this broad scope, the biological activity has only been demonstrated for one single compound (BOP 30K, which is covered by subject 1).

The search has therefore been restricted to the embodiments of claims 1-19 and 23-33, in as far as the proteins (and DNAs) correspond to the definitions given in the claims 17, 18, and 23-31.

This searchable subject matter has been regrouped according to the non-unity specification, in order to establish conceptually individual subjects, each of which now constitutes a potential selection invention.

**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO.**

US 8901453
SA 28156

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 19/12/89. The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO-A- 8800205	14-01-88	AU-A- 7783587	29-01-88
		EP-A- 0313578	03-05-89
EP-A- 0182483	28-05-86	US-A- 4563350	07-01-86
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		AU-A- 4900585	01-05-86
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WO-A- 8505274	05-12-85	AU-B- 575660	04-08-88
		AU-A- 4405285	13-12-85
		CA-A- 1261760	26-09-89
		EP-A- 0182842	04-06-86
		JP-T- 61502588	13-11-86
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		CA-A- 1261549	26-09-89
		JP-A- 61036223	20-02-86
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		US-A- 4774228	27-09-88
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		US-A- 4843063	27-06-89

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For more details about this annex : see Official Journal of the European Patent Office, No. 12/82