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Datasheet for the decision of 4 February 2020

Case Number: T 2162/15 - 3.3.01

Application Number: 08754571.1

Publication Number: 2146728

IPC: A61K35/22, C12N5/08, C12N5/06

Language of the proceedings: EN

Title of invention:
PROGENITOR CELLS FROM URINE AND METHODS FOR USING THE SAME

Applicant:
Wake Forest University Health Sciences

Headword:
Urine progenitor cells/WAKE FOREST UNIVERSITY

Relevant legal provisions:
EPC R. 115(2)
RPBA Art. 15(3), 12(4), 13
EPC Art. 123(2)

Keyword:
Oral proceedings - held in absence of appellant
Amendments - allowable (no)

Decisions cited:
G 0010/93

Catchword:

Europäisches Patentamt
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Beschwerdekammern

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Case Number: T 2162/15 - 3.3.01

D E C I S I O N
of Technical Board of Appeal 3.3.01
of 4 February 2020

Appellant: (Applicant)	Wake Forest University Health Sciences 391 Technology Way, Suite 199 Winston-Salem NC 27101 (US)
Representative:	Gibbs, Richard Marks & Clerk LLP Aurora 120 Bothwell Street Glasgow G2 7JS (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 10 June 2015 refusing European patent application No. 08754571.1 pursuant to Article 97(2) EPC**

Composition of the Board:

Chairman	A. Lindner
Members:	T. Sommerfeld
	L. Bühler

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division in which European patent application No. 08754571.1, based on an international application published as WO 2008/153685, was refused under Article 97(2) EPC. The examining division decided that neither the main request nor the auxiliary request fulfilled the requirements of Articles 56 and 84 EPC.

II. The applicant (hereinafter the appellant) requested that the decision be set aside and that a patent be granted according to the main request or, alternatively, according to the first, second or third auxiliary request, all filed with the statement of grounds of appeal dated 20 October 2015, or, alternatively, that the application be remitted to the examining division for further prosecution.

III. In a communication sent pursuant to Article 15(1) RPBA 2007 in preparation for oral proceedings, the board expressed a detailed opinion as regards Articles 123(2) and 56 EPC.

IV. By letter dated 3 January 2020, the appellant replied to the board's communication and submitted fourth to tenth auxiliary requests, as well as three new documents designated A1 to A3. In a further letter, dated 30 January 2020, the appellant announced that it would not attend the oral proceedings.

V. The oral proceedings took place as scheduled and in the absence of the appellant. At the end of the oral proceedings the chairman announced the board's decision.

VI. The **main request** comprises 13 claims, claim 1 reading as follows:

"1. A method for selectively differentiating urine progenitor cells, comprising:
(a) isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises morphology based selection and/or CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and/or CD44 cell marker selection; and
(b) culturing the isolated urine progenitor cells in a selective medium, wherein said selective medium promotes selective differentiation of said progenitor cells into urothelial cells, smooth muscle cells, endothelial cells or interstitial cells."

Claim 1 of the **first auxiliary request** differs from claim 1 of the main request in that the alternatives "urothelial cells" and "smooth muscle cells" in step (b) have been deleted.

Claim 1 of the **second auxiliary request** differs from claim 1 of the first auxiliary request in that the following amendments have been made to step (a):

"1. ...
(a) isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises detection of the expression of at least one marker selected from the group consisting of ~~morphology based selection and/or~~ CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and/or CD44 ~~cell marker selection~~; and ..."

Claim 1 of the **third auxiliary request** differs from claim 1 of the first auxiliary request in that the following amendments have been made to step (a):

"1. ...
(a) isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises selecting cells which express one or more of ~~morphology based selection and/or~~ CD117 (C-kit)~~;~~ SSEA-4~~;~~ CD105~~;~~ CD73~~;~~ CD90~~;~~ CD133 and~~/or~~ CD44 ~~cell marker selection~~ and/or lack expression of one or more of CD31, CD34 and CD45; and ..."

Claim 1 of the **fourth auxiliary request** differs from claim 1 of the main request as shown:

"1. A method for selectively differentiating urine progenitor cells, comprising:
(a) isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises morphology based selection and/or CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and/or CD44 cell marker selection, wherein the urine progenitor cells have the potential to differentiate into urothelial cells, smooth muscle cells, endothelial cells and interstitial cells; and
(b) culturing the isolated urine progenitor cells ~~in~~ with a selective medium~~, wherein said selective medium promotes selective~~ that supports the growth and differentiation of ~~said~~ the progenitor cells into urothelial cells, smooth muscle cells, endothelial cells or interstitial cells."

The same amendments were also made in claim 1 of the **fifth auxiliary request**, where step (b) was further amended by restricting it to endothelial cells or interstitial cells (as in the first auxiliary request).

Claim 1 of the **sixth auxiliary request** differs from claim 1 of the main request as shown:

"1. A method for ~~selectively~~ differentiating urine progenitor cells into endothelial or interstitial cells, said method comprising:

producing a culture of urine progenitor cells by providing a urine sample and selecting urine progenitor cells from said urine sample by:

(a) selecting cells of interest based upon ~~isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises~~ morphology ~~based selection~~; or

(b) ~~and/or~~ selecting cells expressing CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and/or CD44 ~~cell marker selection~~; and

~~(b)~~ culturing the ~~isolated~~ selected urine progenitor cells ~~in~~ with a selective medium~~, wherein said selective medium promotes selective~~ that supports growth and differentiation of said urine progenitor cells into ~~urothelial cells, smooth muscle cells,~~ endothelial cells or interstitial cells."

Claim 1 of the **seventh auxiliary request** differs from claim 1 of the main request in that step (b) has been amended as shown:

"1. ...

(b) culturing the isolated urine progenitor cells in a ~~selective medium, wherein said selective medium~~ particular growing environment that promotes the

selective differentiation of ~~said~~ the urine progenitor cells into ~~urothelial cells, smooth muscle cells,~~ endothelial cells or interstitial cells."

Claim 1 of the **eighth auxiliary request** differs from claim 1 of the main request in that step (b) has been amended as shown:

"1. ...
(b) ~~culturing~~ differentiating the isolated urine progenitor cells ~~in a selective medium, wherein said selective medium promotes selective differentiation of said progenitor cells~~ into ~~urothelial cells, smooth muscle cells,~~ endothelial cells or interstitial cells."

Claim 1 of the **ninth auxiliary request** essentially differs from claim 1 of the sixth auxiliary request in that the alternative of morphology-based selection has been deleted:

"1. ...
~~(a) selecting cells of interest based upon morphology; or (b)~~ selecting cells expressing CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and~~/or~~ CD44; and
culturing the selected urine progenitor cells with a selective medium that supports growth and differentiation of said urine progenitor cells into endothelial cells or interstitial cells."

Claim 1 of the **tenth auxiliary request** differs from claim 1 of the fourth auxiliary request as shown:

"1. A method for selectively differentiating urine progenitor cells, comprising:

(a) isolating cells from a urine sample to produce isolated urine progenitor cells, wherein said isolating comprises morphology based selection and~~/or~~ CD117 (C-kit), SSEA-4, CD105, CD73, CD90, CD133 and/or CD44 cell marker selection, wherein the urine progenitor cells have the potential to differentiate into urothelial cells, smooth muscle cells, endothelial cells or interstitial cells;

(b) growing the cells in a complex medium comprising progenitor cell medium and keratinocyte serum-free medium KSFM (1:1); and

(c) ~~(b)~~ culturing the isolated urine progenitor cells with a selective medium that supports the growth and differentiation of the progenitor cells into urothelial cells, smooth muscle cells, endothelial cells or interstitial cells."

VII. The appellant's arguments, in so far as they are relevant to the present decision, may be summarised as follows:

The basis for the feature that the "selective medium promotes selective differentiation of said progenitor cells into urothelial cells, smooth muscle cells, endothelial cells or interstitial cells" could be found on page 10, lines 5 to 9, of the application as filed. In addition, the passage bridging page 9, line 23, to page 10, line 4, of the application disclosed examples of media for use with different types of progenitor cells, specifying that selective media were preferred "in order to effect more precise control over the differentiation of the progenitor cell into the desired cell". Finally, page 8, lines 13 to 20, of the application as filed described specific examples of different media to promote selective differentiation of progenitor cells into urothelial cells, smooth muscle

cells, endothelial cells and interstitial cells. These passages not only described the use of a selective medium to support the differentiation of the urine progenitor cells, but also provided a number of specific examples of such media.

VIII. The appellant requested in writing that the decision under appeal be set aside and that a patent be granted on the basis of the main request or, alternatively, on the basis of one of the first to third auxiliary requests, all filed with the statement of grounds of appeal, or, alternatively, on the basis of one of the fourth to tenth auxiliary requests filed by letter of 3 January 2020.

Reasons for the Decision

1. The appeal is admissible.

2. The oral proceedings before the board took place in the absence of the appellant, who had been duly summoned but decided not to attend. The board decided to continue the proceedings in its absence in accordance with Rule 115(2) EPC.

The present decision is based on facts and evidence submitted during the written proceedings and which the appellant has had an opportunity to comment on. Moreover, as stated by Article 15(3) RPBA, 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.

3. Main request - Article 123(2) EPC

3.1 According to the Order of the decision G 10/93 of the Enlarged Board of Appeal (OJ EPO 1995, 172) "[i]n an appeal from a decision of an examining division in which a European patent application was refused, the board of appeal has the power to examine whether the application or the invention to which it relates meets the requirements of the EPC. The same is true for requirements which the examining division did not take into consideration in the examination proceedings or which it regarded as having been met. If there is reason to believe that such a requirement has not been met, the board shall include this ground in the proceedings". Thus, the board is not limited to an examination of the objections raised in the decision under appeal, but has to examine whether the appellant's requests fulfil all the requirements of the EPC. In this context, although the appealed decision only dealt with Articles 56 and 84 EPC, the board raised objections regarding added subject-matter (Article 123(2) EPC) in its communication pursuant to Article 15(1) RPBA.

3.2 Claim 1 of the main request appears to derive from a combination of original claims 1, 2, 5, 6, 8 and 11, which read: "A method for producing a culture of urine progenitor cells comprising: providing a urine sample; and then isolating urine progenitor cells from said urine sample" (claim 1), "... wherein said isolating step is carried out by (a) collecting cells from a urine sample to provide a crude cell sample; and (b) selecting urine progenitor cells from said crude cell sample" (claim 2), "... wherein said selecting step is carried out by selecting cells of interest based upon

morphology" (claim 5) or "... by selecting a marker specific to urine progenitor cells" (claim 6), "... wherein said marker is selected from the group consisting of: C-kit (CD117), SSEA-4, CD105, CD73, CD90, CD133, and CD44" (claim 8) and "... further comprising the step of differentiating said urine progenitor cells into at least one of the group consisting of: urothelial cells and smooth muscle cells" (claim 11). No basis is to be found in the originally filed claims for the feature that a selective medium promotes selective differentiation of said progenitor cells, let alone into endothelial cells or interstitial cells. The only claim of the original set that refers to differentiation into endothelial cells or interstitial cells is claim 12. However, claim 12 is not a method claim but a product claim, which reads: "An isolated urine progenitor cell, wherein said cell is c-kit positive, and wherein said cell can differentiate into two or more lineages selected from the group consisting of: urothelium, smooth muscle, endothelium and interstitial cells." It cannot provide a basis for the disputed feature, because it lacks all the other features of the claim (including the complete cell marker set and the method steps), it requires differentiation potential into at least two lineages (and not only one, as in the new claim) and it does not teach that differentiation is achieved by culturing in a selective medium.

3.3 There is no basis for the disputed feature in the description as filed either. In the statement of grounds of appeal, the appellant indicated the following passages as the basis for the first auxiliary request (which is restricted to differentiation into endothelial and interstitial cells): page 3, lines 11 to 16, in combination with page 5, lines 30 to 34; and

page 8, lines 11 to 13. The first of these passages relates to exactly the same subject-matter as original claim 2. It cannot therefore, for the same reasons as for original claim 2, provide a basis for this feature in new claim 1. The second passage is within a paragraph defining urine progenitor cells (UPCs) and reads: "A UPC is 'pluripotent' in that it is capable of giving rise to various cell types within one or more lineages. For example, UPCs according to some embodiments possess the potential to differentiate into one or more of the following: bladder urothelial, smooth muscle, endothelium, interstitial cells, and even bone, muscle, epithelial cells and other types of cells and tissues." Again, this passage does not provide a suitable basis, as it does not teach any of the features of the claimed method, let alone the use of a selective medium for differentiation into each cell type. As to the last passage, it teaches: "In further embodiments, isolated UPCs are provided in a particular growing environment that promotes the selective differentiation of the progenitor cells." This passage, again, does not teach culturing in a selective medium ("a particular growing environment" not being considered synonymous with a selective culture medium), let alone for differentiation into the specific cell types as claimed.

3.4 In its letter dated 3 January 2020, filed in reply to the board's communication, the appellant indicated further passages of the description as filed as providing a basis for this feature: page 8, lines 13 to 20; page 9, line 23 to page 10, line 4; and page 10, lines 5 to 9. However, the board is still not convinced that these passages constitute an adequate basis. The passage on page 8 follows the passage mentioned above referring to a "particular growing environment" and

discloses specific media that promote the differentiation of UPCs into urothelium, or into smooth muscle-like, endothelial-like or interstitial-like cells. This passage cannot provide a basis for the feature in the general context of claim 1, because it refers to specific media, defined by their components, and not just to a "selective medium" in general; it also does not disclose differentiation into smooth muscle, endothelial or interstitial cells but rather into smooth muscle-*like*, endothelial-*like* or interstitial-*like* cells, which is not necessarily the same. As to the passage starting on page 9, it reads that "it will generally be preferable that the cells be maintained in a simple serum-free medium such as KSFM for urothelial progenitor cells, or medium with 10% FBS for smooth muscle or interstitial progenitor cells such as Dulbecco's Minimal Essential Media (DMEM), Hank's Basic Salt Solution (HBSS), Dulbecco's phosphate-buffered saline (DPBS), RPMI, or Iscove's-modified Dulbecco's medium (IMDM), in order to effect more precise control over the differentiation of the progenitor cell into the desired cell". This passage thus also teaches specific media, defined by their components, for each of urothelial, smooth muscle or interstitial (not endothelial) progenitor cells, and it clearly refers to three different types of progenitor cells which are to be maintained, and not to one single urine progenitor cell type which is to be selectively differentiated into each cell type. Finally, the above-mentioned passage on page 10 reads: "In some embodiments, growth factors or other mitogenic agents are included in the media to promote proliferation and differentiation of distinct populations of cells. In this regard, particular embodiments of the invention embrace culturing urine progenitor cells with selective medium that supports the growth and differentiation of

the urine progenitor cells into urothelial, smooth muscle, interstitial cells, etc." This passage does indeed describe the use of selective media to support growth and differentiation of the urine progenitor cells into three of the cell lineages of the claim, but lacks one cell type, namely the endothelial cells.

3.5 Accordingly, claim 1 of the main request contravenes Article 123(2) EPC.

4. First to tenth auxiliary requests

4.1 Admissibility (Articles 12(4) and 13 RPBA)

4.1.1 The first to third auxiliary requests were filed for the first time with the statement of grounds of appeal. Their admission is thus governed by Article 12(4) RPBA 2007, which gives the board the power to hold inadmissible facts, evidence or requests which could have been presented or were not admitted in the proceedings before the examining or opposition division.

4.1.2 As to the fourth to tenth auxiliary requests, these were filed later during the appeal proceedings, with the letter of reply to the board's communication pursuant to Article 15(1) RPBA 2007. Article 13(1) RPBA 2007 leaves it to the board's discretion to admit any amendment to a party's case after it has filed its grounds of appeal. This discretion is exercised in view of inter alia the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy. Pursuant to Article 13(3) RPBA 2007, amendments sought to be made after oral proceedings have been arranged are not admitted if they raise issues which the board or the other parties

cannot reasonably be expected to deal with without adjournment of the oral proceedings.

4.1.3 The board considers that the first to third auxiliary requests were submitted as a legitimate reaction to the decision of the examining division, in an attempt to overcome the objections raised under Article 56 EPC. Hence, the board decided to admit them into the proceedings.

4.1.4 Moreover, the board also accepts the appellant's arguments that the fourth to tenth auxiliary requests were filed as a legitimate attempt to overcome the new objections raised by the board. In addition, they do not add to the complexity of the case and could be dealt with by the board without the need for adjournment of oral proceedings.

4.1.5 Hence, all the requests submitted by the appellant were admitted into the proceedings.

4.2 Article 123(2) EPC

4.2.1 Claim 1 of all the auxiliary requests still contains the feature of differentiation of the urine progenitor cells into different specific cells by culturing with selective media. As set out above in relation to the main request, the only passage in the application as filed that could provide a basis for this feature is on page 10, lines 5 to 9. However, this passage only refers to differentiation "into urothelial, smooth muscle, interstitial cells, etc.", and therefore does not mention "endothelial cells". Since differentiation into endothelial cells is part of claim 1 of all the auxiliary requests, it follows that there is no basis in the application as filed for this feature.

4.2.2 Claim 1 of all the auxiliary requests thus contravenes Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

M. Schalow A. Lindner

Decision electronically authenticated