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**Datasheet for the decision
of 25 May 2012**

Case Number: T 2464/10 - 3.3.08

Application Number: 05077712.7

Publication Number: 1676920

IPC: C12N 15/62

Language of the proceedings: EN

Title of invention:

Anticoagulant fusion protein anchored to cell membrane

Applicant:

Imperial Innovations Limited

Headword:

Anticoagulant protein/IMPERIAL

Relevant legal provisions:

EPC Art. 76(1), 123(2)

EPC R. 28(b)(c)

Keyword:

"Main request: compliance with Articles 76(1) and 123(2)
(yes)"

Decisions cited:

G 0001/03, G 0002/10

Catchword:

Remaining subject matter test of G 0002/10 applied. The Enlarged Board of Appeal in G 0002/10 did not consider that G 0001/03 provided an exhaustive treatment of the conditions under which an undisclosed disclaimer was to be allowable. In addition to the requirements set out in G 0001/03, G 0002/10 developed the further test of whether the skilled person would, using common general knowledge, regard the remaining claimed subject matter as explicitly or implicitly, but directly and unambiguously, disclosed in the application as filed.



Case Number: T 2464/10 - 3.3.08

D E C I S I O N
of the Technical Board of Appeal 3.3.08
of 25 May 2012

Appellant: Imperial Innovations Limited
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted 26 July 2010
refusing European patent application
No. 05077712.7 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: M. Wieser
Members: T. J. H. Mennessier
D. S. Rogers

Summary of Facts and Submissions

- I. The applicant (appellant) lodged an appeal against the decision of the examining division, whereby the European patent application No. 05 077 712.7 with publication number 1 676 920 was refused. The application, entitled "*Anticoagulant fusion protein anchored to cell membrane*", was filed as a divisional application to the application No. 98 912 600.8, on which the European patent No. 1 000 161 had been granted.
- II. Basis for the refusal was the main request and the three auxiliary requests all filed with the letter of 12 May 2010.
- III. The requests were all refused for reasons of non-compliance with the requirements of Article 123(2) EPC.
- IV. Under cover of a letter of 2 December 2010, the appellant filed a statement setting out the grounds of appeal which was accompanied by a main request and six auxiliary requests. The main request was identical to the main request on which the decision under appeal was based. Oral proceedings were requested as an auxiliary measure.
- V. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA) attached to the summons to the oral proceedings, the Board expressed its preliminary and non-binding views.

VI. In reply to the Board's communication, the appellants filed further submissions with a letter dated 22 February 2012. The submissions were accompanied by a main request and a first auxiliary request. The former main request and first to sixth auxiliary requests were renumbered as the second to eighth auxiliary requests.

VII. With a letter dated 10 April 2012, the appellant submitted a new main request which was identical to the main request filed with the statement of grounds, thus corresponding to the second auxiliary request filed under cover of the appellant's letter of 22 February 2012, and withdrew its request for oral proceedings.

VIII. The main request consisted of 15 claims of which claims 1, 10, 11 and 14 read as follows:

"1. A **non-human** animal comprising a biological tissue, wherein the tissue comprises a cell, the cell expressing one or more proteins comprising a region with anticoagulant activity and a region which can anchor said protein to a cell membrane, wherein the anchor region and anticoagulant region of the protein are derived from different proteins, and wherein the anticoagulant region comprises the sequence of an anticoagulant polypeptide selected from the groups consisting of:

- i) hirudin, tissue factor pathway inhibitor, tick anticoagulant peptide and protein C activator;
- ii) functional derivatives, fragments or analogues of i) which retain anticoagulant activity;
- iii) heparin and antithrombin;

- iv) functional derivatives and fragments of iii) which retain anticoagulant activity; and
 - v) anticoagulant derivatives of thrombin."
- (emphasis added by the Board)

"10. An organ of the non-human transgenic animal of claim 8 or claim 9."

"11. A biological tissue comprising a cell, wherein the cell expresses one or more proteins as defined in claim 1, **wherein the cell is not produced using a process which involves modifying the germ line genetic identity of human beings or which involves use of a human embryo for industrial or commercial purposes.**"

(emphasis added by the Board)

"14. A method of rendering a tissue or organ suitable for transplantation, comprising expressing a protein as defined in claim 1 on the surface of endothelial cells in said tissue or organ, **wherein the method does not involve modifying the germ line genetic identity of human beings or use of a human embryo for industrial or commercial purposes.**"

(emphasis added by the Board)

Claims 2 to 9 and 15 were dependent on claim 1 while claims 12 and 13 were dependent on claim 11.

IX. With a communication faxed on 11 April 2012, the Board informed the appellant that the oral proceedings scheduled on 17 April 2012 were cancelled.

- X. The submissions made by the appellant, insofar as they are relevant to the present decision, may be summarised as follows:

Main request

Requirements of Article 123(2) EPC

Transfection with a vector was provided as an example of a method to render the biological tissue suitable for transplantation. The application as filed provided biological tissue that had been rendered suitable for transplantation via other methods. For example, the biological tissue was comprised in an animal that had been born as a transgenic animal. Generating animals via nuclear transfer was also mentioned. Such animals would not comprise cells that had themselves been "transfected" with a vector but would instead be the descendants of the cells that were transfected with the vector. Thus, the disclosure in the application as filed did not require the animal to comprise a cell that had itself been transfected with a vector, and consequently, the absence of the term "transfection" did not add matter.

There was basis in the application as filed for claiming animals without explicitly stating that they were transgenic (see in particular page 7, lines 25 to 26). Therefore, the omission of the term "transgenic" did not result in an unallowable generalisation.

The basis for claim 11 was the same as the basis for claim 1. An example of biological tissue was disclosed at page 8 as filed, lines 12 to 15, wherein biological

tissue that had been rendered suitable for transplantation by expressing one or more proteins in said biological tissue was described.

By amending claims 11 and 14 to include disclaimers based on the wording of Rules 28(b) and (c) EPC, the only subject-matter which has been disclaimed was that which was excluded from patentability for non-technical reasons.

- XI. The appellant requested that the decision under appeal be set aside and the application be remitted to the examining division for further prosecution on the basis of the main request filed under cover of the letter dated 10 April 2012.

Reasons for the Decision

Main request

Admissibility in the proceedings

1. The main request is identical to the main request filed with the statement of grounds which was itself identical to the main request on which the decision under appeal was based. Therefore, exercising the discretion conferred to it by Article 13(1) RPBA, the Board decides to admit this request, re-filed as the main request on 10 April 2012, into the proceedings.

Compliance with Article 123(2) EPC

2. The question to be answered is whether the subject-matter of each of claims 1 to 15 (see Section VIII, *supra*) is disclosed in the application as filed. The allowability of the disclaimers of claims 1, 11 and 14, and of the other aspects of the claimed subject-matter will be assessed in succession.

Disclaimers

3. Each of claims 1, 11 and 14 contains a disclaimer (as emphasised in Section VIII *supra*). The disclaimer of claim 1 ("non-human") excludes human beings in order to satisfy Article 53(a) EPC while the disclaimers of claims 11 and 14 exclude subject-matter which is not patentable under Article 53(b) EPC taken in combination with Rule 28 EPC, paragraphs b) and c).
4. The three disclaimers which exclude subject-matter not eligible for patent protection and only serve the purpose of removing specific legal obstacles do not contribute to the invention. The "non-human" disclaimer of claim 1, in a self-evident manner, and the disclaimers of claims 11 and 14, for the very reason that they reproduce the specific wording of Rule 28 EPC, do not remove more than is necessary to disclaim subject-matter excluded from patentability for non-technical reasons. In this respect, the Board disagrees with the conclusion reached by the examining division at point 1 of the decision under appeal that the disclaimers of claims 11 and 14 removed more than was necessary.

5. As such the disclaimers of the main request, while meeting the criteria as set forth in decision G 1/03 (OJ EPO 2004, 413; see the Order), do not change the subject-matter of the application as filed, within the meaning of Article 123(2) EPC.

6. In decision G 2/10 of 30 August 2011 (not yet published), it was considered that in decision G 1/03 the Enlarged Board of Appeal did not provide an exhaustive treatment of when a disclaimer violates Article 123(2) EPC and when it does not (see the first paragraph on page 34 of decision G 2/10). Applied to the facts of G 2/10, this meant that the Enlarged Board of Appeal did not consider that decision G 1/03 was exhaustive as to the conditions that needed to be fulfilled for an amendment that consisted of the introduction of an undisclosed disclaimer to be regarded as allowable under Article 123(2) EPC (see the last paragraph on page 47 of decision G 2/10).

7. The present Board interprets these remarks made in decision G 2/10 as an instruction to the Board to apply the further test developed in this decision, in addition to those set out in G 1/03, in order to carry out a full assessment of whether an undisclosed disclaimer meets the requirements of Article 123(2) EPC.

8. The further test to be applied is whether the skilled person would, using common knowledge, regard the **remaining** claimed subject-matter as explicitly or implicitly, but directly and unambiguously, disclosed in the application as filed (see point 4.5.4 on page 39 of decision G 2/10).

8.1.1 The remaining subject-matter test of G 2/10 applied to claim 1

Account being taken of the exclusion associated with the "non-human" disclaimer, claim 1 is directed to any animal, except a human, comprising a biological tissue a cell of which expresses one or more specific chimeric proteins with anticoagulant activity. The animal is referred to in the application as filed without any limitation with the indication that preferably it is a mammal, and more preferably a transgenic pig or a transgenic sheep (see page 7, lines 25 to 28 of the application as filed). The limitation of this general disclosure to non-human animals does not lead to a disclosure of any particular animal. No new technical teaching is introduced. The aforementioned passage in the description as filed provides an explicit support for non-human animals. The preparation of any non-human animal according to claim 1, which includes the introduction into a cell of a genetic construct encoding the desired chimeric anticoagulant protein by gene therapy or as the result of any other method suitable for generating transgenic animals, relies on exactly the same procedure as would be the case for a human (see from line 29 on page 7 to line 11 on page 8 of the application as filed). Thus, regarding the remaining subject-matter of claim 1, the skilled person is not presented in the application as filed with any new disclosure which goes beyond the application as originally filed.

- 8.1.2 The remaining subject-matter test applied to claims 11 and 14

The preparation of a cell which expresses one or more chimeric anticoagulant proteins, as referred to in claim 11, basically relies on the introduction of a construct encoding such a protein. It is disclosed in the application as filed only in general terms. It may or not involve a transfection (see page 7, lines 5 to 15, and page 8, lines 5 to 11, of the application as filed). The remaining subject-matter of claim 11 is limited to the situation where the cell is produced using a process which does not involve either modifying the germ line genetic identity of human beings or using a human embryo for industrial or commercial purposes.

9. A method of rendering a tissue or organ suitable for transplantation which comprises expressing a chimeric anticoagulant protein on the surface of endothelial cells of said tissue or organ, as referred to in claim 14, is disclosed in the application as filed only in general terms (see page 7, lines 12 to 15 of the application as filed). The remaining subject-matter of claim 14 is limited to the situation where the method involves no modification of the germ line genetic identity of human beings or use of a human embryo for industrial or commercial purposes.
10. The limitation imposed by the disclaimers of claims 11 and 14 serves the sole purpose of removing specific subject-matter not eligible for patent protection pursuant to Article 53(b) EPC in combination with Rule 28(b) and (c) EPC. It has no bearing on the remaining subject-matter in that no new technical

teaching is introduced and it leads neither to a disclosure directed to any particular animal nor to an intermediate generalisation that is not explicitly or implicitly disclosed in the application as filed.

11. Thus, it follows from the above, that the disclaimers of claims 1, 11 and 14 of the main request meet the requirements set out in point 1a of the Order of decision G 2/10. Accordingly, these claims satisfy Article 123(2) EPC.

Other aspects

12. The subject-matter of claims 1 to 3 and 15, each of which is directed to a non-human animal, is disclosed on pages 4, 6 and 7 of the description as filed as follows:

An animal comprising a biological tissue "according to the invention" is disclosed on page 7, lines 25 to 26. Said tissue comprises a cell in which a polynucleotide encoding an anticoagulant fusion protein has been transferred. Said cell is derived from a biological tissue, such as an organ, which has been treated by gene therapy (see the paragraph bridging pages 7 and 8), i.e. by transfecting its cells with a vector (see page 7, lines 1 to 4 and 14 to 16, together with page 6, lines 2 to 3) or is a cell of an animal born as a transgenic animal, i.e. an animal whose cells have integrated in their genome the said polynucleotide. The cell is able to express one or more different anticoagulant fusion proteins (see page 7, lines 17 to 19). Said protein comprises a region with anticoagulant activity and a region which can anchor said protein to

a membrane, wherein the anticoagulant region comprises the sequence of hirudin, a tick anticoagulant peptide (TAP), antithrombin, a tissue factor pathway inhibitor (TFPI) or the sequence of a protein C activator, along with their functional derivatives, fragments or analogues thereof (see page 4, lines 6 to 10 and lines 24 to 27). Preferably the TFPI sequence comprises the Kunitz domains I and II thereof (see page 4, lines 18 to 19).

13. The subject-matter of claim 4, which is directed to a non-human animal of any of claims 1 to 3 wherein the anchor region comprises the transmembrane sequence from a membrane protein, is disclosed in the afore-mentioned passages of pages 4, 6 and 7 taken in combination with page 4, lines 28 to 29 which specifies that the anchor region of the protein may include a transmembrane sequence from a membrane protein.

14. The subject-matter of claims 5 to 7, each of which is directed to a non-human animal of any of claims 1 to 4 wherein the tissue is a collection of cells (claim 5) or is defined as fibroblasts, a cornea, a nervous tissue, a heart, a liver or a kidney (see claim 6) or is an organ (see claim 7), is disclosed in the passages of pages 4, 6 and 7 as referred to at points 12 and 13 *supra* taken in combination with page 7, lines 22 to 24, which specifies that the term "biological tissue" includes collections of cells, tissues, and organs, more particularly, fibroblasts, a cornea, a nervous tissue, a heart, a liver, or a kidney.

15. The subject-matter of claims 8 and 9, each of which is directed to a non-human animal of any of claims 1 to 7, wherein the animal is transgenic (claim 8), in particular a transgenic pig or a transgenic sheep (claim 9), is disclosed in the passages of pages 4, 6 and 7 as referred to at points 12 to 14 *supra* taken in combination with page 8 as filed, line 5, which actually specifies that the animal is transgenic and with page 7, lines 27 to 28, which indicates that preferably the transgenic animal is a pig or a sheep.

16. The subject-matter of claim 10 and claims 11 to 13, which are directed to an organ (claim 10) of an animal of claim 8 or claim 9, and to a biological tissue (claims 11 to 13), respectively, comprising a cell expressing one or more proteins as defined in claim 1, is disclosed in the passages of pages 4, 6 and 7 as referred to at points 12 to 15 *supra*.

17. The subject-matter of claim 14, which is directed to a method of rendering a tissue or organ suitable for transplantation (see Section VIII, *supra*), is disclosed in the passages of page 4 as referred to at point 12 *supra* taken in combination with page 8, lines 12 to 17.

18. Regarding the objection raised by the examining division with respect to the omission of the terms "*transgenic*" and "*transfected*" in claim 1, the Board comments as follows:
 - 18.1 According to a first aspect, the animal is born as a transgenic animal generated by methods known in the art (see page 8, lines 5 to 11) involving in particular manipulation of the zygote, the early embryo or

embryonic stem cells. Transgenesis and cloning by nuclear transfer is a further known method. Various suitable approaches, such as microinjection of DNA or nuclear transfer, also do not involve transfection of the cells with a vector. All cells so produced, which per se have themselves not been transfected with a vector, contain incorporated in their genome the exogene polynucleotide encoding the anticoagulant fusion protein.

18.2 Alternatively, the animal is not born as a transgenic animal but has been treated by gene therapy such that a particular group of its cells which is part of a particular biological tissue or of one of its organs has been transfected with a vector, defined on page 6, lines 1 to 2, as a molecule which is capable of transferring a polynucleotide to a host cell. This vector comprises the exogene polynucleotide encoding an anticoagulant fused protein and is capable of expressing said protein. This situation is illustrated, in the sentence on page 8, lines 2 to 4, by the disclosure of the delivery of such a vector to endothelial cells in a pig to produce "*transgenic*" organs.

18.3 Therefore, the invention is firstly not limited to transgenic animals and, secondly transfection with a vector is described in the application only as an example for various different means to introduce the polynucleotide of interest into the cells. Consequently, the Board, contrary to the examining division, reaches the conclusion that neither the omission of the term "*transgenic*" (to qualify the animal) nor the omission of the term "*transfected*" (to qualify the cell) in

claim 1, amounts to an extension of the claimed subject-matter beyond the content of the application as filed.

19. It follows from the above remarks (see points 2 to 18) that the requirements of Article 123(2) EPC are met.

Compliance with Article 76(1) EPC

20. As the description of the parent application as filed is the same as that of the present divisional application as filed, the main request also complies with Article 76(1) EPC.

Conclusions

21. As all other requirements of the EPC (Articles 54, 56, 83 and 84 EPC) have not yet been assessed by the examining division, the case is remitted to the first instance for further prosecution under the provisions of Article 111(1) EPC in accordance with the appellant's request.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the examining division for further prosecution on the basis of claims 1 to 15 of the main request filed under cover of the letter of 10 April 2012.

The Registrar

The Chairman

A. Wolinski

M. Wieser