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**Datasheet for the decision
of 4 September 2009**

Case Number: T 0329/06 - 3.3.04

Application Number: 99913967.8

Publication Number: 1064353

IPC: C12M 3/04

Language of the proceedings: EN

Title of invention:

Vascularized perfused microtissue/micro-organ arrays

Patentee:

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

Opponent:

Forschungszentrum Karlsruhe GmbH

Headword:

Perfused microtissue/MIT

Relevant legal provisions:

EPC Art. 53(a), 123(2), 54, 111

Relevant legal provisions (EPC 1973):

-

Keyword:

"New main request - added subject-matter (no), disclaimer allowable for non-technical reasons, novelty (yes), remittal (yes)"

Decisions cited:

-

Catchword:

-



Case Number: T 0329/06 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 4 September 2009

Appellant: MASSACHUSETTS INSTITUTE OF TECHNOLOGY
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Decision under appeal: Decision of the Opposition Division of the
European Patent Office posted 5 January 2006
revoking European patent No. 1064353 pursuant
to Article 102(1) EPC 1973.

Composition of the Board:

Chairman: U. Kinkeldey
Members: M. Wieser
R. Moufang

Summary of Facts and Submissions

- I. The appeal was lodged by the Patent Proprietor (Appellant) against the decision of the Opposition Division, whereby the European patent No. 1 064 353 was revoked pursuant to Article 102(1) EPC 1973.
- II. The patent has been opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC).

The Opposition Division, in accordance with Article 114(1) EPC, has introduced Article 53(a) EPC 1973 as a new ground of opposition, and has decided that the subject-matter of claim 1 of the main request before them, claims 1 to 29 as granted, was excluded from patentability under Article 53(a) EPC 1973 and Rule 23d(c) EPC 1973.

Moreover, they decided that the subject-matter of claim 1 of each of auxiliary requests 1, 2 and 4 before them was not novel in the light of the disclosure in either document (D1) or (D3), and that the subject-matter of claim 1 of auxiliary request 3 contravened the requirements of Article 123(3) EPC.

- III. The Board expressed their preliminary opinion in a communication dated 31 March 2009.

Oral proceedings were held on 4 September 2009.

- IV. The Appellant requested to set aside the decision under appeal and to maintain the patent on the basis of

claims 1 to 29 of the new main request filed at the oral proceedings.

Should the Board recognise novelty of the subject-matter of the claims of the new main request, the case should be remitted to the department of first instance for further prosecution.

The Opponent (Respondent) requested that the appeal be dismissed.

V. The claims of the new main request differ from the claims as granted only in claims 1 and 25 which read as follows:

"1. An apparatus comprising

a) a matrix formed of a solid support made from an inert material comprising one or more channels,

b) cells within the channels of the matrix provided that the cells are not human embryonic stem cells,

c) means for perfusing the cells within the channels using cross-flow, and

d) means for detecting changes in the cells or in compounds exposed to the cells,

wherein the channels are open at both ends and run through the matrix wherein the size and orientation of the channels in the matrix allow perfusion of the cells with nutrients and oxygen sufficient to maintain the viability of the cells.

25. A method for propagating stem cells other than human embryonic stem cells comprising culturing the stem cells in the apparatus of any of claims 1-22."

Claims 2 to 22 refer to preferred embodiments of the apparatus according to claim 1; claims 23 and 24 refer to a method using the claimed apparatus and claims 26 to 29 relate to preferred embodiments of the method of claim 25. All these claims are identical to the corresponding claims as granted.

VI. The present decision refers to the following documents:

- (1) K.F. Weibezahn et al., KFK-Nachrichten, vol. 26, no. 1, 1994, pages 10 to 14
- (2) K.F. Weibezahn et al., 4th International Conference on Micro Electro, Opto, Mechanical Systems and Components, Berlin 19 to 21 October 1994, pages 873 to 878
- (3) WO 93/07258

VII. The submissions made by the Appellant may be summarised as follows:

The disclaimer introduced into claims 1 and 25 was allowable according to the established case law of the Boards of Appeal. As a result of this disclaimer the objection raised by the Opposition Division under Article 53(a) EPC and Rule 28(c) EPC (Rule 23d(c) EPC 1973) was no longer relevant.

The device disclosed in document (1), which was also referred to in documents (2) and (3), did not contain means for perfusing cells within the channels using cross-flow and was therefore not novelty destroying for the subject-matter of claims 1 to 29 of the new main request.

The decision under appeal did not consider the question of inventive step. Therefore, should the Board decide that the claims of the main request were directed to novel subject-matter, the case had to be remitted to the department of first instance for further prosecution.

VIII. The submissions made by the Respondent may be summarised as follows:

Document (1) disclosed a device wherein the flow around the tissue layers cultured therein was controlled by computer means. Thereby the problem of controlled in- and outflow had been solved. Document (1), although not explicitly mentioning perfusion and cross-flow, described these processes in unequivocal and unmistakable way and anticipated therefore the claimed subject-matter contrary to the requirements of Article 54 EPC.

The Appellant, already during the opposition procedure before the department of first instance, had ample opportunity to file amended claims in order to overcome the objections under Article 54 EPC raised by the Opposition Division and by doing so to provide a basis for the Opposition Division to judge the claimed subject-matter under Article 56 EPC. The Board should

thus restrain from remitting the case to the department of first instance for further prosecution but rather decide all issues of the present case on its own.

Reasons for the decision

Amendments - Articles 123(2), 123(3) and 84 EPC

1. Claim 1 of the new main request differs from claim 1 according to the printed patent specification. An obvious typographical mistake (replacement of "non" by "run") has been corrected and the definite article "the" has been introduced before the word "size". These amendments have already been carried out during the opposition procedure and were found by the Opposition Division to be allowable (see point (1) of the appealed decision).

None of the parties commented on these amendments.

2. Moreover claim 1, in addition to claim 1 as granted, contains a disclaimer in its section b) wherein it is "provided that the cells are not human embryonic stem cells". In a similar way the subject-matter of claim 25 has been restricted to a method wherein the propagated stem cells are "other than human embryonic stem cells".
3. The Enlarged Board of Appeal in its decision G 2/06 (OJ EPO 2009, 306) has decided that Rule 28(c) EPC (formerly Rule 23d(c) EPC 1973) forbids the patenting of claims directed to products which - as described in the respective application - at the filing date could be prepared exclusively by a method which necessarily

involved the destruction of **human** embryos. In the view of the present Board it can be deduced from this decision that methods involving such destruction are also to be regarded as not patentable.

4. Claim 1 as granted was directed to an apparatus comprising **cells** within the channels of a matrix. Claim 25 as granted was directed to a method for propagating **stem cells**. This clearly included **embryonic stem cells** of **human** origin. In the passage bridging pages 31 and 32 of the application as published it is stated that embryonic stem cells (ES cells) are obtained from embryos at a very early stage.

Since in the application as published the only teaching of how to prepare embryonic stem cells, including human embryonic stem cells, is the use (involving their destruction) of embryos at a very early stage, it is concluded that at the filing date of the application underlying the patent in suit **human embryonic stem cells** could be prepared exclusively by a method which necessarily involved the destruction of human embryos. This has the result that the invention of claims 1 and 25 as granted falls under the prohibition of Article 53(a) EPC taken in combination with Rule 28(c) EPC (cf. also G 2/06 (see *supra*), in particular point 29 of the reasons).

5. Neither the disclaimer introduced by the Appellant into claims 1 and 25 of the new main request in order to avoid an objection under Article 53(a) EPC, nor the subject-matter excluded by it has a basis in the application as published.

6. The Enlarged Board of Appeal in decision G 1/03 (OJ EPO 2004, 413) was concerned with the question whether an amendment to a claim by the introduction of a disclaimer is unallowable under Article 123(2) EPC for the sole reason that neither the disclaimer nor the subject-matter excluded by it from the scope of the claim have a basis in the application as filed.

The Enlarged Board of Appeal came to the conclusion that a claim containing a disclaimer may not be refused under Article 123(2) EPC for this sole reason, but that such claim, for instance, may be allowable to disclaim subject-matter which, under Article 53(a) EPC, is excluded from patentability for non-technical reasons (see decision G 1/03, *supra*; point (2.4.1)).

7. In agreement with decision G 1/03 (*supra*) the amended claims 1 and 25, both containing a disclaimer not removing more than what is necessary to disclaim subject-matter falling under the prohibition of Article 53(a) EPC in combination with Rule 28(c) EPC (cf also decision G 2/06, *supra*), meet the requirements of Article 123(2) EPC.

8. As the introduction of a disclaimer by way of its nature restricts the scope of protection conferred by a claim, the requirements of Article 123(3) EPC are met.

As required by decision G 1/03 (*supra*; point 2.4 of the Order) claims 1 and 25 meet the requirements of clarity and conciseness of Article 84 EPC.

Against the claims as amended by the introduction of the disclaimers no objections under Article 53(a) EPC

and Rule 28(c) EPC (formerly Rule 23d(c) EPC) have been raised.

Novelty - Article 54 EPC

9. Claim 1 refers to an apparatus comprising a matrix having one or more channels running through it. The apparatus further comprises cells within said channels and means for the perfusion of these cells with oxygen and nutrients using cross-flow, sufficient to maintain the viability of the cells.

10. Document (1) discloses three-dimensional cell-cultures in a so-called tissue-model (Gewebemodell). The model consists of cells contained in a specific microstructure. This structure is built of a multitude of micro-containers with a porous bottom which act as a support for the cells to be cultured. However, also micro-containers without porous bottom are disclosed (figure 3). The structures with the cell-tissue layers are introduced into a specially shaped supply vessel, which is shown in figure 2. In this supply vessel the structures are in contact with two isolated medium reservoirs, one above and one below the microstructure. The flow of the corresponding media around the tissue layers is under computer control. In this manner, the outlined problem of a controlled in- and outlet is technically solved and, in addition, the prerequisites are created for the construction and the variation of directed metabolic concentration gradients over the cell layer (page 11, left paragraph).

11. "Perfusion" designates the process of flow of a liquid through a hollow entity, in the present case the

channels running through the matrix of the claimed apparatus. The direction of flow of the liquid through or across the channels is designated as "cross-flow". These definitions have been agreed on by both parties.

12. The Appellant argued that, as a matter of elementary physics, a liquid will not flow passively. Thus a force needs to be exerted upon it in order for it to flow. The "means for perfusing the cells" according to point c) of claim 1 have to create a pressure difference between the two independent tangential perfusion circuits such that flow of liquid occurs from one space to the other. The channels comprising cells are thereby perfused in cross-flow mode.

In the absence of such means, the resistance of the tissue layer would prevent the liquid to flow from one space to the other. Consequently, in the device disclosed in figure 2 of document (1), not containing means for perfusing the cells, medium 1 entering the apparatus on the top of the left side would leave it on the top right side and medium 2 entering on the bottom of the left side would leave it on the bottom right side. Thus no perfusion by cross-flow of the cells contained in the micro-containers will take place. However, in case the two media contain specific molecules in different concentrations, a directed metabolic concentration gradient will be created across the cell layer by molecular diffusion, which is a net transport of molecules from a region of higher concentration to one of lower concentration by random molecular motion. Contrary to a flow process, like perfusion, diffusion does not require any additional energy supply.

13. The Respondent argued that, although the processes of cross-flow and perfusion are not literally disclosed in document (1), they nevertheless are described therein in an unequivocal and unmistakable manner. The apparatus shown in figure 2 of document (1) when run with two different media, one above and one below the tissue structures, would almost automatically cause perfusion of the media through the tissue in cross-flow mode. This would be the case all the more so in a device wherein the containers do not contain any bottom and where at the beginning of the culturing process not the entire micro-containers are filled with cell tissue. Moreover, in such embodiment the flow resistance of the tissue structure within the micro-containers would be much lower than described by the Appellant.
14. The patent discloses the working mode of the claimed apparatus in figure 2. Figure 2B shows the apparatus operating in cross-flow mode. Perfusion through the arrays is driven by the pressure differential between two independent tangential perfusion circuits, one on either side of the scaffold (page 7, column 12, lines 24 to 29). Figure 2C shows the apparatus in the forced flow mode, which the Board considers to be a special case of cross-flow mode, in which the entire flow from a single perfusion circuit is diverted through the array (page 7, column 12, lines 32 to 35).

The apparatus according to document (1), which identically is the subject of documents (2) and (3), does not explicitly refer to means for perfusing the cells within the channels, as required by claim 1, point c), but mentions a computer controlled inlet and

outlet mechanism. Although it might be possible to configure such means so that they create a pressure difference between two independent tangential perfusion circuits such that flow of liquid occurs from one space to the other, thereby perfusing cells contained in micro-containers or channels situated between the two spaces, this is not disclosed in document (1) or in any other prior art document on file.

The arguments of the Respondent (see point (12) above) that cross-flow and perfusion, although not literally disclosed in document (1), are described therein in an unequivocal and unmistakable manner, seem to be based on the assumption that these processes would proceed in an apparatus as described in document (1) when properly adapted to the requirements described in the patent in suit.

15. According to the case law of the Boards of Appeal it is not justifiable to decide whether a document is prejudicial to novelty on the basis of probability. In order to decide that the subject-matter of a claim lacks novelty, the department concerned, having taken all facts and arguments put forward during the proceedings into consideration, has to be sure about the facts justifying a decision that a given subject-matter is not novel (cf decision T 464/94 of 21 May 1997; point (16) of the reasons).

16. In the light of the facts and arguments presented by the parties, this Board is not convinced that the apparatus disclosed in documents (1), (2) or (3) contains means for perfusing the cells within the

channels as required in point c) of claim 1 of Appellant's new main request.

The apparatus of claim 1 and of dependent claims 2 to 22 is therefore novel within the meaning of Article 54 EPC. The same applies to claims 23 to 29, referring to methods using said apparatus.

Remittal - Article 111 EPC

17. According to Article 111(1) EPC the Board of Appeal may either exercise any power within the competence of the department which was responsible for the decision appealed or remit the case to the department for further prosecution. Remittal to the department of first instance is at the discretion of the Board.

Although Article 111(1) EPC does not guarantee an absolute right to have all the issues in the case considered by two instances, it is well recognised that any party should preferably be given the opportunity to have two readings of the important elements of the case. The essential function of appeal proceedings is to consider whether the decision which has been issued by the first instance department is correct. Hence, a case is normally remitted, if essential questions regarding the patentability of the claimed subject-matter have not yet been examined and decided by the department of first instance (cf decision T 1091/00, 2 July 2002).

In particular, remittal is taken into consideration by the boards in cases where a first instance department issues a decision solely upon one particular issue

which is decisive for the case against a party and leaves other essential issues outstanding. If, following appeal proceedings, the appeal on the particular issue is allowed, the case is normally remitted to the first instance department for consideration of the undecided issues (cf decision T 1091/00, supra).

18. The Opposition Division in the decision under appeal has only dealt with the requirements of Article 53(a), 54 and 123(3) EPC. Thus, inventive step, a fundamental requirement for the grant or maintenance of a patent, has not yet been examined by the department of first instance. Consequently, the examination was not carried out in a way to put the Board in a position to decide now, on the basis of a comprehensive examination of the first instance, whether or not this substantial requirement of the EPC is met by the patent, which, considering procedural economy, would be the most preferable situation.

19. The Respondent has argued that the case should not be remitted as the Appellant had ample opportunity during the opposition procedure to file an amended set of claims, which would have met the requirements of Article 54 EPC and which would have set the Opposition Division in a position where it could have examined the requirements of Article 56 EPC.

The Board does not agree. If the Appellant would have filed an amended, which in the present case would have been a restricted set of claims, which would probably have met the requirements of Article 54 EPC, this would have allowed the department of first instance to

examine the requirements of Article 56 EPC with regard to this restricted set of claims. However, this would have had the consequence that the Appellant had no possibility to have the subject-matter of the claims of his main request examined by the department of first instance with regard to the requirements of Article 56 EPC.

The Board in the present case cannot see any sign of deliberate procedural delay by Appellant. Therefore, in line with the decision T 1091/00 (*supra*), although being aware that this could lead to a considerable delay of the procedure, the Board considers it to be justified and appropriate to allow the set of claims of the new main request to be examined by two instances, and decides therefore, at its discretion under Article 111(1) EPC, to remit the case to the first instance for further prosecution.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.
2. The case is remitted to the department of first instance for further prosecution on the basis of the new main request filed at the oral proceedings.

Registrar:

Chair:

P. Cremona

U. Kinkeldey