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D E C I S I O N
of 15 April 2005

Case Number: T 1331/04 - 3.3.8

Application Number: 92907075.3

Publication Number: 0567599

IPC: C12N 15/27

Language of the proceedings: EN

Title of invention:
Megakaryocyte stimulating factors

Applicant:
Genetics Institute, LLC

Opponent:
-

Headword:
MSF/GENETICS INSTITUTE

Relevant legal provisions:
EPC Art. 123(2), 54, 87, 88, 111

Keyword:
"Main request - allowability of a disclaimer (no)"
"Auxiliary request - amendments - added subject-matter (no)"

Decisions cited:
G 0002/98, G 0001/03, G 0002/03

Catchword:
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Case Number: T 1331/04 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 15 April 2005

Appellant: Genetics Institute, LLC
87 Cambridge Park Drive
Cambridge, MA 02140 (US)

Representative: Denholm, Anna M.
Wyeth Pharmaceuticals
Patents & Trade Marks Dept.
Huntercombe Lane South
Taplow, Maidenhead
Berkshire SL6 0PH (GB)

Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 28 June 2004 refusing European application No. 92907075.3 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: L. Galligani
Members: M. R. Vega Laso
S. C. Perryman

Summary of Facts and Submissions

I. European Patent Application No. 92 907 075 was published as international application WO 92/13075 (EP A 0 567 599) with the title "Megakaryocyte stimulating factors". In a decision posted on 28 June 2004 the application was refused by the examining division on the grounds that the amendments to claim 1 of the sole request then on file offended against Article 123(2) EPC.

II. In the view of the examining division, the extension of the scope of the original claim 1 by deletion of the technical feature "*having an amino terminal sequence encoding a secretory leader and initiating methionine*" was not supported by the disclosure in the application as filed. Even though it acknowledged that according to the description of the application (see page 9, lines 22-24), the natural Exon I may be completely absent, the examining division did not accept that this would amount to the complete absence of a secretory leader. The passage mentioned by the applicant in support of the introduced amendment (page 12, lines 21 to 25) did not indicate that a (recombinant) megakaryocyte stimulating factor (MSF) only made up of parts encoded by Exons II, III and IV was the desired protein of the application. Furthermore, this passage did not refer to the sequence in Figure 1, but to a predominantly homodimeric form.

III. The appellant (applicant) lodged an appeal against the decision of the examining division and with the statement of grounds, filed on 29 October 2004, it submitted a new main request (claims 1 to 13) and an

auxiliary request (claims 1 to 10). Except for minor amendments, the new main request corresponded essentially to the main request as rejected by the examining division. As a subsidiary request, the appellant requested oral proceedings under Article 116 EPC.

Claim 1 of the **main request** read:

"1. An MSF protein, substantially free from association with other proteinaceous materials and contaminants with which it is associated in natural sources, said protein comprising the amino acid sequence of Exon II, Exon III and Exon IV of Figure 1, wherein said protein does not comprise the sequence consisting of

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AAT TCT  CTC TCA  CCA AGT  GGC TTT  GTC CCC  CTC GTT  AGA TTG
Asn Ser  Leu Ser  Pro Ser  Gly Phe  Val Pro  Leu Val  Arg Leu

CTC CCT  TTC TAT  AAA GTG  GTT TGG  CCA TAT  TTA CGC  CAG TAT
Leu Pro  Phe Tyr  Lys Val  Val Trp  Pro Tyr  Leu Arg  Gln Tyr

TGT ATA  ATT TTA  GAT TTA  TCA AGC  TGT GCA  GGG AGA  TGT GGG
Cys Ile  Ile Leu  Asp Leu  Ser Ser  Cys Ala  Gly Arg  Cys Gly

GAA GGG  TAT TCT  AGA GAT  GCC ACC  TGC AAC  TGT GAT  TAT AAC
Glu Gly  Tyr Ser  Arg Asp  Ala Thr  Cys Asn  Cys Asp  Tyr Asn

TGT CAA  CAC TAC  ATG GAG  TGC TGC  CCT GAT  TTC AAG  AGA GTC
Cys Gln  His Tyr  Met Glu  Cys Cys  Pro Asp  Phe Lys  Arg Val

TGC ACT  GCG GAG  CTT TCC  TGT AAA  GGC CGC  TGC TTT  GAG TCC
Cys Thr  Ala Glu  Leu Ser  Cys Lys  Gly Arg  Cys Phe  Glu Ser

TTC GAG  AGA GGG  AGG GAG  TGT GAC  TGC GAC  GCC CAA  TGT AAG
Phe Glu  Arg Gly  Arg Glu  Cys Asp  Cys Asp  Ala Gln  Cys Lys

AAG TAT  GAC AAG  TGC TGT  CCC GAT  TAT GAG  AGT TTC  TGT GCA
Lys Tyr  Asp Lys  Cys Cys  Pro Asp  Tyr Glu  Ser Phe  Cys Ala

GAA GTG  CAT AAT  CCC ACA  TCA CCA  CCA TCT  TCA AAG  AAA GCA
Glu Val  His Asn  Pro Thr  Ser Pro  Pro Ser  Ser Lys  Lys Ala

CCT CCA  CCT TCA  GGA GCA  TCT CAA  ACC ATC  AAA TCA  ACA ACC
Pro Pro  Pro Ser  Gly Ala  Ser Gln  Thr Ile  Lys Ser  Thr Thr

AAA CGT  TCA CCC  AAA CCA  CCA AAC  AAG AAG  AAG ACT  AAG AAA
Lys Arg  Ser Pro  Lys Pro  Pro Asn  Lys Lys  Lys Thr  Lys Lys

GTT ATA  GAA TCA  GAG GAA  ATA ACA  GAA GGT  AGG AAG  ATG ACA
Val Ile  Glu Ser  Glu Glu  Ile Thr  Glu Gly  Arg Lys  Met Thr

GAT ATA  ATC AAA  GGA GCT  TTC TTA  GAT GAA  GTA ACT  TGT AGG
Asp Ile  Ile Lys  Gly Ala  Phe Lys  Asp Glu  Val Thr  Cys Arg
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said protein being characterized by the ability to stimulate growth and development of colonies of megakaryocyte cells."

Dependent claims 2 to 4 related to specific embodiments of the MSF protein of claim 1. Independent claims 5 and 6 were directed to further MSF proteins being defined solely by structural features. Independent claims 7 and 8 related to MSF DNA sequences, and independent claims 9 and 10 to a process for producing an MSF protein and the produced protein, respectively. Independent claims 11, 12 and 13 related to, respectively, a cell, a pharmaceutical composition and a use for the MSF proteins of the invention.

IV. The appellant was summoned to oral proceedings. In a communication annexed to the summons, the board indicated the matters to be discussed at the oral proceedings, and drew attention to some issues in connection with the assessment as to whether the disclaimer in claim 1 was allowable under Article 123(2) EPC in the light of decisions G 1/03 and G 2/03 (OJ EPO 2004, 413 and 448).

V. At the oral proceedings held on 15 April 2005, the appellant submitted a new auxiliary request (claims 1 to 10) that replaced the previous auxiliary request on file.

Claim 1 of the **auxiliary request** read:

"1. An MSF protein, substantially free from association with other proteinaceous materials and contaminants

with which it is associated in natural sources, said protein comprising the amino acid sequence encoded by Exon I, Exon II, Exon III and Exon IV of Figure 1, said protein being characterized by the ability to stimulate growth and development of colonies of megakaryocyte cells."

Dependent claim 2 was, except for minor editorial amendments, substantially identical to claim 4 of the main request. Claims 3 to 10 were, except for the deletion of alternative (h) in the previous claim 7 and further minor editorial amendments, substantially identical to claims 6 to 13 of the main request.

VI. The following document is referred to in the present decision:

(D1): WO 91/02001

VII. In writing und during oral proceedings the appellant argued that the examining division had not taken into account what would be understood as disclosed in the application as filed by the notional skilled addressee. The application provided support and also specifically and deliberately disclosed a meaningful number of embodiments of the invention that involved sequences, for which Exon I was absent and explicitly not required. The notional skilled addressee of the specification would understand from the factual context and background of the invention that inclusion of Exon I was not an essential feature. By insisting on the recitation of Exon I in claim 1, the examining division was denying the applicant a meaningful portion of patent coverage for inventions actually disclosed and

supported in the specification and which had therapeutic value.

There was clear support for the subject-matter of claim 1 of the main request both in the specification as filed and in the US application 07/643,502, the priority of which was claimed in the present application. Having regard to the statements on page 21, lines 1 to 7; page 19, line 13; and page 71, lines 5 to 8, as well as to Tables I and III of the priority application, the skilled person would understand that MSF proteins comprising the amino acid sequences encoded by Exon II, Exon III, and Exon IV as sequences essential to the biological activity of the protein were part of the invention. Furthermore, in Figure 1 of the priority application a DNA fragment containing those three exons was indicated.

VIII. The appellant requested that the decision under appeal be set aside und that a patent be granted on the basis of either the main request filed on 29 October 2004 or of the auxiliary request submitted at the oral proceedings on 15 April 2005.

Reasons for the Decision

Main request

1. In view of the decision of the examining division, the sole question at issue is whether the amendments made to claim 1 are in breach of Article 123(2) EPC, ie whether claim 1 as amended contains subject-matter

which extends beyond the content of the application as filed.

2. The examining division decided that the subject-matter of the amended claim 1, in particular MSF proteins lacking a secretory leader were not disclosed in the application as filed. The board does not agree with this view. On page 11, lines 27 to 30 of the application, a class of recombinant, genetically-engineered MSFs characterized by the complete absence of **an** Exon I, ie of a sequence encoding a secretory leader and initiating methionine is disclosed, such MSFs being said to be useful for intracellular expression in bacterial cells, such as E. coli. Furthermore, a specific embodiment of this class of MSFs is disclosed on page 19, lines 2 to 8 of the application as filed, the exemplified recombinant MSF-234 protein being characterized by an amino acid sequence consisting of the amino acid sequences encoded by Exons II, III and IV. Thus, the application as filed does provide support for MSF proteins as claimed in claim 1 which lack a secretory leader and initiating methionine, so that the reasons given by the examining division to justify the refusal of the application are factually incorrect.

3. Nevertheless, the board cannot set aside the decision of the first instance without ascertaining beforehand that all features introduced into claim 1 of the main request do in fact fulfil the requirements of Article 123(2) EPC. Whereas the examining division had considered the disclaimer introduced into original claim 1 on the basis of document (D1) to be acceptable,

for the reasons stated below, the board comes to a different conclusion.

4. The disclaimer in question was introduced during the examination procedure in order to delimit claim 1 against the disclosure of document (D1). The disclaimer has no basis in the application as filed. According to decisions G 1/03 and G 2/03 (*supra*) of the Enlarged Board of Appeal, a disclaimer which has not been disclosed in the original application may be allowable under Article 123(2) EPC in order to restore novelty by delimiting a claim against state of the art under Article 54(3) and (4) EPC or against an accidental anticipation under Article 54(2) EPC. Hence the question arises whether document (D1) constitutes state of the art that allows the introduction of the disclaimer without breach of Article 123(2) EPC.

5. Document (D1) is an international application filed on 7 August 1990 and **published on 21 February 1991**, ie between the first and second priority dates claimed in the present application. The international application has been published in an official language of the EPO, and the national fee has been paid (Article 158(2) EPC). Thus, according to Article 158(1) EPC document (D1) constitutes state of the art under Article 54(3) and (4) EPC for the subject-matter of claim 1 to the extent that this subject-matter is entitled to the priority rights of the US application 07/643,502 filed on 18 January 1991 (in the following "first priority application"), and otherwise constitutes state of the art under Article 54(2) EPC.

6. In the latter case, the allowability of the disclaimer is at stake, as document (D1), which describes the purification of urinary MSF protein and the nucleotide sequences of cloned fragments of the human MSF gene as well as partial amino acid sequences derived therefrom, cannot be considered an "accidental anticipation" as defined in decisions G 1/03 and G 2/03 (*supra*). Hence, the question as to whether claim 1 is entitled to the priority of the first priority application becomes relevant to the assessment of the allowability of the disclaimer.

7. In accordance with Article 87 EPC, a European patent application is only entitled to priority in respect of the same invention as was disclosed in the previous application. The requirement of "the same invention" means that a priority can be acknowledged in respect of a claim only if the skilled person can derive the subject-matter of the claim directly and unambiguously, using common general knowledge, from the previous application as a whole (G 2/98, OJ EPO 2001, 413). If one or more priorities are claimed, the right of priority covers only those elements of the European patent application which are included in the application or applications whose priority is claimed (Article 88(3) EPC), the elements of the invention either appearing among the claims formulated in the previous application or being specifically disclosed in the documents of the previous application as a whole (Article 88(4) EPC).

8. Claim 1 at issue relates to an MSF protein which comprises the amino acid sequence encoded by Exon II, Exon III and Exon IV, and has the ability to stimulate

growth and development of colonies of megakaryocyte cells. None of the claims of the first priority application is directed specifically to a MSF protein comprising the amino acid sequence encoded by Exon II, Exon III and Exon IV, and only one MSF protein falling under present claim 1 is claimed, namely an MSF protein consisting of the amino acid sequence encoded by Exons I to VI (see claim 2, alternative (c) in the priority application).

9. Furthermore, the board judges that the first priority application **as a whole** does not allow the skilled person to derive directly and unambiguously, using common general knowledge, subject-matter included in the present claim 1, ie MSF proteins either consisting of or comprising an amino acid sequence encoded by Exon II, Exon III and Exon IV, other than an MSF protein which consists of the amino acid sequence encoded by Exons I to VI. Unlike the present European application, the first priority application does not include any statement to the effect that the amino acid sequences essential to the biological activity of the MSF proteins of the invention are encoded by Exons II, III and IV, nor is there any specific indication from which the skilled person could infer, using common general knowledge, such information. Moreover, elements of the invention included in claim 1 for which the priority is claimed, in particular MSF proteins comprising the amino acid sequence encoded by Exon II, Exon III and Exon IV linked to additional sequences other than those encoded by Exons I, V, and VI, are not disclosed.

10. In the board's view, the passages of the first priority application cited by the appellant do not provide a specific disclosure of subject-matter included in claim 1. Page 21, lines 1 to 7 of the priority application contains mere speculations about the 5' and 3' borders of the mature MSF protein. It is said that, since the amino acid sequence encoded by Exon I is not found in the mature protein, Exon II would be its 5' border, the 3' border being located before the 800th nucleotide of Table III, ie in Exon VI.

11. The passages on pages 19 and 71 as cited by the appellant and the indication below the restriction map in Figure 1 refer to the probe tryptic sequences hybridizing with the isolated 18.2 kb genomic insert, which are said to be located within Exons II, III and IV, and to the use of the predicted cDNA sequences for the identification of additional clones that contain sequences flanking said exons. Table I of the priority application contains a nucleotide sequence corresponding to Exons I to III and the intervening intron sequences, as well as partial amino acid sequences derived therefrom, and in Table III a nucleotide sequence corresponding to Exons I to VI and the encoded amino acid sequence is shown.

12. Thus, none of the cited passages of the priority application discloses an MSF protein according to claim 1, other than the protein encoded by Exons I to VI, nor do they contain a specific indication to the effect that the presence of the amino acid sequences encoded by Exons II to IV is an essential feature of the claimed MSF proteins.

13. In view of the above, the board must conclude that the subject-matter of claim 1, the emphasis being technically put on the presence of the amino acid sequence encoded by Exons II, III and IV, does not enjoy the priority of the US application 07/643,502. Thus, document (D1) constitutes prior art under Article 54(2) EPC (see point 5. above). Since the content of this document cannot be considered as an "accidental anticipation" (see point 6. above), the disclaimer in claim 1 is not allowable under Article 123(2) EPC. The main request must therefore fail.

Auxiliary request

14. Claim 1 of the auxiliary request is supported by the application as filed; see eg original claim 4, alternative (h) read in the context of the application as filed. Claims 2 to 9 find support in original claims 3 to 10, and the subject-matter of claim 10 is disclosed in the passage on page 35, lines 7 to 12 read in combination with the disclosure on page 34, lines 7 to 10 of the application as filed. Thus, the requirements of Article 123(2) EPC are met.

15. Having found the claims of the auxiliary request filed in appeal in conformity with Article 123(2) EPC, the board decides, in accordance with Article 111(1) EPC, to remit the case to the first instance in order for the further requirements of the EPC to be examined with respect to the claims of the auxiliary request (see Article 111(2) EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the first instance for further prosecution on the basis of claims 1 to 10 of the auxiliary request submitted at the oral proceedings on 15 April 2005.

The Registrar: The Chairman:

A. Wolinski L. Galligani