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Datasheet for the decision of 1 July 2024

Case Number: T 1694/22 - 3.3.08

Application Number: 14860799.7

Publication Number: 3066472

IPC: G01N33/566, C12Q1/6883, A61K31/451

Language of the proceedings: EN

Title of invention:
Compositions and methods for detecting and/or treating inflammation

Patent Proprietor:
The General Hospital Corporation

Opponent:
Dr. H. Ulrich Dörries

Headword:
Kidney inflammation/GENERAL HOSPITAL

Relevant legal provisions:
EPC Art. 56

Keyword:
Inventive step - reasonable expectation of success (yes)

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Case Number: T 1694/22 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 1 July 2024

Appellant: (Opponent)	Dr. H. Ulrich Dörries Fünf Höfe, Theatinerstr. 16 80333 München (DE)
Respondent: (Patent Proprietor)	The General Hospital Corporation 55 Fruit Street Boston, MA 02114 (US)
Representative:	Barker Brettell LLP 100 Hagley Road Edgbaston Birmingham B16 8QQ (GB)
Decision under appeal:	**Interlocutory decision of the Opposition Division of the European Patent Office posted on 16 May 2022 concerning maintenance of the European Patent No. 3066472 in amended form**

Composition of the Board:

Chair	T. Sommerfeld
Members:	A. Schmitt
	D. Rogers

Summary of Facts and Submissions

I. The appeal lodged by the opponent (appellant) lies from the opposition division's interlocutory decision that European patent No. 3 066 472 (the patent) in the version of the main request filed during opposition proceedings and the invention to which it relates meet the requirements of the EPC. The patent proprietor is the respondent in the appeal proceedings.

Claim 2 of the main request underlying the decision under appeal reads as follows:

"2. A method of detecting renal inflammation in a subject, the method comprising;
(i) assaying, in a urine sample obtained from a subject, a level of UDP-glucose;
(ii) comparing the level of UDP-glucose with a reference level; and
(iii) identifying the subject as (a) having renal inflammation if the level of UDP-glucose
is above the reference level; and (b) not having renal inflammation if the level of UDP-glucose is at or below the reference level."

II. In the statement of grounds of appeal, the appellant challenged the decision under appeal with respect to the inventive step of claim 2, *inter alia*.

III. The respondent did not reply to the appeal.

IV. The board issued a summons to oral proceedings, as requested by the appellant. Subsequently, the board cancelled the oral proceedings and informed the parties that the proceedings would be continued in writing.

V. The following documents are referred to in this decision:

D1 Arase et al., J Immunol. 182, 2009, 7074-84

D3 Müller et al., Am J Respir Cell Mol Biol. 33, 2005, 601-9

D4 Charlton et al., Brain Res. 764, 1997, 141-8

VI. The appellant provided arguments supporting its view that the subject-matter of claim 2 *inter alia* of the main request underlying the decision under appeal did not involve an inventive step over the disclosure in document D1, alone, or in combination with the disclosures in any of documents D3 and D4.

VII. The respondent did not make any submissions in the appeal proceedings.

VIII. The parties' requests, where relevant to the decision, were as follows.

The appellant requested that the decision under appeal be set aside and that the patent be revoked.

The respondent did not make any requests.

Reasons for the Decision

1. Since only the appellant has requested oral proceedings and the board is of the view that the decision under appeal should be set aside and the patent revoked, it was possible to arrive at a decision without holding oral proceedings.

Main request
Inventive step (Article 56 EPC) - claim 2
Closest prior art

2. The only document put forward in the decision under appeal and by the appellant as a starting point for the assessment of inventive step in the claimed methods is document D1.

3. Document D1 discloses that the expression levels of the membrane receptor P2Y14 (P2RY14 in document D1) and the cytokine IL-8 are higher in endometrial tissue samples from patients with pelvic inflammatory disease than in those of subjects without any inflammatory diseases (Figures 1 and 2 of document D1), and that the P2Y14-ligand UDP-glucose induces IL-8 production in endometrial epithelial cells through P2Y14 signalling (see first full paragraph in left-hand column on page 7079 to first paragraph in left-hand column on page 7080). UDP-glucose-induced IL-8 secretion and neutrophil chemotaxis were confirmed in mice *in vivo* (pages 7080 to 7081; Figures 6 and 7 of document D1).

4. From these results, the authors of document D1 propose a "*novel model for stimulating innate mucosal immunity*" in the female reproductive tract (FRT), in which damaged cells release UDP-glucose into the extracellular space, P2Y14 expression is up-regulated

in undamaged epithelial cells, and released UDP-glucose stimulates IL-8 production via epithelial P2Y14 (see Figure 8 and its legend).

Difference, technical effect and objective technical problem

5. Document D1 does not concern a method of detecting renal inflammation, or the assessment of the relative levels of a marker in a urine sample. Thus, the claimed method differs from that disclosed in document D1 in that it is a method of detecting renal inflammation, and in that the level of UDP-glucose is determined in a urine sample of a subject and compared with a reference level and the presence or absence of renal inflammation is determined from this comparison (see section I. for the full wording of the claim).

6. The technical effect of these differences is that renal inflammation is detected. In view of this, the objective technical problem can be formulated as suggested by the appellant (first half-sentence in section 25 on page 8 of the statement of grounds of appeal) as the provision of a method for identifying renal inflammation.

Obviousness

7. Document D1 shows that, in addition to the endometrium, P2Y14 is expressed in various other organs, including the kidney, where it is expressed in mucosal epithelial cells of convoluted tubules (supplemental Figure 1(D) of document D1). Expression of P2Y14 in the kidney is confirmed in document D4 (section 3.3 and Figure 2 on page 144 of document D4).

8. From their experimental results, the authors of document D1 draw the following conclusion: "*Given that P2RY14 is expressed in the surface epithelium of various tissues/organs other than the FRT (supplemental Fig. 1), UDP-glucose and P2RY14 may be novel front line players able to trigger innate mucosal immunity in other luminal organs as well*" (see sentence that bridges left- and right-hand columns on page 7082 of document D1). With reference to document D3, they also point to the fact that IL-8 is produced by UDP-glucose via P2Y14 in airway epithelial cells, which supports the posited more general role of UDP-glucose and P2Y14 in mucosal immunity (first full sentence in right-hand column on page 7082 of document D1, reference [20] in this sentence is document D3).

9. Hence, document D1 posits that UDP-glucose and P2Y14 play a general role in inflammation in various mucosal tissues, and specifically highlights the fact that P2Y14 is expressed in mucosal epithelial cells in the kidney. In view of this teaching, the appellant is right that the skilled person would have reasonably expected the UDP-glucose-P2Y14 system also to play a role in mucosal immunity in the kidney (see for example sections 27 to 33 on pages 8 and 9 of the statement of grounds of appeal).

10. Moreover, since this system is triggered by UDP-glucose that is released into the extracellular space by damaged cells, thereby increasing the extracellular UDP-glucose concentration (see paragraph that bridges pages 7081 and 7082 of document D1), the appellant is right that the skilled person would also have expected higher UDP-glucose concentrations to be present in the lumen of the kidney and, as a consequence of the fact that small blood molecules are extracted from the blood

into the urine in the kidney glomeruli, also in the urine of subjects having renal inflammation, compared to that of healthy subjects (see for example sections 39 to 42 on pages 10 and 11 of the statement of grounds of appeal).

11. Starting from the disclosure in document D1, the skilled person, motivated to provide a method for identifying renal inflammation (see point 6. above), arrives at the claimed method in an obvious manner.

12. In the decision under appeal, the opposition division considered that, since many factors might lead to acute kidney injury and the mechanisms of sterile inflammation were unknown, it was unclear whether a diagnostic test for renal inflammation could be based on P2Y14 levels, and that the expression of P2Y14 in normal non-inflamed tissue would not provide the skilled person with any knowledge on whether P2Y14 was expressed differently in inflamed tissue or whether P2Y14-related inflammation played a role in renal inflammation (points 26 to 28 of the decision under appeal). The same considerations applied to UDP-glucose levels in kidney inflammation (point 39 of the decision under appeal).

13. These arguments are not persuasive, however. The claim is not concerned with the detection of a specific type of inflammation such as acute or sterile kidney inflammation or kidney injury. The reference to these specific kidney conditions is thus besides the point, especially since document D1 posits that the UDP-glucose-induced IL-8 release via P2Y14 is a *general* mechanism of innate mucosal immunity in luminal organs (see point 8. above). The fact that P2Y14 is indeed expressed in the kidney is, in the board's view, a

strong pointer that this general mechanism also plays a role in the kidney.

14. Furthermore, the opposition division is right that the expression of P2Y14 in non-inflamed kidney tissue does not provide the skilled person with any knowledge on whether P2Y14 expression is increased in inflamed kidney tissue. However, this is not relevant either, since certainty is not required in matters of assessing inventive step. Rather, the question to be assessed is whether the skilled person would have reasonably expected UDP-glucose to be released and P2Y14 expression to be increased when there is kidney inflammation.

15. As assessed above (see points 7. to 11.), from the teaching in document D1, the skilled person would have reasonably expected UDP-glucose-induced IL-8 release via P2Y14 also to play a role in innate mucosal immunity in the kidney and therefore at least UDP-glucose, which is released into the extracellular space from damaged cells, to be present in higher amounts in the urine of subjects with kidney inflammation than in that of healthy subjects, and that, accordingly, the levels of UDP-glucose in the urine could be used to detect kidney inflammation.

16. The subject-matter of claim 2 of the main request does not involve an inventive step (Article 56 EPC).

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The patent is revoked.

The Registrar: The Chair:

L. Malécot-Grob T. Sommerfeld

Decision electronically authenticated