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**Datasheet for the decision
of 30 June 2017**

Case Number: T 0102/14 - 3.3.06

Application Number: 10158444.9

Publication Number: 2218495

IPC: B01D71/80, B01D61/02,
B01D69/14, C02F1/44

Language of the proceedings: EN

Title of invention:
Biomimetic membranes

Applicant:
Applied Biomimetic A/S

Headword:
Membrane for water purification / Applied Biomimetic A/S

Relevant legal provisions:
EPC Art. 83

Keyword:
Sufficiency of disclosure - (no)

Decisions cited:
T 0766/91

Catchword:



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Case Number: T 0102/14 - 3.3.06

D E C I S I O N
of Technical Board of Appeal 3.3.06
of 30 June 2017

Appellant: Applied Biomimetic A/S
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Decision under appeal: Decision of the Examining Division of the
European Patent Office posted on 1 August 2013
refusing European patent application No.
10158444.9 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman L. Li Voti
Members: P. Ammendola
S. Fernández de Córdoba

Summary of Facts and Submissions

I. This appeal lies from the decision of the Examining Division to refuse European divisional patent application no. 10 158 444.9.

II. During examination the following documents had, *inter alia*, been cited:

D1: Nardin, C. and Meier, W.: "HYBRID MATERIALS FROM AMPHIPHILIC BLOCK COPOLYMERS AND MEMBRANE PROTEINS", *Reviews in Molecular Biotechnology*, vol. 90, no. 1, March 2002, pages 17-26;

and

D3: WO 01/32146 A2.

III. In its decision refusing the pending Main Request and Auxiliary Request because of lack of sufficient disclosure, the Examining Division found (reasons, points 1.1.3 and 2) that

"the disclosure as a whole is **not** sufficient in the sense of Art.83 EPC for enabling a skilled person to obtain biomimetic membranes suitable for water purification...

The objection under Art. 83 EPC...applies to the application as a whole and, therefore, also to the auxiliary request on file."

The Examining Division noted, *inter alia*, (see penultimate paragraph on page 4 of the reasons of the decision) that the sole information in the description

as originally filed as to how to prepare the claimed membrane, was limited to the indication

"... in [0061] ... that a 5 nm thick monolayer of synthetic triblock copolymer and protein should be deposited on the surface of a 25 mm commercial ultrafiltration disk using a Langmuir-Blodgett trough, then cross-linked with UV light and finally covered with a 220 nm pore size PVDF membrane.

There is no further teaching in the description on how to prepare a solution of tri-block copolymer incorporating proteins, nor prior art documents have been acknowledged, which could help to overcome the lack of detail in this regard."

Having established the lack of sufficient details in the application, the Division considered (first paragraph on page 5 of the decision) the Applicant's allegation that it would be well-known to the person skilled in the art which kind of tri-block copolymers should be used to reproduce the claimed membrane (for instance that these tri-block copolymers should not be too thick and should be friendly to the proteins). It is then apparent from the subsequent reasoning in the decision under appeal, that the existence of this common general knowledge alleged by the Applicant, was found demonstrated neither by D1 nor by the other scientific articles and patents (including D3) on file, because (see the initial passage in the third paragraph on page 5):

"According to the established jurisprudence of the Boards of Appeal, common general knowledge is represented by basic handbooks and textbooks on the

subject in question, it does not normally include patent literature and scientific articles (see e.g. T766/91)."

Nevertheless, starting at the subsequent sentence in the same paragraph the Examining Division also considered that

"... the division will assume, to the benefit of the applicant, that the general knowledge is represented by the prior art documents on file.

However, **none** of these documents teach how to prepare a membrane comprising a tri-block copolymer matrix incorporating porin proteins using a Langmuir-Blodgett trough.

Therefore, in the opinion of the division, the skilled person would inevitably need to start a research work."

Also in view of the above reasons, the Examining Division concluded (page 7, second paragraph) that

"the absence of a workable example and adequate knowledge from the prior art or the description of the application, results in an undue burden on the skilled person trying to reproduce the invention."

IV. Claim 1 according to the **Auxiliary Request** refused by the Examining Division reads as follows:

"1. A biomimetic membrane for water purification, comprising:

a block copolymer matrix simulating a natural biological membrane and natural protein environment; and membrane proteins incorporated into said matrix to form a membrane/protein composite; in which said membrane proteins are selected from the aquaporin family of proteins, and said matrix is formed from tri-block copolymers having hydrophilic outer blocks and hydrophobic inner blocks, and is impermeable to water."

Herein below "*tri-block copolymers having hydrophilic outer blocks and hydrophobic inner blocks*" are also indicated in brief as **tri-block copolymers**.

- V. The Applicant (**Appellant**) lodged an appeal against this decision. With its statement of grounds of appeal it filed as Main Request and Auxiliary Request the two set of claims already considered by the Examining Division in its decision, as well as the document

D11: "Statement by Professor Carlo Montemagno",
dated 11/13/13,

describing the general protocol for experiments in which the inventors of the present patent application made membranes using a Langmuir-Blodgett trough at the time of the invention and a specific sample of the claimed biomimetic membrane made.

- VI. In a communication of 28 April 2017 issued by the Board in preparation for the then forthcoming oral proceedings of 30 June 2017, the Board expressed, *inter alia*, the following opinion (see points 5.5, 5.5.1, 5.5.4):

"In the preliminary opinion of the Board, a skilled person attempting to follow the instructions in [0061] of the application would immediately realize the absence therein of many essential details.

Manifestly missing essential information is, in particular, that relating to the chemical structure of a suitable tri-block copolymer (i.e. kind of repeating units and molecular weights of the blocks, kinds and amounts of the UV cross-linkable groups present therein and their location along the macromolecules)...

Thus, in the preliminary opinion of the Board the application as filed not only fails to disclose with sufficient details (in [0061]) the sole example of the preparation of the claimed membrane, but also makes no reference to any specific document possibly providing information apt at complementing the example's incomplete disclosure".

VII. With letter of 19 May 2017 the Appellant, *inter alia*, filed nine new documents and stated (see passage bridging pages 1 and 2) that it expected to refer to specific case law during the Oral Proceedings.

VIII. With a communication of the Board's Registry dated 1 June 2017, the Appellant was informed *inter alia* that, since these additional nine documents had not been accompanied with any indication of which specific arguments were allegedly supported by these citations and of the passages in these latter providing such support, the Board had severe concerns as to the admissibility into the proceedings of the late filed documents.

IX. The Appellant replied with letter of 7 June 2017 requesting again the admission of the newly-filed documents into the proceedings and to rely on the case law listed in the previous letter.

X. At the oral proceedings held before the Board on 30 June 2017, the Appellant:

- did not maintain its request that these latter nine documents be admitted into the proceedings and did not rely on the case law listed in the letter of 19 May 2017;
- withdrew the Main Request, and
- **requested** that the decision under appeal be set aside and that a patent be granted on the basis of the claims of the Auxiliary Request as filed with the statement of grounds of appeal (identical to the Auxiliary Request refused by the Examining Division).

XI. The Appellant's submissions of relevance for the present decision can be resumed as follows.

The limited instructions in the example in [0061] sufficed to the skilled person for reproducing the claimed membrane in which aquaporins were in their functional state. The skilled person in question had to be considered to be represented by a team of experts formed by a polymer chemist and a biochemist expert in biological membranes. Hence, the skilled person was certainly aware of the well-known research work reviewed in D1 (in the following **Meier's work**), in which vesicles of poly(2-methyloxazoline)-poly(dimethyl-siloxane)-poly(2-methyloxazoline) tri-

block copolymers (i.e. **PMOXA-PDMS-PMOXA** tri-block copolymers) had already been successfully used for incorporating membrane proteins.

Hence, also the skilled person attempting to replicate the present invention would have certainly recognised that these tri-block copolymers were suitable for the claimed invention.

Indeed, as also confirmed in D11, the inventors of the present application at the time that the invention was made fabricated biomimetic membranes by combining PMOXA-PDMS-PMOXA and aquaporins following the procedure also partially described in [0061] of the application. In particular, to optimize the molecular weight of the three polymer blocks forming the PMOXA-PDMS-PMOXA in order to achieve a monolayer with a thickness of about 4-5nm, suitable for incorporating aquaporins in a functional state and also chosen in said example of paragraph [0061], required, at most, some limited experimental work.

As to the possibility of preparing embodiments of the claimed membrane using tri-block copolymers different from PMOXA-PDMS-PMOXA, the Appellant submitted the following:

- (a) Interfacing the common general knowledge of the polymer chemist and the biochemist expert in biological membranes enabled the skilled person to predict which other tri-block copolymers were most likely to possess all the characteristics required for simulating the mosaic structure of the natural cell membranes containing aquaporins and, thus, to host aquaporins in their functional state. Only a limited amount of experimental work would be

needed, if at all, to verify or optimize such predictions.

- (b) The existence of common general knowledge sufficient for such predictions would also be confirmed by the fact that e.g. the authors of D3 had been able to provide extensive teachings as to which sorts of polymer blocks could be used to prepare other tri-block copolymers apt at forming biomimetic membranes, in addition to the PMOXA-PDMS-PMOXA.
- (c) Thus, no or only a limited amount of experimental work was also required for preparing embodiments of the claimed membrane using hydrophilic-hydrophobic-hydrophilic tri-block copolymers different from PMOXA-PDMS-PMOXA.

Accordingly, the disclosure in the patent in suit of the claimed biomimetic membrane was sufficient.

Reasons for the Decision

Appellant's only request (claims according with the Auxiliary Request filed with the statement of grounds of appeal)

- 1. Lack of sufficient disclosure (Article 83 EPC)
 - 1.1 The Board notes preliminarily the following:
 - (a) Claim 1 (full text under IV, *supra*) is directed to a biomimetic membrane for water purification comprising a block copolymer matrix having aquaporin proteins incorporated therein. It is apparent to the skilled reader of this claim that

the applicability of the membrane "*for water purification*" is due to these proteins, i.e. that the aquaporins incorporated in the membrane have to be in a functional state (this latter wording is used e.g. in paragraph [0004] of the application's description). It is thus also apparent to the skilled reader of claim 1, wherein the matrix of tri-block copolymers is required to be "*simulating natural biological membrane and natural protein environment*", that the (implicitly) required functional state of the aquaporins depends essentially on the nature of the block copolymer matrix, i.e. that the matrix of tri-block copolymer is functionally defined so as to include any matrix of tri-block copolymer that is able of "*simulating a natural biological membrane and protein environment*" to the extent required at incorporating the aquaporins in a functional state. This construction of claim 1 is not only in line with the whole content of the description of the application, but is also the same underlying the submissions of the Appellant (see XI, *supra*).

- (b) The only explicit disclosure in the whole patent application as to how to produce the claimed biomimetic membranes is contained in paragraph [0061] reading :

"[0061] *The preferred form of the invention has the form of a conventional filter disk because it is most easily assayed for functionality that way. To fabricate such a disk, a 5nm thick monolayer of synthetic triblock copolymer and protein is deposited on the surface of a 25mm commercial ultrafiltration disk using a Langmuir-Blodgett trough. The monolayer on the disk*

is then exposed to 254nm UV light to cross-link the polymer and increase its durability. Lastly, a 220nm pore size PVDF membrane is epoxy glued to the disk surface to ensure safe handling and prevent leakage at the edges".

- (c) If only the missing indication in this paragraph of the chemical structure of the "*synthetic triblock copolymer*" is sufficient at rendering apparent that the disclosure in [0061] is too incomplete to allow *per se* to carry out the invention. It is also undisputed that the remainder of the application does not mention any single specific example of tri-block copolymer, let aside of a tri-block copolymer **suitable** for forming the claimed membrane with functional aquaporins. The Appellant accepted also during oral proceedings that not every possible tri-block copolymer would be suitable for the claimed invention.
- (d) Also the prior art mentioned in the application - only relating to the incorporation of functional membrane proteins into lipid vesicles (see e.g. [0018]) or lipid membranes (see e.g. [0027]) - neither relates to synthetic block copolymer matrices having membrane proteins incorporated therein, nor directly or indirectly refers to any other prior art related to synthetic block copolymers.

1.2 Hence, it is apparent that the patent application *per se* does not contain any direct or indirect indication, in particular, as to which (among all the possibly conceivable) tri-block copolymers can be used to carry

out the invention according to the instructions in [0061]. This is undisputed by the Appellant.

1.3 Nevertheless, according to the Appellant's line of reasoning (see XI, *supra*), the Examining Division had erred in concluding that the limited instructions in [0061] did not suffice to the skilled person for reproducing the claimed membrane. In the Appellant's opinion, the skilled person to which the present patent application was directed was a team of experts formed by a polymer chemist and a biochemist familiar with biological membranes. Thus, the common general knowledge of which this skilled person was also certainly aware (herein below **the alleged common general knowledge**) embraced:

- The well-known background art, reported in a number of scientific articles (Meier's work) and patents (such as D3) and reviewed in D1, as to the possibility of specifically using PMOXA-PDMS-PMOXA tri-block copolymers for producing matrices (in the form of vesicles) capable of incorporating membrane proteins; the relevance of this background art was also apparent from the fact, described in D11, that the inventors of the present patent application had actually used the PMOXA-PDMS-PMOXA "at the time that the invention was made".
- Sufficient general knowledge to enable the skilled person to predict or to readily identify which tri-block copolymers, possibly also different from the PMOXA-PDMS-PMOXA tri-block copolymers, were most likely to possess all the characteristics required for simulating the mosaic structure of the natural cell membranes containing aquaporins; the existence of this general knowledge was apparent, in

particular, from the extensive teachings in pages 5 to 8 of D3 as to the blocks possibly suitable for forming amphiphilic biocompatible copolymers such as tri-block copolymers.

- 1.4 The Board holds *arguendo* that the Appellant's has correctly identified the relevant skilled person. However, the Board also finds that the Appellant has provided no convincing evidence as to the existence of the alleged common general knowledge.
- 1.4.1 Indeed, according to the established jurisprudence of the Boards of Appeal also indicated by the Examining Division (see III, *supra*), normally scientific articles and reviews or patent documents constitute *per se* no evidence of what is part of the common general knowledge of the relevant skilled person.
- 1.4.2 The Board also notes that the allegation that a skilled person would have been certainly aware of Meier's work reviewed in D1 - and specifically that it was common knowledge that PMOXA-PDMS-PMOXA tri-block copolymers were the tri-block copolymers of choice to be used for incorporating membrane proteins - appears at odds with the undisputable fact (already indicated at "d)" in point 1.1, *supra*) that the present application does not even contain some indirect reference to the existence of any background art related to synthetic tri-block copolymers.
- 1.4.3 Hence, the mere existence of D1 itself and of the individual scientific articles concerning Meier's work or of patents relating to such a research work (including those already cited before the Examining Division, such as the patent D3 also referred to in these appeal proceedings) is insufficient at

demonstrating that the common knowledge of the skilled person included the use of PMOXA-PDMS-PMOXA tri-block copolymers as suitable for producing matrices capable of incorporating membrane proteins (let alone that included any other more general teachings possibly contained e.g. in D1 or in D3).

- 1.4.4 As to the further argument of the Appellant (see 1.3, *supra*) that the lists of alternative blocks for the block copolymers disclosed in D3 (see the section entitled "A. Hydrophilic and Hydrophobic blocks" starting at page 5), which also included PMOXA-PDMS-PMOXA (see examples), were an (indirect) evidence of the existence of the alleged common general knowledge, it is apparent to the Board that, since D3 is a patent application, the disclosure in this document is not necessarily reflecting the common general knowledge. Indeed, also the teachings in this patent application as to the lists of alternative blocks for the block copolymers, may as well be based on some experimental evidence or theoretical knowledge or hypothesis only known to the inventors of D3. Moreover, the general disclosure in D3 as to the possible polymer blocks does not relate exclusively to the incorporation of proteins into vesicles made of amphiphilic biocompatible copolymers, but concerns the incorporation of very different types of molecules into these vesicles (page 14, line 31 to page 15, line 11).

Thus, the general disclosure in D3 referred to by the Appellant appears not necessarily to imply the existence of the alleged common general knowledge concerning tri-block copolymers.

- 1.4.5 Hence, in the absence of any other document or argument rendering plausible that Meier's work and/or the

general disclosure or the examples in D3 were indeed part of the common general knowledge of the skilled person, the Appellant's line of reasoning resumed at 1.3, *supra*, appears based on unsupported allegations and thus, not convincing.

- 1.5 Therefore, the Board comes to substantially the same conclusion as the Examining Division, i.e. that the skilled person attempting to follow the partial instructions in [0061] of the description of the application, is obliged to start a research programme. In particular, already upon considering that several aspects of the structure of the tri-block copolymer (such as the kind of repeating units, the molecular weights of the blocks and, possibly, also the kind and amount of the UV cross-linkable groups present therein and their location along the macromolecules) may undisputedly be expected to influence the ability of the matrix made therefrom to simulate the "*natural biological membrane and natural protein environment*" to the extent required for incorporating therein the aquaporins in a functional state, the Board holds that a possibly very extensive research work (e.g. in the scientific and technical literature and by means of experiments) appears necessary if only for just identifying which sort of tri-block copolymers are most likely to be suitable for carrying out the invention.
- 1.6 Accordingly, the Board concludes that the Appellant has failed in rendering plausible that the claimed biomimetic membrane might be reproduced without undue burden.
- 1.7 In D11 the Appellant stated that "at the time that the invention was made" the claimed membrane had been prepared by using a PMOXA-PDMS-PMOXA tri-block

copolymer made according to the procedure (partially) described in [0061] of the present application. Therefore, the Board has also considered, *arguendo*, the hypothetical case, submitted by the Appellant, that the relevant skilled person was indeed aware that PMOXA-PDMS-PMOXA tri-block copolymers had already been used (as described in D1/Meier's work and D3) for fabricating matrices apparently capable of hosting membrane proteins in a functional state, and thus has also assumed, *arguendo*, that such person, upon reading the application, would have immediately conceived (and succeeded in it without any undue burden of experimental work) fabricating e.g. the same embodiment of the claimed membrane described in D11.

However, even in this case, the possibility of carrying out exclusively embodiments of the claimed invention by using PMOXA-PDMS-PMOXA tri-block copolymers, would still not commensurate with the breadth of claim 1 under consideration. Indeed, the subject-matter of this claim clearly extends (see also in "(a)" at point 1.1, *supra*) to any membrane in which aquaporins are incorporated into any tri-block copolymer's matrix that is able of "*simulating a natural biological membrane and natural protein environment*" to the extent required for incorporating the aquaporins in a functional state.

Hence, the disclosure of the claimed biomimetic membrane in the patent application would remain insufficient even when assuming, for the sake of an argument in favour of the Appellant, that the relevant skilled person, similarly to the inventors of the present patent application, were able to carry out without undue burden the embodiments of the subject-matter of claim 1 at stake in which the tri-block copolymer was PMOXA-PDMS-PMOXA.

1.8 For the above reasons, the Appellant's sole request is thus found to contravene Article 83 EPC and must be refused.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:



D. Magliano

L. Li Voti

Decision electronically authenticated