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Datasheet for the decision of 14 September 2011

Case Number: T 0840/07 - 3.3.04

Application Number: 02777137.7

Publication Number: 1430084

IPC: C07K 14/705, A61K 38/18, A61P 37/06

Language of the proceedings: EN

Title of invention:
Peptides capable of modulating immune response

Applicant:
CellAct Pharma GmbH

Headword:
Immunomodulatory peptide/CELLACT PHARMA

Relevant legal provisions:
EPC Art. 82
EPC R. 44(1), 103(1)(a)

Relevant legal provisions (EPC 1973):
-

Keyword:
"Unity of invention (yes)"
"Remittal (yes)"
"Reimbursement of appeal fee (no)"

Decisions cited:
-

Catchword:
-

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Case Number: T 0840/07 - 3.3.04

D E C I S I O N
of the Technical Board of Appeal 3.3.04
of 14 September 2011

Appellant: (Applicant)
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Decision under appeal:
Decision of the Examining Division of the European Patent Office posted 7 December 2006 refusing European patent application No. 02777137.7 pursuant to Article 97(2) EPC.

Composition of the Board:

Chairman: C. Rennie-Smith
Members: B. Claes
R. Gramaglia

Summary of Facts and Submissions

I. The appeal lies from the decision of the examining division to refuse European patent application 02777137.7, published as WO 03/025000. The decision is on the application as filed with amended claims 1-10 of a main and auxiliary request both filed with a letter of 27 October 2006.

Claim 1 of the main request read:

"1. **An immunomodulatory peptide** of up to 50 amino acid residues comprising a fragment of the amino acid sequence of HLA-(Human Leukocyte associated Antigen) class II alpha 2 chain, said peptide comprising or consisting of an amino acid sequence shown in SEQ ID NO:3 or SEQ ID NO:4, or a fragment of at least 6 consecutive amino acids thereof wherein said peptide is capable of inhibiting proliferation of peripheral blood mononuclear cells (PBMCs)." (*emphasis added by the board*)

Claim 1 of the auxiliary request read:

"1. **An immunomodulatory peptide** of up to 50 amino acid residues comprising a fragment of the amino acid sequence of HLA-(Human Leukocyte associated Antigen) class II alpha 2 chain, said peptide comprising or consisting of (i) an amino acid sequence shown in SEQ ID NO:3 or SEQ ID NO:4; (ii) a fragment of at least 10 consecutive amino acids of(i), or (iii) an amino acid sequence of (i) or (ii) containing conservative amino acid substitutions, wherein said peptide is capable of inhibiting proliferation of peripheral blood

mononuclear cells (PBMCs)." (*emphasis added by the board*)

II. The examining division refused the application for the sole reason that the claims lacked unity within the meaning of Article 82 EPC for the following reasons:

Claim 1 of the request before the examining division, defined chemical alternatives, i.e. a so-called Markush grouping, and unity of invention should be considered to be present if the alternatives are of a similar nature.

The problem underlying the application resided in the provision of compounds for the inhibition of an immune response. As a solution, peptides derived from HLA-class II alpha 2 chain, up to 50 amino acids long, were provided. The technical feature which *a priori* could be considered to unify different solutions was thus a peptide derived from HLA-class II alpha 2 chain being up to 50 amino acids long.

However, such a solution had already been proposed in prior art document (D2), i.e. US 5,827,516, which disclosed a 23-mer peptide derived from the HLA-class II alpha 2 chain corresponding to amino acids 158-180 of SEQ ID NO:1 of the application. The peptide was useful for therapeutic intervention in disease conditions characterized by autoreactivity, such as rheumatoid arthritis or multiple sclerosis, and might also be used to reduce transplant rejection (see (D2) SEQ ID NO: 231, table 8 and column 2).

The objective problem to be solved was therefore the provision of further peptides derived from the HLA-class II alpha 2 chain that are up to 50 amino acids long. While peptides of SEQ ID NO:3 and 4 had a common activity or property, i.e. the inhibition of the proliferation of peripheral blood mononuclear cells and the inhibition of the proliferation of immune cells respectively, a significant structural element shared by both peptides, which could fulfil the role of a "special technical feature" in the sense of Rule 30(1) EPC 1973, was missing. There was no common amino acid sequence motif present in SEQ ID NO:3 and 4 that might be considered as a significant structural element that was shared by said peptide and that could link both peptides together. As there were no other special technical features, inventions (1) and (2), directed to peptides of SEQ ID NO:3 and SEQ ID NO:4 respectively, were not so linked as to form a single general inventive concept (Rule 30(2) EPC 1973).

The examining division noted that an additional search on 30 October 2006 had revealed several documents that were "detrimental to the issue of novelty" and cited three specific documents. The examining division specified however that the application was not refused under Article 54(1) and (2) EPC vis-à-vis these documents, because the applicant had had no chance to comment on the objection.

The examining division was furthermore of the opinion that the applicant was given sufficient opportunity in writing and by telephone to file a request that met the requirements of the EPC and decided not to issue a

further communication or to telephone the applicant again prior to the oral proceedings.

III. The appellant filed a new main request with the notice of appeal dated 16 February 2007 and two auxiliary requests with the statement of grounds of appeal dated 17 April 2007.

Claim 1 of the new main request read:

"1. **Use of a peptide** of up to 100 amino acid residues, wherein said peptide is capable of inhibiting proliferation of peripheral blood mononuclear cells (PBMCs), and having at least 6 consecutive amino acids of the amino acid sequence of HLA-(Human Leukocyte associated Antigen) class II alpha 2 chain, **for the preparation of a pharmaceutical composition for inhibition of an immune response** by interfering with the interaction of TIRC7 with its ligand." (*emphasis added by the board*)

IV. The board summoned the appellant for oral proceedings to take place on 14 September 2011.

V. Further arguments were filed by the appellant with a letter dated 30 May 2011. On 12 September the appellant informed the board that it would not attend the oral proceedings.

VI. The appellant (applicant) requested that the decision under appeal be set aside and a patent be granted on the basis of the main request filed with the notice of appeal dated 16 February 2007 or on the basis of the first or second auxiliary requests filed with the

statement of grounds of appeal dated 17 April 2007. The appellant requested furthermore reimbursement of the appeal fee.

VII. The appellant's arguments as far as they are relevant for the present decision can be summarised as follows:

Unity of invention

The decision held erroneously that a technical feature in the sense of Article 82 and Rule 30(2) EPC 1973 had to be a "significant structural element" in the form of a common amino acid sequence motif. This was apparently also the reason for rejecting the auxiliary request, which had been filed with a letter of 4 September 2006 in response to the summons to attend oral proceedings and which was now the main request in the appeal proceedings (cf. result of consultation of 23 October 2006).

Document (D2) taught to solve the problem of inhibiting an undesired immune response by introducing **into**, or intracellularly expressing **in**, antigen presenting cells (APC) of a patient a sort of self-peptides, which were assumed to prevent association of the MHC class II alpha/beta chain complex. The blocking peptides of document (D2) therefore specifically blocked the binding of immunogenic peptides **inside** APCs by binding to the well defined peptide-binding pockets of the MHC class I or II molecules resulting in MHC molecule/blocking peptide complexes which were only subsequently expressed on the cell surface of APCs.

In contrast, the peptides of the invention were required to interact with TIRC7 in order to prevent its interaction with its natural ligand (see description e.g. page 3, line 27 to page 4, line 12). The peptides of the present invention and those disclosed in (D2) were directed towards different sites of pharmacological action.

The claims of the main request before the board now were "use" claims, contrary to the claims underlying the impugned decision. The purpose of the use of the peptides was now explicitly the "preparation of a pharmaceutical composition for inhibition of an immune response *by interfering with the interaction of TIRC7 with its ligand*"(*emphasis added by the board*). This feature was common to all peptides and specific sequences described in the claims.

Neither document (D2), nor any other cited prior art document, did indicate or suggest any interference between the peptides and TIRC7.

The novel and inventive feature of the present invention was the effect that the peptides were characterized by the functional feature of being capable of interfering with the interaction of TIRC7 with its ligand. This was now explicitly reflected in the claims and was thus to be considered to constitute the contribution of the claimed invention as a whole over the prior art. Consequently, it was not only novel and inventive over the prior art including document (D2) but also a "special technical feature" in the sense of Rule 30(1) EPC 1973, second sentence.

This special technical feature, i.e. the capability of interfering with the interaction of TIRC7 with its ligand, was also present if the peptides base amino acid sequence of HLA class II alpha 2 chain was further defined by reference to either of SEQ IDs NO: 3 and 4. Consequently, the requirements of Article 82 and Rule 30 EPC were fully met.

Reimbursement of the appeal fee

The reimbursement of the appeal fee pursuant to Rule 67 EPC 1973 (now Rule 103(1)(a) EPC) was equitable by reason of a substantial procedural violation.

The applicant had been adversely affected by the manner in which the examination proceedings had been conducted. Although the applicant made every effort to comply with each communication, the examining division "went on throwing spanner [*sic*] in the works" so that the application had to fail.

After the applicant had dealt with the unsubstantiated objections against the breadth of the claims in the second communication, the examining division took the applicant by surprise by summons to oral proceedings with an annexed communication introducing for the first time document (D2) as the justification for the oral proceedings and another "reason" for rejection of the application. The applicant filed two new sets of claims with its letter of 4 September 2006, asked for the examination to be continued in writing and for a telephone discussion of any minor issues, but requested oral proceedings in the examination division considered refusal of the application.

In the subsequent first telephone consultation on 23 October 2006, the applicant's representative explained that the summons to attend oral proceedings was premature and allowance should be made for the applicant's limited resources. No reason was given why the requests filed on 4 September 2006 were bad. The primary examiner refused to cancel the oral proceedings and to continue the proceedings in writing and gave the applicant until 27 October 2006 to file new sets of claims. The applicant's representative filed an amended second auxiliary request on 26 October 2006 and a further telephone consultation took place on 27 October 2006 in which he was told that this request was inadmissible and he was given a last chance to file amended claims by 16.00 hours on that date.

The present appeal proceedings would not have been necessary if only the examining division would have conformed to the usual practice in the EPO and discussed the substantive issues in a sensible or at least reasonable way. In any case, the unjustified summons to attend oral proceedings on the grounds of a newly-introduced document on which the applicant had not been given a previous opportunity to comment during the written proceedings alone amounted to a substantial procedural violation, not to mention the attitude of the primary examiner with respect to applicant's attempts to cancel the oral proceedings.

The examining division had deprived the applicant of fair and reasonable proceedings by its piecemeal delivery of objections and cited documents, culminating in the issue of the summons to attend oral proceedings

for reason of a document, i.e. document D2, which had not been considered before and had not been cited in the search report. This amounted to a substantial procedural violation, in particular in view of the fact that the objections raised in the previous communications of the examining division had all been dealt with by the applicant.

Moreover, in response to the summons to attend oral proceedings, the examining division was respectfully requested to grant the applicant at least one further opportunity to continue the substantive examination in writing because of the newly cited document (D2). However, contrary to the well-established principle to provide an applicant sufficient opportunities to address the objections raised by the examining division for the first time, the examining division simply stated that it "does not want to cancel the oral proceedings and does not want to continue the procedure in writing" (result of telephone conversation of 23 October 2006).

As can be inferred from the subsequent result of consultation of 27 October 2006, the opportunity given by the examining division to the applicant to file a new set of claims on short notice only and of having a further telephone interview was not quite helpful and at last resulted in the contested decision.

VIII. Oral proceedings were held on 14 September 2011. The representative of the appellant had informed the board on 12 September 2011 that she would not attend the oral proceedings.

Reasons for the Decision

Unity of invention

1. Pursuant to Article 82 EPC the European patent application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept. Rule 44(1) EPC gives an interpretation of the concept of unity of invention where a group of inventions is claimed. In such cases 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, i.e. those features which define a contribution which each of the claimed inventions as a whole makes over the prior art.

2. 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; alternatively a lack of unity may follow from an objection *a posteriori*, i.e. after having taken the prior art revealed by the search into closer consideration.

3. The examining division has reasoned its finding of lack of unity of invention based on an objection *a posteriori*. It found in the impugned decision in the context of the subject-matter of the claims before them that document (D2) discloses a peptide having SEQ ID NO:231 which would read on the structure as defined for the claimed peptides. It then argued that although the claimed peptides had a **common activity or property**, i.e.

the inhibition of the proliferation of peripheral blood mononuclear cells, a significant structural element shared by the peptides (in the case of the requests before the examining division having or being derived from peptides having the sequence SEQ ID NO:3 and 4) was missing which could fulfil the role of a special technical feature in the sense of Rule 30(1) EPC 1973 since there was no **common amino acid sequence motif** present in the two specifically recited peptide sequences.

4. Claim 1 of the main request now before the board is, contrary to the "product"-format of the claims before the examining division (see section I), drafted in a "medical use" format, i.e. in the so-called Swiss-type claim format and concerns the use of a peptide of up to 100 amino acid residues which (i) is capable of inhibiting proliferation of peripheral blood mononuclear cells and (ii) has at least 6 consecutive amino acids of the amino acid sequence of HLA-class II alpha 2 chain, for the preparation of a pharmaceutical composition for **inhibition of an immune response by interfering with the interaction of TIRC7 with its ligand** (see section III; *emphasis added by the board*).

5. The question to be examined is therefore whether the subject-matter of claim 1, the uses of a variety of peptides, lacks unity of invention in view of the disclosure of document (D2).

6. Document (D2) discloses as a solution to the problem of inhibiting an undesired immune response to introduce **into,** or express intracellularly **in,** antigen presenting cells (APC) of a patient a kind of self-peptides,

including the specific peptide having the SEQ ID NO:231, which are assumed to prevent association of the major histocompatibility complex (MHC) class II alpha/beta chain complex, whereby the class II molecule/blocking peptide complex subsequently might be expressed on the cell surface without eliciting an immune response (see document (D2) e.g. column 2, lines 43-60 and column 3, lines 10-12 and the examples which are clearly restricted to the delivery of the peptides into APCs). The system disclosed in document (D2) ensures "*that peptides are produced only* ***within*** *cells, and are not present outside the cells where they could stimulate antibody production by contact with B cells*" (emphasis added, see document (D2), column 3, lines 46-49). The blocking peptides of document (D2) therefore specifically block the binding of immunogenic peptides **inside** of APCs by binding to the well-defined peptide-binding pockets of the MHC class I or II molecules resulting in MHC molecule/blocking peptide complexes which were only subsequently expressed on the cell surface of APCs.

7. The board considers that the peptide with SEQ ID NO:231 disclosed in document (D2) reads on to the structural definition of the peptides as defined in the wording of claim 1 of the main request before it. Furthermore, the board accepts that the peptides disclosed in document (D2) are used for inhibiting the immune response. The claimed subject-matter and the disclosure in document (D2) therefore address the same problem of providing peptides for inhibiting an immune response.

8. In contrast to the peptides of document (D2) however, the claimed invention is based on the finding that

peptides derived from HLA-class II alpha 2 chain interfere with the interaction of TIRC7 with its ligand, thereby resulting in inhibiting an immune response. The therapeutic use of the peptides of the invention is thus characterised by their property of interfering with the interaction of TIRC7 with its ligand. However, the use of the peptides disclosed in document (D2) is based on an interaction of these peptides within the cells where they would not be available for interaction with TIRC7.

9. The board therefore agrees with the appellant that the peptides as defined in claim 1 of the main request now before the board and those as disclosed in document (D2) are directed towards different sites of pharmacological action and that document (D2) neither discloses nor suggests such peptides having the functionality property of interfering with the interaction of TIRC7 with its ligand. The various peptides as now defined in claim 1 of the main request before the board are therefore equally functionally defined so that there is a technical relationship between them which defines a contribution over the prior art, i.e. a "special technical feature in the sense of Rule 44(1) EPC.

10. The board notes that the above finding renders it unnecessary for the board to examine whether or not the "common activity or property" as identified by the examining division of the peptides in the claims before it, i.e. the inhibition of the proliferation of peripheral blood mononuclear cells, could serve as a special technical feature in the sense of Rule 44(1) EPC or whether or not the mere lack of a "common amino acid sequence motif" between the specific peptides

recited in the claims before the examining division could form the basis for denying unity of invention.

11. Accordingly, the board considers the claims of the main request before it to comply with the requirements of unity of invention pursuant to Article 82 EPC.

Reimbursement of the appeal fee

12. The appellant's complaints about the examining division's conduct of the examination proceedings are understandable but inconsistent. It is clear that the appellant wished to avoid the cost of attending oral proceedings but none the less requested oral proceedings if (as was the case) the examining division considered refusing the application. The specific complaint of a substantial procedural violation by the introduction of document (D2) into the proceedings with the summons to attend oral proceedings cannot, in the board's view, be correct. The examining division is entitled to identify additional prior art and to raise objections based on it. Contrary to the appellant's argument, it did have time to consider the new document - the summons was issued on 2 June 2006 and the applicant replied in writing on 4 September 2006.

13. One aspect of the proceedings which the appellant does not specifically criticise but which troubles the board is the exceedingly short deadlines imposed by the examining division in the telephone consultations for filing further requests before the oral proceedings - on 23 October 2006 a deadline of 27 October 2006, and on 27 October 2006 a deadline of 16.00 hours the same day. It is notable that on both occasions the applicant

met those deadlines but they were clearly both far too short to allow a representative to consult his client, take adequate instructions and draft and file new requests.

14. The impression the objective reader obtains from reading the file of the examination proceedings is of mutual frustration. On one side the examining division wanted to bring the proceedings to a conclusion and, after three rounds of communications and replies and two telephone consultations shortly before the oral proceedings, both followed by further written submissions, it clearly considered the oral proceedings necessary to provide that conclusion. On the other side, the applicant wanted to avoid oral proceedings to save costs and, if necessary, would not attend oral proceedings for costs reasons. If maintained, as they were, those attitudes were irreconcilable.

The appellant's submission that the present appeal could have been avoided if the examining division had allowed further discussion is wholly speculative. Moreover, and the deciding factor, the appellant's request which has succeeded in this appeal is the same as the main request which it filed on 4 September 2006 and later replaced. It did not pursue that request to the point where it became the subject of a decision. Thus the appellant had no choice but to appeal if it wanted the result it has now obtained. To reimburse the appeal fee would give the appellant a fee-free appeal which would be inequitable. The request for reimbursement must accordingly be refused.

Remittal of the case to the department of first instance

15. The present application was refused on the sole ground that the claimed subject-matter lacked unity of invention (Article 82 EPC). It can be taken from the history of the examination procedure and from the impugned decision itself that the examining division has not come to a final opinion concerning the substantial patentability requirements. Accordingly, the board considers it appropriate to remit the present case to the examining division for further prosecution on the basis of the application documents that formed the basis for the present decision.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the department of first instance for further prosecution on the basis of claims 1 to 10 of the main request filed with the notice of appeal dated 16 February 2007.

3. The request for reimbursement of the appeal fee is refused.

The Registrar The Chairman

P. Cremona C. Rennie-Smith