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Datasheet for the decision of 17 June 2024

Case Number: T 1373/22 - 3.3.05

Application Number: 15733576.1

Publication Number: 3154694

IPC: B01L3/00, C12M1/00, G01N1/40, B01D39/00

Language of the proceedings: EN

Title of invention:
PRODUCTS AND METHODS TO ISOLATE MITOCHONDRIA

Applicant:
Children's Medical Center Corporation
Beth Israel Deaconess Medical Center, Inc.

Headword:
Isolation of mitochondria/Medical Center

Relevant legal provisions:
EPC Art. 123(2), 87, 56, 113(1)
RPBA 2020 Art. 13(2)

Keyword:
Amendments - allowable (yes)
Inventive step - (yes)
Right to be heard - substantial procedural violation (no)
Amendment after summons - exceptional circumstances (yes)

Decisions cited:

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 1373/22 - 3.3.05

D E C I S I O N
of Technical Board of Appeal 3.3.05
of 17 June 2024

Appellant: (Applicant 1)	Children's Medical Center Corporation 55 Shattuck Street Boston, MA 02115 (US)
Appellant: (Applicant 2)	Beth Israel Deaconess Medical Center, Inc. 330 Brookline Avenue Boston, MA 02215 (US)
Representative:	Marks & Clerk LLP 15 Fetter Lane London EC4A 1BW (GB)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 20 December 2021 refusing European patent application No. 15733576.1 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairman	T. Burkhardt
Members:	G. Glod
	S. Fernández de Córdoba

Summary of Facts and Submissions

I. The applicants' (appellants') appeal lies from the examining division's decision refusing European patent application No. 15 733 576.1 for lack of inventive step.

II. The following documents cited in the decision are of relevance here:

D1: US 2,854,143 A
D2: Stitt, M. et al., Methods in Enzymology, vol. 174, 1989, pages 518-552, XP000864424
D3: US 2001/0047966 A1
D9: Declaration of Alexander Schueller of 28 October 2021
D13: Declaration of Alexander Schueller of 30 November 2021

III. With the statement of grounds of appeal the appellants submitted, among other things:

D14: Declaration of Alexander Schueller of 28 April 2022

IV. During oral proceedings on 17 June 2024, the appellants submitted a new, now main, request labelled "Auxiliary Request 20". Claim 1 reads as follows:

"*1. A method for isolating a viable, respiration-competent mitochondrion, the method comprising: providing a cell homogenate comprising a viable mitochondrion; providing a filtration apparatus comprising:*

a tubular body configured to be received in a centrifuge tube and comprising a lumen and first and second ends, each end comprising an opening;
a first filter disposed and secured within the lumen, wherein the filter has a pore-size between 30 µm and 50 µm; and
a second filter disposed and secured within the lumen adjacent to the first filter and having a pore-size between 5 µm and 20 µm; introducing the cell homogenate into the opening at the first end such that the cell homogenate contacts and is filtered through the first filter and subsequently the second filter to thereby form a filtrate; and
collecting the viable, respiration-competent mitochondrion in the filtrate, thereby isolating the viable, respiration-competent mitochondrion."

Claims 2 to 8 relate to preferred embodiments. Claim 9 reads as follows:

"*9. A filtration apparatus for isolating an intact, viable, respiration-competent mitochondrion from mammalian tissue comprising:*
a tubular body configured to be received in a centrifuge tube and comprising a lumen and first and second ends, each end comprising an opening;
a first filter disposed and secured within the lumen, wherein the filter has a pore-size between 30 µm and 50 µm;
a second filter disposed and secured within the lumen adjacent to the first filter and having a pore-size between 5 µm and 20 µm, and
a third filter disposed and secured within the lumen between the first filter and the second filter and having a pore-size which is selected from 18 µm, 20 µm,

22 µm, 25 µm, 28 µm, 30 µm, 33 µm, 35 µm, 38 µm, 40 µm, 42 µm, 45 µm, 48 µm, or 50 µm."

Claims 10 to 13 relate to preferred embodiments of claim 9.

V. The appellants' arguments are reflected in the reasoning below.

VI. The appellants request that the decision under appeal be set aside and that a patent be granted on the basis of the main request submitted as auxiliary request 20 during oral proceedings.

Reasons for the Decision

1. Article 13(2) RPBA

Under Article 13(2) RPBA any amendment to a party's appeal case made after notification of a communication under Article 15, paragraph 1 shall, in principle, not be taken into account unless there are exceptional circumstances, which have been justified with cogent reasons by the party concerned.

In the case at hand exceptional circumstances are present. Indeed, in the communication pursuant to Article 15(1) RPBA and during oral proceedings, the board had raised new objections, in particular under Article 123(2) EPC, which triggered the filing of a new request at a very late stage (Case Law of the Boards of Appeal of the EPO, 10th edition, 2022, V.A.4.5.4 a)).

The now-main request is taken into account.

2. Article 123(2) EPC

The requirements of Article 123(2) EPC are met for the following reasons.

2.1 Claim 1 is based on claim 1 as filed in combination with page 2, line 19 of the application as originally filed. The wording "between 30 µm and 50 µm" and "between 5 µm and 20 µm" is based on claim 1 as filed and the disclosure on page 2, line 26 to page 3, line 1 of the description as originally filed. The fact that a range is given in claim 1 as filed means that the filter has a pore size which is one value within the range.

2.2 Claims 2 to 7 are based on claims 2 to 7 as filed. The multiple dependencies are justified by the disclosure on page 4, lines 9 to 19 of the application as filed.

2.3 Claim 8 is based on page 2, lines 30 to 32 in combination with page 3, lines 5 to 7. Although several selections have to be made, example 2 provides an indication that the selection claimed in claim 8 is the preferred one.

2.4 Claim 9 is based on claim 8, page 3, lines 1 to 5 and page 9, lines 10 and 11 of the application as originally filed.

2.5 Claims 10 to 12 are based on claims 12, 14 and 16 as filed.

2.6 Claim 13 including the "and/or" is directly and unambiguously derivable from page 3, lines 9 to 12 and page 7, line 14 to page 8, line 3 of the application as originally filed.

3. Article 56 EPC

3.1 Claim 1

3.1.1 The invention relates to a method for isolating viable, respiration-competent mitochondria.

3.1.2 D1 is a possible starting point for the question of inventive step. It discloses particle separation by slowly diffusing a liquid vehicle containing frozen particles through a series of filters which selectively retain the particles thereon according to filter pore and particle size (column 1, lines 40 to 44). Possible particles include mitochondria (column 1, line 54). The goal is to obtain viable elements (column 1, lines 64 to 67). Figure 1 shows an apparatus comprising four filters 33, 35, 37 and 39 of decreasing pore size. The pore sizes of the filters are 40 to 60 µm, 10 to 15 µm, 4 to 5.5 µm and 0.9 to 1.4 µm, respectively (column 2, lines 34 to 47). The specific application described relates to the separation of blood cellular elements (column 3, lines 1 to 3) according to their size into white cells, red cells and blood platelets, which are separately retained on the different filters (column 3, lines 43 to 56).

3.1.3 The problem to be solved by the invention defined in claim 1 is to provide a method for a different application.

3.1.4 It is proposed to solve the problem by a method according to claim 1 characterised in that a viable, respiration-competent mitochondrion is collected.

3.1.5 It is accepted that the problem is successfully solved.

3.1.6 The proposed solution is not obvious for the following reasons.

As explained above, the device of the figure of D1 is aimed at separating blood cellular elements and isolates the respective ingredients on different filter layers. Consequently, the skilled person wishing to adapt the specific application of D1 to isolate a single species, namely mitochondria, would use a single filter with a suitable pore size to isolate mitochondria. They would have no incentive to keep the plurality of filters.

3.1.7 D2 is also a possible starting point for the question of inventive step. D2 relates to the disruption and fractionation of protoplasts. The protoplasts are first disrupted on a 17 µm mesh nylon net, then filtered through an 8 µm membrane filter and ultimately filtered through a 0.45 µm membrane filter (page 528, first full paragraph).

3.1.8 The problem to be solved by the invention defined in claim 1 is to provide a method for isolating viable, respiration-competent mitochondria from cell homogenates.

3.1.9 It is proposed to solve the problem by a method according to claim 1 characterised in that the cell homogenate is filtered through a first filter having a pore size between 30 µm and 50 µm.

3.1.10 In view of D14 and the examples present in the application, it is accepted that the problem is successfully solved.

3.1.11 The claimed solution is not obvious for the following reasons.

D2 does not teach a first filter having a pore size between 30 µm and 50 µm. There is also no reason to include a filter with such a large pore size in D2, since D2 relates to protoplasts (plant cells) which are to be ruptured and subsequently fractionated.

There is also no reason for the skilled person starting from D2 to use a homogenate as starting material.

Although D1 mentions a filter 33 having a pore size between 40 and 60 µm, this filter is for separating white blood cells (column 3, lines 50 to 52). Consequently, the skilled person trying to obtain mitochondria would not see the need to add a filter with such a large pore size.

D3 does not mention mitochondria and does not provide the solution to the problem posed.

3.1.12 The subject-matter of claim 1 involves an inventive step.

3.2 Claim 9

3.2.1 The invention relates to a filtration apparatus suitable for isolating an intact, viable, respiration-competent mitochondrion from mammalian tissue.

3.2.2 D1 is a possible starting point for the question of inventive step. As set out in point 4.1.2, D1 discloses an apparatus made of four filters (figure 1).

3.2.3 The problem to be solved is to provide an apparatus for faster isolation of viable, respiration-competent mitochondria from mammalian cells.

3.2.4 It is proposed to solve the problem by an apparatus according to claim 1, characterised in that the middle filter has a pore size which is selected from 18 µm, 20 µm, 22 µm, 25 µm, 28 µm, 30 µm, 33 µm, 35 µm, 38 µm, 40 µm, 42 µm, 45 µm, 48 µm, or 50 µm.

3.2.5 It is accepted that the problem is successfully solved.

In the apparatus of figure 1 of D1, mitochondria would be retained by filter layer 39 having a pore size of only 0.9 µm to 1.4 µm, which is smaller than the size of mitochondria. In the device of D1 it is thus cumbersome (and less fast) to isolate viable mitochondria.

3.2.6 The proposed solution is not obvious.

D1 does not provide any incentive to change the setup by using a middle filter with the claimed pore size when isolating viable mitochondria.

D2 at least does not disclose a filter with the pore size missing in D1.

D3 is silent about mitochondria. There is thus no reason to include a middle filter with the claimed pore size in the setup of figure 1 of D1.

3.2.7 As explained above under points 3.1.7 to 3.1.11, there is no reason to modify the apparatus of D2 by adding a first filter with the claimed pore size.

3.2.8 D3 relates to the isolation of cell components (claim 1) and is also a possible starting point for the question of inventive step. D3 discloses a filter with decreasing pore size (figure 1). The filtration unit is made of a three-layered sheet. The top layer may have a pore size of from 100 to 300 µm, the second layer a pore size of from 30 to 100 µm, and the third layer a pore size of from 5 to 30 µm (paragraph [0011]).

3.2.9 The problem to be solved is to provide an apparatus for faster isolation of viable, respiration-competent mitochondria from mammalian cells.

3.2.10 It is proposed to solve the problem by an apparatus according to claim 9, characterised in that it comprises a first filter having a pore size between 30 µm and 50 µm.

3.2.11 It is accepted that the problem is successfully solved. D3, rather, relates to the isolation of nucleic acid from plasmids (see example 1). The first filter of 100 to 300 µm is expected to have little effect when isolating an intact, viable, respiration-competent mitochondrion from mammalian tissue. Therefore the main purification would be obtained by the subsequent filters having a pore size of from 30 to 100 µm and of from 5 to 30 µm, which equates to a two-filter system. As set out in D9 and D13, the filtration through three filters as claimed allows faster filtration than filtration through two filters.

3.2.12 The proposed solution is not obvious.

D3 does not relate to mitochondria. There is no incentive to change the pore size of the disclosed filters.

D1 provides no incentive to add a first filter having a pore size between 30 µm and 50 µm to the apparatus of D3.

D2 does not deal with mammalian cells and does not teach the pore sizes as claimed.

3.2.13 The subject-matter of claim 9 involves an inventive step.

3.3 The subject-matter of claims 1 and 9 is based on an inventive step. Consequently, the same applies to claims 2 to 8 and 10 to 13, directly or indirectly referring to claims 1 or 9, respectively. The requirements of Article 56 EPC are met.

4. Article 113(1) EPC - substantial procedural violation

The appellants argue that the examining division committed a substantial procedural violation because of a lack of reasoning with regard to auxiliary request 7 (item 3.1 of the decision under appeal).

Even though the examining division could have provided more information as to its reasoning with regard to the features added, it is evident that these features were not seen as providing an additional technical effect when starting from either D1 or D3, as compared with the claimed subject-matter of the main request ("for the same reasons").

Thus the board cannot recognise any substantial procedural violation.

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 with the order to grant a patent on the basis of claims 1 to 13 of the now-main request submitted as auxiliary request 20 during oral proceedings and a description to be adapted thereto.

The Registrar: The Chairman:

L. Malécot-Grob T. Burkhardt

Decision electronically authenticated