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Datasheet for the decision of 5 June 2007

Case Number: W 0013/06 - 3.3.04

Application Number: PCT/IB2005/001306

Publication Number: WO 2005/069724

IPC: C07K 14/47

Language of the proceedings: EN

Title of invention:
Novel nucleotide and amino acid sequences, and assays and methods of use thereof for diagnosis of cardiac disease

Applicant:
Compugen LTD.

Opponent:
-

Headword:
Nucleotide and amino acid sequences/COMPUGEN

Relevant legal provisions:
PCT Art. 17(3)(4)
PCT R. 13, 40
EPC Art. 154(3)
EPC R. 105(3)

Keyword:
"Unity of invention (no)"

Decisions cited:
G 0001/89, W 0013/87

Catchword:
-

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Beschwerdekammern | Boards of Appeal | Chambres de recours

Case Number: W 0013/06 - 3.3.04

International Application No. PCT/IB2005/001306

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 5 June 2007

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Decision under appeal: **Protest according to Rule 40.2(c) of the Patent Cooperation Treaty made by the applicants against the invitation (payment of additional fees) of the European Patent Office (International Searching Authority) dated 11 November 2005 .**

Composition of the Board:

Chair: U. Kinkeldey
Members: G. Alt
T. Bokor

Summary of Facts and Submissions

I. International patent application no. PCT/IB2005/001306 published as WO 2005/069724 and having the title "Novel nucleotide and amino acid sequences, and assays and methods of use thereof for diagnosis of cardiac disease" was filed on 27 January 2005 with 37 claims.

Claims 1, 18, 24, and 28 to 32 read as follows:

"1. An isolated polynucleotide comprising a transcript selected from the group consisting of SEQ ID NOs: 22-25, 353 or 386, or a polynucleotide at least about 95% homologous thereto."

"18. A kit for detecting heart disorders, comprising a kit detecting overexpression of a splice variant according to any of claims 1-11."

"24. A method for detecting heart disorders, comprising detecting overexpression of a splice variant according to any of claims 1-11."

"28. A biomarker capable of detecting heart disorders, comprising the nucleic acid sequences or a fragment thereof, or amino acid sequences or a fragment thereof of any of claims 1-12."

"29. A method for screening for heart disorders, comprising detecting heart disorder cells using the biomarkers or antibodies of any of claims 1-12."

"30. A method for diagnosing heart disorders, comprising detecting heart disorder cells using the biomarkers or antibodies of any of claims 1-12."

"31. A method for monitoring disease progression, or treatment efficacy, or relapse of heart disorders, or any combination thereof, comprising detecting heart disorder cells using the biomarkers or antibodies or a method or assay according to any of claims 1-12."

"32. A method of selecting a therapy for heart disorders, comprising detecting heart disorder cells with any of the above biomarkers or antibodies or a method or assay according to any of claims 1-12 and selecting a therapy according to said detection."

II. On 11 November 2005, the European Patent Office (EPO), acting in its capacity as International Searching Authority (ISA) under Article 16 PCT and Article 154 EPC, informed the applicant that the application did not comply with the requirement of unity of invention (Rule 13.1 PCT) and invited the applicant to pay within a time limit of one month forty-three additional search fees, in accordance with Article 17(3)(a) PCT and Rule 40.1. PCT.

III. In the invitation to pay additional fees, the ISA listed the forty-four inventions to which the application related. Inventions 1 and 4 were defined as follows:

"Invention 1: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 22, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides."

"Invention 4: Claims 1 (partially), 18-21 (partially), 24-37 (partially)

Polynucleotides comprising Seq Id Nr 25, kits comprising said polynucleotides and diagnostic and therapeutical applications of said polynucleotides."

The reasons for the finding of non-unity by the ISA were that the single general concept which could be identified as linking together the sequences in the claims was that they were putative variants of troponin I or sequences for use in detecting said variants, and that this concept was not novel because cardiac troponin I variants were already known from the prior art. Reference was made to the passages of the documents of Bhavsar et al., GENOMICS (1996) 35: 11-23, and Toyota et al., J. MUSCLE RES. CELL MOTIL. (1999) 20: 755-760, as indicated in the search report.

Furthermore, the sequences in claim 1 did not seem to share any structural features which were per se novel and inventive, and which could thus constitute for claim 1 a special technical feature in the sense of Rule 13.2 PCT. The nucleotides 1 to 171 which were common to sequence ID Nos: 22 to 25 and 353 were already known from the sequence of cardiac troponin I (TNNI3) disclosed for example in WO-A-01/32927, cited in the search report. Likewise, the region

corresponding to nucleotides 563 to 892 of SEQ ID No: 22 was already known from WO-A-01/32927 and did not constitute, for the sequences in claim 1, a special technical feature in the sense of Rule 13.2 PCT.

In view of the prior art, the problem to be solved by claim 1 was considered to be the provision of further troponin I variants. Each of the sequences claimed in claim 1 constituted an independent solution to this problem. The different solutions did not share a technical relationship involving one or more of the same or corresponding special technical features in the sense of Rule 13.2 PCT. Thus, the requirement of unity of invention referred to in Rule 13.1 PCT was not fulfilled.

Analogous argumentation applied to the remainder of the sequences defined in the claims. The sequences claimed in claims 2 to 14 did not seem to share any structural features which were per se novel and inventive and could thus constitute a special technical feature in the sense of Rule 13.2 PCT.

Hence the ISA considered that the application contained forty-four inventions as identified above.

IV. The communication of 11 November 2005 also contained the results of the partial international search, which was established for the invention first mentioned in the claims, i.e. invention (1) relating to sequence ID NO: 22.

V. On 8 December 2005, the ISA issued a communication to the applicant which made reference to a telephone call of 2 December 2005 and contained information on the protest procedure.

VI. In a letter dated 7 December 2005, the applicant expressed its protest to the ISA's finding that the application related to forty-four inventions. If the examiner continued to maintain that there were forty-four inventions, then the applicant would select invention number four (SEQ ID NO: 25) for prosecution. A cheque covering the protest fee and one additional search fee was enclosed.

The applicant argued that the application related to only one invention and that the examiner was in error with regard to the cited prior art by Bhavsar et al. and Toyota et al., because the "isoforms" which were known referred to different genes, not to splice variants of the same gene. "Troponin I" was not a single gene, but referred to a family of genes, which included genes preferentially expressed in cardiac, slow twitch muscle and fast twitch muscle tissues.

In the document by Bhavsar et al., Table 1 did not show splice variants, but exon/intron boundaries; the splicing sites shown clearly indicated that only one protein product was known for this gene. Similarly, Figure 1 only showed the exon organization, but did not indicate that any splice variants were known. The term "isoform" as used in the document did not refer to a splice variant of a known gene, as the article indicated on page 19, left hand column, last paragraph

that the gene itself was isolated and was therefore new at the time of publication of the article.

In the document by Toyota et al., cardiac and fast skeletal muscle troponin I isoforms were also clearly indicated as separate genes. The term "TnI" again did not refer to a single gene, but rather to a family of genes.

VII. On 21 March 2006, the ISA invited the applicant to pay a protest fee (unless such fee had already been paid) and informed the applicant that a prior review had confirmed that the invitation to pay additional search fees was justified. It was indicated that the fee had already been paid on 9 December 2005.

Reasons for the Decision

1. The protest is admissible.

2. According to Rule 13.1 PCT, the international patent application shall relate to one invention only or to a group of inventions so linked as to form a single inventive concept. If the ISA considers that the claims lack unity of invention, it is empowered, under Article 17(3)(a) PCT, to invite the applicant to pay additional fees.

3. Lack of unity may be directly evident *a priori*, i.e. before the examination of the merits of the claims in comparison with the state of the art revealed by the search (cf., for example, decision W 13/87 of 9 August 1988). Alternatively, having regard to decision G 1/89

of the Enlarged Board of Appeal (OJ EPO 1991, 155), the ISA may also raise an objection *a posteriori*, i.e. after having taken the prior art revealed by the search into closer consideration. The Enlarged Board of Appeal indicated that such consideration represents only a provisional opinion on novelty and inventive step which is in no way binding upon the authorities subsequently responsible for the substantive examination of the application (point 8.1. of the Reasons for the decision). In point 8.2 of the Reasons, the Enlarged Board mentioned that such invitation to pay additional fees should always be made "with a view to giving the applicant fair treatment" and should only be made in clear cases.

4. According to Rule 13.2 PCT, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art.

5. The question to be decided by the board here is whether the subject-matter of those inventions for which search fees have been paid by the applicant, namely inventions (1) and (4) as listed by the ISA (see Section III above), can be considered to be part of the same general inventive concept.

6. Inventions (1) and (4) relate to polynucleotides comprising the sequences of SEQ ID NOs: 22 and 25, respectively, which, according to the description, represent transcripts encoding variants of the known cardiac troponin I protein (see page 230, line 15, to page 231, line 5; page 237, lines 3 to 5; page 238, lines 8 to 10). The sequences were identified by a computational process using the information of EST libraries to find genes and/or splice variants that are specifically expressed in cardiac tissue (page 96, lines 19 to 25).

7. The board agrees to the ISA's finding that cardiac troponin I (CTnI) variants were already known from the prior art. The document by Toyota et al. (cited in the partial international search report contained in the invitation to pay additional fees; see Sections III and IV above) discloses deletion mutants of cardiac troponin containing CTnI amino acid residues 1-79, 43-207 and 80-207 (termed "CTnI-head", "CTnI-tail-1" and "CTnI-tail-2", respectively), which were transiently expressed (see the abstract and Figure 1). DNA corresponding to these variants was prepared by PCR with a previously known cardiac troponin I cDNA as template, and fused into expression vectors (see page 756, right-hand column, paragraph 2).

8. In view of this prior art, the technical problem underlying inventions (1) and (4) was the provision of alternatives to the known variants of cardiac troponin I.

9. As solutions to the above problem, invention (1) provides a polynucleotide comprising the sequence of SEQ ID NO: 22, whereas invention (4) provides a polynucleotide comprising the sequence of SEQ ID NO: 25.

10. The board cannot recognize a structure or effect common to the polynucleotides according to inventions (1) and (4), which could represent a "special technical feature" within the meaning of Rule 13.2 PCT.

11. The board notes that according to the application, the claimed sequences have been obtained using the information of EST libraries, whereas the document by Toyota et al. discloses that the variants of cardiac troponin I were prepared using PCR with a previously known cardiac troponin I cDNA as template. It has also been submitted by the applicant in its letter of protest that splice variants of cardiac troponin I had not been disclosed in the prior art.

Although it is acknowledged by the board that by using a different process, products may be obtained which show distinct features representing traces of their process of manufacture, it is not apparent to the board that in the present case, the process used in the application contributed to the formation of structural elements which are shared by the polynucleotides of SEQ ID NOs: 22 and 25 and which do not also occur in the prior art products.

Therefore, the board must conclude that the solutions to the above technical problem as provided by inventions (1) and (4) do not share a technical relationship involving one or more of the same or

corresponding special technical features in the sense of Rule 13.2 PCT.

12. The applicant has pointed out in its letter of protest that the "isoforms" of troponin I mentioned in the prior art documents by Bhavsar et al. and Toyota et al. referred to different genes preferentially expressed in cardiac, slow twitch muscle and fast twitch muscle tissues, and that the term "isoform" did not refer to splice variants of the same gene.

While this is not disputed, the board notes that this argumentation neither addresses the ISA's reasoning based on the finding that the prior art already disclosed variants of cardiac troponin I, notably the deletion mutants as disclosed in the document by Toyota et al., nor provides any information as to which structural elements not occurring in the variants of the prior art are shared by the polynucleotides of inventions (1) and (4).

As set out in point 11 above, the mere fact that the claimed variants have been obtained by a different process as the variants of cardiac troponin I disclosed in the prior art, cannot, in the present case, establish a unifying link between inventions (1) and (4).

13. Consequently, the international application does not comply with the requirement of Rule 13.1 PCT, and the invitation to pay additional fees with respect to invention (4) was justified.

Order

For these reasons it is decided that:

The protest under Rule 40.2(c) PCT is dismissed.

The Registrar: The Chair:

P. Cremona U. Kinkeldey