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Datasheet for the decision of 7 November 2007

Case Number: T 1593/05 - 3.3.04

Application Number: 99956908.0

Publication Number: 1137421

IPC: A61K 35/12

Language of the proceedings: EN

Title of invention:
Uses of fibroblasts or supernatants from fibroblasts for the suppression of immune responses in transplantation

Applicant:
Osiris Therapeutics, Inc.

Opponent:
-

Headword:
Fibroblasts in transplantation/OSIRIS

Relevant legal provisions:
EPC Art. 54 (1)(2), 113(1), 123(2)
RPBA Art. 11(3)

Keyword:
"All requests - novelty (no)"

Decisions cited:
T 0609/02

Catchword:
-

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Case Number: T 1593/05 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 7 November 2007

Appellant: Osiris Therapeutics, Inc.
2001 Aliceanna Street
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Representative: LOUIS, PÖHLAU, LOHRENTZ
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Decision under appeal: **Decision of the Examining Division of the European Patent Office posted 23 June 2005 refusing European patent application No. 99956908.0 pursuant to Article 97(1) EPC.**

Composition of the Board:

Chairman: U. Kinkeldey
Members: G. Alt
G. Weiss

Summary of Facts and Submissions

I. European patent application No. 99 956908.0 was filed as an international application under the PCT with the No. PCT/US 99/25963 and was published as WO 00/29001 with the title "Uses of fibroblasts or supernatants from fibroblasts for the suppression of immune responses in transplantation".

II. The examining division refused the application under Article 97(1) EPC. The refusal was based on the grounds that claims 1 and 16 of the sole request on file were not clear, that the subject-matter of claim 33 was not novel, and that the subject-matter of claims 1 to 32 did not involve an inventive step.

III. The appellant (applicant) lodged an appeal against the decision. With the statement setting out the grounds for appeal two new auxiliary requests were filed, while claim 1 of the main request corresponded to claim 1 already considered by the examining division. Claim 33 of the main request and the corresponding claims in auxiliary requests I and II had been reformulated as a second medical use claim.

IV. Claim 1 of the main request and of auxiliary requests I and II, respectively, read (amended parts have been highlighted by the board):

"1. Use of fibroblasts or a supernatant from a fibroblast culture for the manufacture of a pharmaceutical for treating a recipient to reduce an immune response in the recipient to a transplanted donor tissue.

1. Use of **isolated** fibroblasts or a supernatant from an **isolated** fibroblast culture for the manufacture of a pharmaceutical for treating a recipient to reduce an immune response in the recipient to a transplanted donor tissue.

1. Use of **isolated** fibroblasts or a supernatant from an **isolated** fibroblast culture for the manufacture of a pharmaceutical for treating a recipient to reduce an immune response in the recipient to a transplanted donor tissue, **wherein the fibroblasts are allogeneic to both the donor of the transplant and the recipient**."

V. In the statement setting out the grounds for appeal the appellant argued against the decision of the examining division by giving reasons as to why the subject-matter of claim 33 (and of the corresponding claims in auxiliary requests I and II) was novel and as to why the subject-matter of all claims involved an inventive step.

The appellant requested that the decision of the examining division be set aside and that a patent be granted either according to the main request or according to either of auxiliary requests I or II. Oral proceedings were also requested.

VI. The appellant was summoned to oral proceedings, but informed the board that he would not take part.

VII. The board issued a communication informing the appellant inter alia of its preliminary view that the subject-matter of claim 1 of all requests was

considered not to be novel over the disclosure in document D1.

VIII. The appellant did not reply to the board's communication.

IX. Oral proceedings were held in the absence of the appellant. At the end of the oral proceedings the decision was announced.

Reasons for the Decision

Article 113(1) EPC

1. The appellant had been duly summoned, but was not present at the oral proceedings. The board could take a decision at the oral proceedings without violating the appellant's right to be heard as laid down in Article 113(1) EPC in view of Article 11(3) of the Rules of Procedure of the Boards of Appeal (1973), adopted by decision of the Presidium of 28 October 2002 and approved by decision of the Administrative Council of 12 December 2002 (OJ EPO 2003, 61), stating that the board is not obliged to delay any step in the proceedings, including its decision, by reason only of the absence at the oral proceedings of any party duly summoned who may then be treated as relying only on its written case.

Main request

Articles 54 (1)(2) EPC

2. According to one of its alternative embodiments, the subject-matter of claim 1 relates to the use of fibroblasts for the manufacture of a pharmaceutical for treating a recipient to reduce an immune response in the recipient to a transplanted donor tissue.

3. Document D1 relates to a method for minimizing rejection of transplanted cells by using immunoprivileged cells. It is stated on page 4, lines 13 to 15 of document D1: "In the preferred embodiment described herein, cells forming cartilage such as chondrocytes or fibroblasts are used to form an immunoprotective barrier". Thus, document D1 discloses the use of fibroblasts for the same application as in the present application.

For that purpose the fibroblasts are dissociated by treatment using collagenase or trypsin, seeded onto a fibrous matrix or seeded onto the bottom of a culture dish and grown under standard conditions until a layer of the desired thickness is obtained (pages 4 and 5 of document D1). Thus, document D1 discloses that the cells are manufactured into a pharmaceutical before they are used to avoid rejection of transplanted tissue.

Hence, document D1 discloses the subject-matter of claim 1.

4. According to established case law (Case law of the boards of appeal of the EPO, 5th edition 2006, I.C.2.12) a further requirement to be fulfilled before a disclosure can be considered as novelty-destroying is that its teaching is reproducible, i.e. that the disclosure in the prior art is such that it can be carried out. The need for an enabling disclosure in the prior art is in conformity with the requirement expressed in Article 83 EPC that patent applications or patents have to disclose the invention in a manner sufficiently clear and complete for it to be carried out by a person skilled in the art. Given that the requirement of sufficiency of disclosure is the same for the prior art and for a patent application or a patent, it is also necessary that the same standard is applied in deciding whether or not this requirement is fulfilled.

5. Claim 1 is directed to a so-called second medical use. For the acceptance of a sufficient disclosure of a therapeutic application, the application or the patent and/or common general knowledge must provide some information rendering it technically plausible for the skilled person that the claimed compounds can be applied for the claimed therapeutic use (T 609/02 of 27 October 2004, point 9 of the reasons).

5.1 The analysis of document D1 under this point of view reveals the following:

Example 1 reports the in vitro culture of an immunoprotective tissue - in this case chondrocytes -, how the donor tissue alone - in this case islets of Langerhans - and how both together, the

immunoprotective tissue and transplant cells, are worked up for transplantation: the tissue to be transplanted is "wrapped" in a monolayer of cells. Examples 2 and 3 show the functional survival of the transplant tissue in vitro and in vivo, i.e. insulin production is detected. Although these examples relate to chondrocytes they are, in the board's view, equally suited to demonstrate the usefulness of fibroblasts in the claimed method. The gist of the invention set out in document D1 is the use of immunoprivileged tissue to protect the transplant tissue from an attack by the immune system. Fibroblasts are, as well as chondrocytes, known to have such an immunoprivileged status (see document D1, page 4, lines 9 to 15). Hence, the board is convinced that according to the standard established by case law for the acceptance of sufficiency of disclosure of a claim directed to second medical use, the relevant subject-matter identified in document D1 is disclosed in an enabling way.

6. The board therefore concludes that the subject-matter of claim 1 lacks novelty in view of the teaching in document D1. Consequently, the requirements of Articles 54 (1)(2) EPC are not fulfilled.

Auxiliary request I

Articles 54 (1)(2) and 123(2) EPC

7. Compared to claim 1 of the main request, the fibroblasts and the supernatant are further characterized in claim 1 of auxiliary request I in that they are "isolated" and that the supernatant is from an "isolated" fibroblast culture. The question as to the

meaning of the term "isolated" arises for the following reason:

7.1 For the board there is a difference between the **teaching** in document D1 and that derivable from the **description** of the present application. While in document D1 it is contemplated to form a layer of fibroblasts which is then used as a whole to wrap the tissue to be transplanted, the fibroblasts according to the application appear to be used in a dissociated way. It is stated on page 3, lines 1 to 4: "To this objective, the present invention provides a method for reducing or ameliorating an immune response by providing to the recipient donor tissue or organ that is perfused with or includes fibroblasts."

7.2 Thus, with a view to establishing whether or not the above-mentioned distinction may be reflected by present claim 1, the board has considered the meaning of the newly added term "isolated".

8. The interpretation of terms in a claim and the meaning of the claim as a whole is made from the perspective of the skilled person reading the claim with his/her common general knowledge. Having regard to this criterion, the skilled person would, in the board's view, understand that in the context of the claim, i.e. in relation to cells, the term "isolated" signifies "taken out of the context in which the cells naturally occur" or, in other words, isolated from the body. Hence, since the skilled person would have per se no doubt about this meaning, any differing interpretation of the term by reference to the description is not appropriate.

9. The examination of the requirements of Articles 123(2) and 54 (1)(2) EPC on the basis of this interpretation reveals the following:

9.1 It is apparent from the application document as originally filed, as a whole, that the fibroblasts are taken from the body before they are used as such in the transplant situation. It is for example stated on page 3 that the recipient tissue or organ is perfused with the fibroblasts or that the fibroblasts are administered to the recipient of the donor tissue. The disclosure of the use of culture supernatant from a fibroblast culture already implies that the fibroblasts had been isolated because otherwise they could not be propagated in vitro to prepare a culture in order to obtain culture supernatant which is then used. Therefore, the requirements of Article 123(2) EPC are fulfilled.

9.2 As to the novelty of the subject-matter of claim 1, it is disclosed in document D1 that for the application in the method disclosed in that document fibroblasts are obtained by biopsy or from established cell lines.

9.3 For subject-matter to be novelty-destroying it must be clearly and unambiguously derivable from the prior art. This is true for explicit but also for implicit information. Implicit information is information which is not explicitly spelt out for example in a document but which is nevertheless part of it because it comes to the skilled person's mind when reading what is explicitly said.

The skilled person knows that cell lines are made from isolated cells, i.e. the cells of a cell line are isolated and also that the effect of a biopsy is that cells are removed from the body.

Consequently, although it is not explicitly stated, in the board's view, the skilled person derives implicitly from document D1 that isolated fibroblasts are used in the method disclosed in the document.

10. Since the remaining features of claim 1 are disclosed in document D1 too (see point 3 above) and since the teaching of document D1 relevant here is reproducible for the reasons given in point 5.1 above, the subject-matter of claim 1 is considered not to be novel. Consequently, the requirements of Article 54 EPC are not fulfilled.

Auxiliary request II

Article 123(2) EPC

11. Compared to claim 1 of auxiliary request I, the expression "wherein the fibroblasts are allogeneic to both the donor of the transplant and the recipient" has been added at the end of the claim. In view of the finding that claim 1 of auxiliary request I complies with the requirements of Article 123(2) EPC and given that the expression cited above can be found in claim 5 as originally filed, the board concludes that claim 1 of auxiliary request II also complies with the requirements of Article 123(2) EPC.

Articles 54 (1)(2) EPC

12. The term "allogeneic" used according to the feature newly added to claim 1 has a generally recognized meaning for a skilled person in the field of immunology. It generally describes the relationship between tissues, and specifically in a transplant situation it means for example that donor tissue is genetically non-identical to the recipient tissue. Allogeneic tissue therefore stimulates the recipient's immune cells to react with the allogeneic cells. The term is used in this meaning in the application. It is for example explained on page 2, lines 28 to 32 of the application: "The fibroblasts can be either autologous or allogeneic to the recipient. The allogeneic fibroblasts can also be obtained from a source other than the donor [...]."

Accordingly, the feature in claim 1 "wherein the fibroblasts are allogeneic to both the donor of the transplant and the recipient" means, as stated on page 2 of the application, that the fibroblasts "need not be matched either to the donor type or the recipient type" or, in other words, as set out on page 3 of the application, that the fibroblasts can be obtained from a "third party".

13. The fibroblasts suited for the use according to document D1 are characterised as follows on page 4, lines 16 to 18:

"Cells are typically obtained by biopsy, most preferably from the patient into which the cells are to be implanted, although they can also be obtained from

established cell lines or related individuals." (emphasis added by the board).

The question arises whether the skilled person would consider this disclosure, especially in view of the reference to an "established cell line", as the disclosure of cells allogeneic to both the donor and the recipient.

13.1 The term "established cell lines" is not defined in document D1. Therefore, according to the general principle for the interpretation of documents in the evaluation of novelty, its meaning is determined by the understanding of the skilled person in view of his/her common general knowledge at the priority date of the patent application (Case law of the boards of appeal of the EPO, 5th edition 2006, I.C.2).

13.2 The relevant common knowledge is in the board's view the following:

Cells derived from a body and which are cultivated in vitro are called a "primary cell culture". After its first subculture the primary culture becomes a "cell line", this expression being a common technical term. Cell lines may normally only be propagated for a limited number of cell generations before the cells die. Either spontaneously or by chemical or viral induction cell lines may alter this property in culture and may acquire the ability to grow continuously. Many passages of the cells, usually at least 70, are necessary before a cell line transforms into a "continuous" cell line. It takes further passages before it is definitely established that a continuous

cell line consists of a single cell type that has the potential for unlimited subcultivation and that the cells are genetically stable or, in other words, that a cell line has become an "established" cell line. In view of his/her common general knowledge as described above, the skilled person is also aware of the fact that the generation of an established cell line is a difficult and time-consuming task and may not always be successful. It is also part of the skilled person's common general knowledge that once an established cell line has been generated, it may be deposited with a culture deposit organization such as the American Type Culture Collection (ATCC) or it may be commercially available and thus at the disposal of other parties.

14. In the light of this common general knowledge, especially as regards the difficulty of creating an established cell line, in the board's view, the skilled person would have understood that the term "established cell line" in document D1 refers to an already existing cell line which can, for example, be commercially purchased. Since the cells of such a cell line are inevitably not specifically adapted to a given transplantation situation, the term "established cell line" would necessarily have also conveyed to the skilled person the information that in one embodiment the cells to be used in the method according to document D1 are derived from a source which must be different from the donor and the recipient. Thus, in view of the information conveyed by the term "established cell line" and in view of the disclosure in document D1 of fibroblasts as suitable cells (see point 3 above), the skilled person would, in the board's view, have clearly and unambiguously derived

from document D1 that fibroblasts which neither match the donor nor the recipient may be used in the method disclosed in document D1. Hence, document D1 is considered to disclose the feature according to claim 1 "wherein the fibroblasts are allogeneic to both the donor of the transplant and the recipient.

15. In view of the fact that the remaining features of claim 1 are also disclosed in document D1 (see points 3, 7.2, 8., 9.2 and 9.3 above) and since the teaching of document D1 relevant here is reproducible for the reasons given in point 5.1 above, document D1 is considered to anticipate the subject-matter of claim 1. Consequently, the requirements of Articles 54 (1)(2) EPC are not fulfilled.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chair:

D. Meyfarth U. Kinkeldey