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Datasheet for the decision of 30 May 2017

Case Number: T 0470/14 - 3.3.04

Application Number: 09153790.2

Publication Number: 2172476

IPC: C07K14/00, C07K11/00, C07K7/00, A61K48/00

Language of the proceedings: EN

Title of invention:
Compositions and methods for WT1 specific immunotherapy

Applicant:
Corixa Corporation

Headword:
Immunotherapy/COREXIA

Relevant legal provisions:
EPC Art. 76(1), 111(1)

Keyword:
Extension beyond content of earlier application as filed - (no)
Remittal to the department of first instance - (yes)

Decisions cited:
G 0001/05, G 0001/06

Catchword:

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Case Number: T 0470/14 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 30 May 2017

Appellant: (Applicant)	Corixa Corporation CSC, The United States Corporation 2711 Centerville Road Wilmington, DE 19808 (US)
Representative:	Walker, Ross Thomson Forresters IP LLP Skygarden Erika-Mann-Strasse 11 80636 München (DE)
Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 28 October 2013 refusing European patent application No. 09153790.2 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chairwoman	G. Alt
Members:	B. Claes
	M. Blasi

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application No. 09 153 790.2, published as EP-A-2 172 476. The application has the title "*Compositions and methods for WT1 specific immunotherapy*" and is a divisional application of earlier European patent application No. 02 797 061.5, which was filed as international application PCT/US02/35194 and published as WO03/037060 (hereinafter "the earlier application").

II. Claim 1 of the application as filed read:

"1. A fusion protein comprising an immunogenic portion of a Wilms' tumor (WT1) antigen and a fusion partner, wherein said fusion partner consists of the amino acid sequence SEQ ID NO:506."

Claims 2, 4, 5 and 8 to 11 were likewise independent claims which directly or indirectly referred to the fusion protein of claim 1.

III. In the decision under appeal, the examining division held that the earlier application as filed contained a basis for a fusion protein comprising SEQ ID NO:506 combined with particular portions of the WT1 antigen but not with any immunogenic portion thereof. Therefore, the subject-matter of claim 1 and of claims 2 to 11 - all referring to the fusion protein of claim 1 - extended beyond the content of the earlier application as filed (Article 76(1) EPC).

IV. The applicant (hereinafter "appellant") argued that the decision of the examining division was incorrect because the claimed subject-matter was disclosed in the earlier application as filed when read as a whole.

V. Oral proceedings before the board took place on 30 May 2017. As announced beforehand, nobody was present on behalf of the appellant. At the end of the oral proceedings the Chairwoman announced the decision.

VI. The appellant had requested in writing that the decision under appeal be set aside and that the case be remitted to the examining division for further prosecution.

Reasons for the Decision

1. The appeal is admissible.

2. The duly summoned appellant did not attend the oral proceedings. In accordance with Rule 115(2) EPC and Article 15(3) RPBA the board decided to continue the proceedings in the appellant's absence.

Added subject-matter (Article 76(1) EPC) - claim 1

3. In the decision under appeal the examining division held that the earlier application as filed contained no basis for a fusion protein comprising any immunogenic portion of the Wilms' tumor (WT1) antigen *in general* and SEQ ID NO:506, *i.e.* the subject-matter of claim 1 (see section II).

4. The finding of the examining division was based, in essence, on the sole two references in the earlier application as filed to the amino acid sequence of

SEQ ID NO:506, *i.e.* the sequence of the truncated twin arginine translocation (TAT) signal peptide. The first reference was in claim 10 of the earlier application as filed and was for a fusion protein comprising SEQ ID NO:506 as one fusion partner and a polypeptide according to claims 1, 2 or 4 as the other partner, whereby claims 1, 2 and 4 defined *particular immunogenic portions* or particular variants of the WT1 antigen. The second reference in example 38 of the earlier application as filed related to the fusion of the truncated TAT having the SEQ ID NO:506 to a *particular N-terminal portion* of the WT1 antigen.

5. The examining division held therefore that a basis could be identified for fusion proteins of SEQ ID NO:506 with *particular fusion partners*, however not for fusions of any immunogenic portion of the WT1 antigen to the truncated TAT signal peptide having sequence SEQ ID NO:506. This claimed subject-matter thus extended beyond the content of the earlier application as filed, contrary to Article 76(1) EPC.

6. The board agrees with the examining division to the extent that in the claims and in example 38 of the earlier application as filed, *i.e.* the parts which mention SEQ ID NO:506, no literal basis can be identified for the wording of claim 1.

7. However, in order for the subject-matter of claim 1 to comply with Article 76(1) EPC such a literal basis is not required. In fact, it has rather been established in the case law of the boards that the subject-matter of a divisional application must be **directly and unambiguously derivable** from the earlier application as filed (see decision G 1/06, OJ EPO 2008, 307, e.g. headnote). The "content" of the earlier application as

filed within the meaning of Article 76(1) EPC concerns the whole technical content of this application (see decision G 1/05, OJ EPO 2008, 271, point 9.2 of the Reasons).

8. The board considers the content of the following passages referred to in the general part of the description in the earlier application as filed relevant to determine whether the claimed subject-matter constitutes added subject-matter (in the following citations all the emphases are added by the board).

8.1 In the section "*Field of the Invention*" (see description, page 1, lines 9 to 13), it is stated that: "*The present invention relates generally to the immunotherapy of malignant diseases such as leukemia and cancers. The invention is more specifically related to* ***compositions for generating or enhancing an immune response to WT1****, and to the use of such compositions for preventing and/or treating malignant diseases.*"

8.2 On page 2, lines 10 to 20, the section "*Brief summary of the invention*" starts with: "*Briefly stated, this invention provides compositions and methods for the diagnosis and therapy of diseases such as leukemia and cancer.* ***In one aspect, the present invention provides polypeptides comprising an immunogenic portion of a native WT1****, or a variant thereof that differs in one or more substitutions, deletions, additions and/or insertions such that the ability of the variant to react with the antigen-specific antisera and/or T-cell lines or clones is not substantially diminished. Within certain embodiments of the present invention, the polypeptide comprises at least an immunogenic portion of WT1 wherein the immunogenic portion is contained*

within amino acids 2-281 of WT1." The passages that follow specify certain examples of immunogenic portions of WT1 and variants thereof.

8.3 On page 15 of the description in the section entitled, "*Detailed description of the invention*" (lines 11 to 13) it is furthermore stated that: "*WT1 Polypeptides of the present invention generally comprise at least a portion of a Wilms' Tumor gene product (WT1) or a variant thereof.*" and in lines 22 to 25: "*The present invention is based on the discovery that* ***an immune response raised against a Wilms Tumor (WT) gene product*** *(e.g., WT1) can provide prophylactic and/or therapeutic benefit for patients afflicted with malignant diseases characterized by increased WT1 gene expression.*"

8.4 The board considers that the passages in the earlier application as filed cited above thus identify, as a primary aim of the invention, the provision of polypeptides which comprise any immunogenic portion of WT1 or variants thereof - without the origin thereof being limited to a particular region of the WT1 protein - in order to provide prophylactic and/or therapeutic benefit for patients afflicted with diseases related to WT1 gene expression.

8.5 On page 16, in line 4, a section of the description of the earlier application as filed with the heading "*WT1 Polypeptides*" begins with: "*Within the context of the present invention, a WT1 polypeptide is a polypeptide that comprises at least* ***an immunogenic portion of a native WT1*** *(i.e., a WT1 protein expressed by an organism that is not genetically modified), or a variant thereof, as described herein. A WT1 polypeptide may be of any length, provided that it comprises at least an immunogenic portion of a native protein or a*

variant thereof." and continues in lines 25 to 27 as follows: "***Polypeptides as provided herein may further be associated (covalently*** *or noncovalently****) with other polypeptide*** *or non-polypeptide compounds.*" In this context "Immunogenic portion" is then defined starting on line 28 of page 16: "An "*immunogenic portion", as used herein is a portion of a polypeptide that is recognized (i.e., specifically bound) by a B-cell and/ or T-cell surface antigen receptor. Certain preferred immunogenic portions bind to an MHC class I or class II molecule.*"

8.6 The board considers that this section taught the skilled person that a WT1 polypeptide in accordance with the invention comprised at least one immunogenic portion of WT1 which could be associated with other polypeptides.

8.7 On page 21, lines 11 to 17, the earlier application as filed refers to conjugation of WT1 polypeptides: "*As noted above, **WT1 polypeptides may be conjugated to a signal (or leader) sequence at the N-terminal end of the protein which co-translationally or post-translationally directs transfer of the protein.** A polypeptide may also, or alternatively, be conjugated to a linker or other sequence for ease of synthesis, purification or identification of the polypeptide (e.g., poly-His), or to enhance binding of the polypeptide to a solid support. For example, a polypeptide may be conjugated to an immunoglobulin Fc region.*"

8.8 Fusion proteins are explicitly mentioned starting on page 23, lines 16 to 19: "*Within other illustrative embodiments, a polypeptide may be a fusion polypeptide that comprises multiple polypeptides as described*

herein, or ***that comprises at least one polypeptide as described herein and an unrelated sequence,*** *such as a known tumor protein.*" What follows are passages listing a variety of utilities for the particular added fusion partners and methods for producing such. Page 25, lines 3 to 7, states: "*The fusion polypeptide can comprise a polypeptide as described herein together with an unrelated immunogenic protein* [...]. *Examples of such proteins include tetanus, tuberculosis and hepatitis proteins* [...]." From page 25, line 8 to page 27, line 5, reference is then further made to particular examples of immunological fusion partners. In the passage on page 27, lines 6 to 8 it is then stated: "*Within another illustrative embodiment the fusion partner comprises a twin arginine translocation (TAT)* ***signal peptide*** *from the TorA signal peptide in E. coli on the N-terminus;* [...]." And lastly, in the next paragraph on page 27 reference is then made to other particular **targeting signals** useful as fusion partners (see page 27, lines 12 to 18).

9. The board concludes therefore that the general part of the description of the earlier application as filed clearly and unambiguously discloses in a general manner fusion proteins composed of i) any immunogenic portion of a WT1 antigen; and ii) a fusion partner consisting of a useful peptide.

10. For both of these generally defined binding partners in the fusion protein the earlier application as filed discloses examples in the general description. The example section of the earlier application as filed also indicates such binding partners.

10.1 Page 86, starting in line 20, clarified in general that: "*The following Examples are offered by way of illustration and not by way of limitation.*" An example of a fusion partner consisting of a useful peptide, i.e. a particular signal peptide is then given in Example 34, starting on page 173, which is entitled "*WT1 Expression Constructs Using Twin Arginine Translocation (TAT) Signal Peptide*". The example begins by stating (page 173, lines 24 to 26): "*This example describes the construction of WT1-TAT vectors and expression of WT1-TAT from these vectors. These constructs have utility in the expression of WT1-TAT molecules for the use in vaccination strategies.*"

10.2 Example 38, on page 182, entitled "*Construction of the Stumpy-WT1-F Vector for the Expression of WT-1F in E. coli*", introduces the skilled person to the "Stumpy" WT1-F vector (lines 12 to 28): "*This example describes the construction of an expression vector* ***containing a truncated twin arginine translocator (TAT) signal peptide fused to the WT1-F reading frame*** *(2-281 N-terminal portion of the WT1 protein). This vector can be used to produce a single species truncated TAT-WT1-F protein for use in immunization strategies for the treatment of malignancies associated with expression of WT1. As described previously in Example 34, the TAT signal sequence was used to make various WT1 vectors. When these TAT vectors were used in expression, multiple forms of the protein were observed. N-terminal sequencing of these forms showed that each of the three separate proteins being expressed were truncations of the TAT peptide. These cleavages were occurring at each of the twin arginine sites.* ***Thus, a truncated TAT vector was constructed to shorten the TAT signal peptide from 39 amino acids to 12 amino acids to avoid generation of these cleavage products during***

expression. *The TAT "Stumpy" vector was generated by maintaining the first 12 residues of the TAT signal peptide up to the first twin arginine. This vector was constructed as follows:* [...]". Then, on page 183, line 11, SEQ ID NO:506 is identified contextually as a TAT signal peptide, albeit truncated. This is also corroborated by claims 8 to 10 of the earlier application as filed. In fact, it is clear from Example 38 that, in one aspect of the invention, it was preferable to include a fusion protein which had a truncated version of the TAT signal, *i.e.* SEQ ID NO:506.

11. The board considers that the earlier application as filed in the passages and section referred to above, rather than inextricably linking the disclosure of the truncated version of the TAT signal peptide, *i.e.* SEQ ID NO:506, to the exemplified WT1-F reading frame (*i.e.* the 2 to 281 N-terminal portion) of the WT1 protein, discloses that SEQ ID NO:506 is a generally useful signal peptide in fusions because it retains the required signal activity while avoiding the generation of particular cleavage products during expression when using the complete TAT signal in *E. coli*. Accordingly, the board considers the disclosure of the signal peptide with the sequence SEQ ID NO:506 as a particular example of the second fusion partner ii) referred to in point 10 above.

12. In view of the above considerations, the board is satisfied that there is clear and unambiguous disclosure in the earlier application as filed of a fusion protein having a) any immunogenic portion of a WT1 antigen; and b) a fusion partner comprising SEQ ID NO: 506.

13. The board accordingly concludes that the requirements of Article 76(1) EPC are fulfilled.

14. The sole reason for refusing the application was that it was found not to comply with Article 76(1) EPC. The examining division has not expressed any opinion on the other substantive patentability requirements under the EPC. Under these circumstances, and in view of the of the appellant's request, the board considers it appropriate to remit the case to the examining division for further prosecution in accordance with Article 111(1), second sentence, EPC.

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 for further prosecution.

The Registrar: The Chairwoman:

P. Cremona G. Alt

Decision electronically authenticated