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**Datasheet for the decision
of 2 May 2019**

Case Number: T 2114/14 - 3.3.04

Application Number: 09717471.8

Publication Number: 2235043

IPC: C07K14/00, A61K39/00

Language of the proceedings: EN

Title of invention:

Self-assembling peptide nanoparticles useful as vaccines

Applicant:

Alpha-O Peptides AG

Headword:

Self-assembling peptide nanoparticles/ALPHA-O PEPTIDES

Relevant legal provisions:

EPC Art. 84

Keyword:

Claims - clarity: main request, auxiliary requests 1 to 4 (no)

Decisions cited:

T 0068/85, T 0560/09

Catchword:



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Case Number: T 2114/14 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 2 May 2019

Appellant: Alpha-O Peptides AG
(Applicant) Lörracherstrasse 50
4125 Riehen (CH)

Representative: Latscha Schöllhorn Partner AG
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Decision under appeal: **Decision of the Examining Division of the
European Patent Office posted on 16 June 2014
refusing European patent application No.
09717471.8 pursuant to Article 97(2) EPC.**

Composition of the Board:

Chair G. Alt
Members: R. Morawetz
L. Bühler

Summary of Facts and Submissions

- I. The appeal of the applicant ("appellant") lies against the decision of the examining division refusing European patent application No. 09 717 471.8, which was filed as international application PCT/EP2009/050996 and published as WO 2009/109428 ("application").
- II. In the decision under appeal, the examining division held that the set of claims of the main request and of auxiliary request 1 before it lacked clarity (Article 84 EPC).
- III. With the statement of grounds of appeal, the appellant filed a main request and auxiliary requests 1 to 4.

Claim 1 of the main request reads as follows:

"1. A self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula (I) consisting of a continuous chain comprising a peptidic oligomerization domain D1, a linker segment L, and a peptidic oligomerization domain D2

D1-L-D2 (I),

wherein D1 is a peptide having a tendency to form oligomers (D1)_m of m subunits D1, D2 is a peptide having a tendency to form oligomers (D2)_n of n subunits D2, m and n each is a figure between 2 and 10, with the proviso that m is not equal n and not a multiple of n, and n is not a multiple of m, L is a bond or a short linker segment consisting of 1 to 6 amino acids, **either D1 or D2 or both D1 and D2 is a coiled-coil that incorporates one or more helper T lymphocyte epitopes (HTL epitopes) and/or cytotoxic T lymphocyte epitopes**

(CTL epitopes) within the oligomerization domain, and wherein D1 and D2 are optionally further substituted; wherein a HTL epitope is a peptide measured by biophysical methods or predicted by NetMHCIIpan to bind to any of the MHC II molecules with IC50 values better than 50 nM; and a CTL epitope is a peptide measured by biophysical methods or predicted by NetMHCpan to bind to any of the MHC I molecule with IC50 values better than 50 nM." [emphasis added]

Claim 1 of auxiliary request 1 reads as follows:

"1. A self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula (I) consisting of a continuous chain comprising a peptidic oligomerization domain D1, a linker segment L, and a peptidic oligomerization domain D2

D1-L-D2 (I),

wherein D1 is a peptide having a tendency to form oligomers (D1)_m of m subunits D1, D2 is a peptide having a tendency to form oligomers (D2)_n of n subunits D2, m and n each is a figure between 2 and 10, with the proviso that m is not equal n and not a multiple of n, and n is not a multiple of m, L is a bond or a short linker segment consisting of 1 to 6 amino acids, either D1 or D2 or both D1 and D2 is a coiled-coil that incorporates one or more helper T lymphocyte epitopes (HTL epitopes) and/or cytotoxic T lymphocyte epitopes (CTL epitopes) within the oligomerization domain, and wherein D1 and D2 are optionally further substituted; wherein a HTL epitope is a peptide measured by biophysical methods or predicted by NetMHCIIpan to bind to any of the MHC II molecules with IC50 values better than 50 nM; and a CTL epitope is a peptide measured by

biophysical methods or predicted by NetMHCpan to bind to any of the MHC I molecule with IC50 values better than 50 nM; and the HTL and/or CTL epitope is incorporated into the coiled-coil domain by aligning the sequence of the HTL and/or CTL epitope with the coiled coil heptad repeat pattern such that this domain is predicted by the coiled coil prediction program COILS to form a coiled coil with higher probability than 0.9 for all its amino acids with at least one of the window sizes 14, 21 or 28." [emphasis added]

Claim 1 of auxiliary request 2 reads as follows:

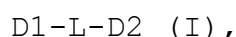
"1. A self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula (I) consisting of a continuous chain comprising a peptidic oligomerization domain D1, a linker segment L, and a peptidic oligomerization domain D2

D1-L-D2 (I),

wherein D1 is a peptide having a tendency to form oligomers (D1)_m of m subunits D1, D2 is a peptide having a tendency to form oligomers (D2)_n of n subunits D2, m and n each is a figure between 2 and 10, with the proviso that m is not equal n and not a multiple of n, and n is not a multiple of m, L is a bond or a short linker segment consisting of 1 to 6 amino acids, **either D1 or D2 or both D1 and D2 is a coiled-coil that incorporates one or more helper T lymphocyte epitopes (HTL epitopes) and/or cytotoxic T lymphocyte epitopes (CTL epitopes) within the oligomerization domain, and wherein D1 and D2 are optionally further substituted; wherein the HTL and/or CTL epitope is selected from proteins with the sequences SEQ ID NO:99-202 and 228-295." [emphasis added]**

Claim 1 of auxiliary request 3 reads as follows:

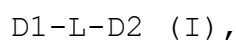
"1. A self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula (I) consisting of a continuous chain comprising a peptidic oligomerization domain D1, a linker segment L, and a peptidic oligomerization domain D2



wherein D1 is a peptide having a tendency to form oligomers (D1)_m of m subunits D1, D2 is a peptide having a tendency to form oligomers (D2)_n of n subunits D2, m and n each is a figure between 2 and 10, with the proviso that m is not equal n and not a multiple of n, and n is not a multiple of m, L is a bond or a short linker segment consisting of 1 to 6 amino acids, **either D1 or D2 or both D1 and D2 is a coiled-coil that incorporates one or more cytotoxic T lymphocyte epitopes (CTL epitopes) selected from proteins with the sequences SEQ ID NO:228-248 within the oligomerization domain, and wherein D1 and D2 are optionally further substituted."** [emphasis added]

Claim 1 of auxiliary request 4 reads as follows:

"1. A self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula (I) consisting of a continuous chain comprising a peptidic oligomerization domain D1, a linker segment L, and a peptidic oligomerization domain D2



wherein D1 is a peptide having a tendency to form oligomers (D1)_m of m subunits D1, D2 is a peptide having a tendency to form oligomers (D2)_n of n subunits D2, m and n each is a figure between 2 and 10, with the proviso that m is not equal n and not a multiple of n, and n is not a multiple of m, L is a bond or a short linker segment consisting of 1 to 6 amino acids, **either D1 or D2 or both D1 and D2 is a coiled-coil that incorporates a T-cell epitope with the sequence SEQ ID NO:228 within the oligomerization domain, and wherein D1 and D2 are optionally further substituted."**
[emphasis added]

IV. The following document is referred to in this decision:

D16 Burkhard P. *et al.*, TRENDS in Cell Biology (2001), vol. 11, pages 82 to 88.

V. The board issued a summons to oral proceedings accompanied by a communication pursuant to Article 15(1) RPBA informing the appellant of its preliminary opinion on the case. As regards the functional feature "*having a tendency to form oligomers*" of claim 1 of the main request, the board noted that "*document D16, referred to in the application (see page 8, lines 8 to 9) as evidence that peptidic oligomerization domains are well-known solely discloses a few specific coiled-coil folding motifs*" (see point 13).

VI. In response, the appellant withdrew its request for oral proceedings, stating that it would not attend the oral proceedings and requesting "*to return to the written procedure*".

VII. Oral proceedings were held on 2 May 2019. The appellant was neither present nor represented, as announced beforehand in writing. At the end of the oral proceedings, the chair announced the board's decision.

VIII. The appellant's written arguments may be summarised as follows:

Main request and auxiliary requests 1 to 4

Clarity (Article 84 EPC) - claim 1

The scope of claim 1 could not otherwise be defined more precisely without restricting the scope of the claim than by using the general functional term "*oligomerization domain*".

The requirements for clarity were summarised in decision T 560/09, Reasons, point 2.

A skilled person reading claim 1 would immediately understand the meaning of the term "*oligomerization domain*" in the context of the claims.

The meaning of the term "*oligomerization domain*" was further explained on page 7, lines 25 to 31, and page 8, lines 8 to 14, of the description. The description gave clear guidance on how to determine whether a peptide sequence represented an oligomerisation domain having a tendency to form oligomers. Thus, the function could be verified by procedures adequately specified in the description and known to the skilled person in the art.

IX. The appellant requested in writing that the decision under appeal be set aside and that the case be remitted

to the examining division with an order to grant a patent on the basis of the set of claims of the main request, or, alternatively, of the set of claims of any of auxiliary requests 1 to 4, all filed with the statement of grounds of appeal. The appellant further requested "to return to the written procedure".

Reasons for the Decision

1. The appeal complies with Articles 106 to 108 and Rule 99 EPC and is therefore admissible.

*Absence from the oral proceedings - Right to be heard
(Article 113(1) EPC)*

2. The duly summoned appellant was neither present nor represented at the oral proceedings. The board considered it expedient to conduct the scheduled oral proceedings in their absence in order to reach a final decision on this appeal, treating them as relying on their written case (Rule 115(2) EPC and Article 15(3) RPBA). Hence, the party's right to be heard was respected (Article 113(1) EPC).

The appellant's request to return to the written procedure

3. In response to the summons to the oral proceedings, which was accompanied by a detailed communication by the board pursuant to Article 15(1) RPBA, the appellant requested "*to return to the written procedure*", albeit without providing arguments in support of this request or indeed any further arguments.
4. The board considered that it was in a position to reach a decision during the oral proceedings and could not identify any reason why it should postpone the decision

and return to the written procedure. Accordingly, the board decided to reject the appellant's request.

Main request

Clarity (Article 84 EPC) - claim 1

5. Article 84 EPC states that the claims - which define the matter for which protection is sought - must be clear.
6. Claim 1 is directed to a self-assembling peptide nanoparticle consisting of aggregates of a multitude of building blocks of formula [D1-L-D2] consisting of a continuous chain comprising a peptidic oligomerisation domain D1, a linker segment L, and a peptidic oligomerisation domain D2 (see section III).
7. The appellant argues that the term "*oligomerization domain*" used in claim 1 is clear from the claim itself and furthermore that the description provides guidance on how to determine whether a peptide sequence represents an oligomerisation domain having a tendency to form oligomers.
8. The claim defines the peptidic oligomerisation domains D1 and D2 not structurally, e.g. in terms of their amino acid sequence, but functionally as peptides "*having a tendency to form oligomers*" and further that "*either D1 or D2 or both D1 and D2 is a coiled-coil*" [emphasis added].

What the peptidic oligomerisation domain D1 or D2 is, if it is not "a coiled-coil" (see the alternative "*either D1 or D2*") is not further defined in claim 1 or its dependent claims.

9. The board considers that the skilled person is aware through their common general knowledge of the structural motifs leading to coiled-coil formation of peptides, the coiled-coil being among the most simple and common motif in protein structures. Thus, the board agrees that the skilled person understands the meaning of an "*oligomerization domain*" which is further defined as being a coiled-coil in the context of the claims.
10. The board is, however, not persuaded that the meaning of an oligomerisation domain that is described as "*having a tendency to form oligomers*" but is not further defined as being a coiled-coil is also clear to the skilled person, for the following reasons.
11. It is established jurisprudence of the Boards of Appeal - and the board sees no reason to deviate from it - that for a feature defined in functional terms to be considered as clear a skilled person must be able to understand the teaching of the claim but also be able to implement it. Thus, the feature must provide instructions that are sufficiently clear for the expert to reduce them to practice without undue burden, if necessary with reasonable experiments (see decision T 68/85, OJ EPO 1987, 228, Reasons, point 8.4.3). It has further been held, for example in decision T 560/09 referred to by the appellant, that the function stated by a functional feature must be able to be verified by tests or procedures adequately specified in the description or known to the skilled person. In other words, the feature must be comprehensible and must also

be non-ambiguous in that it can be determined without any ambiguity whether the claimed functional requirement is satisfied or not (see Reasons, point 2, second paragraph).

12. The functional feature "*having a tendency to form oligomers*" itself does not provide instructions to the skilled person that would allow him to identify such oligomerisation domains. The board has also not seen any evidence that the skilled person, as a matter of common general knowledge, can distinguish without any ambiguity peptides "*having a tendency to form oligomers*" from peptides not having such a tendency or is aware of procedures allowing them to do so.
13. The board is also not persuaded by the appellant's argument that the application discloses how to determine whether a peptide sequence represents an oligomerisation domain having a tendency to form oligomers.
14. The board notes that the passage of the application relied on by the appellant as providing guidance for the skilled person (page 7, lines 25 to 31) discloses that "*a tendency to form oligomers means that such peptides can form oligomers depending on the conditions, e.g. under denaturing conditions they are monomers, while under physiological conditions they may form, for example trimers. Under predefined conditions they adopt one single oligomerization state, which is needed for nanoparticle formation. However, their oligomerization state may be changed upon changing*

conditions, e.g. from dimers to trimers upon increasing salt concentration (Burkhard P. et al, Protein Science 2000, 9:2294-2301) or from pentamers to monomers upon decreasing pH [emphasis added].

15. It is thus apparent that the tendency of a peptide to form oligomers depends *inter alia* on the conditions chosen, including the salt concentration and the pH of the solution comprising the peptide. Thus, since oligomerisation depends on the experimental parameters chosen, a standard test is required to allow unambiguous identification of the peptides having "*a tendency to form oligomers*". However, the application does not further define the conditions under which the tendency of peptides to form oligomers is assessed, other than that they are "*predefined*". Accordingly, the skilled person is not given precise directions and has to select the conditions themselves. Depending on the particular conditions chosen, a peptide's tendency to form oligomers will vary.

16. The board thus considers that the application provides no guidance or standard test that ensures that peptides "*having a tendency to form oligomers*" can be identifying unambiguously. Moreover, the only peptides that are identified in the application as having such a tendency are those having a coiled-coil motif. Indeed while, according to the application, peptidic oligomerisation domains "*are well-known*" (see page 8, lines 8 to 13), the board notes that all the oligomerisation domains specifically disclosed in this context in the application are coiled-coil folding motives. Finally, document D16, referred to in the application as evidence that peptidic oligomerisation domains "*are well-known*", only discloses a few specific coiled-coil folding motifs. This was pointed out in the

board's communication (see section V) and has not been contested by the appellant.

17. The board thus considers that neither the feature "*having a tendency to form oligomers*" nor the description provides instructions that are sufficiently clear to allow the skilled person to determine whether the claimed functional requirement is satisfied or not.
18. For the reasons set out above, the board concludes that the definition in claim 1 of the oligomerisation domain as a peptide "*having a tendency to form oligomers*" leaves the skilled person in doubt as to which peptides - other than those having a coiled-coil motif - are meant. Consequently, claim 1 does not comply with the clarity requirement of Article 84 EPC.

Auxiliary requests 1 to 4

Clarity (Article 84 EPC) - claim 1

19. In claim 1 of each of auxiliary requests 1 to 4 the oligomerisation domain is defined by the same functional feature "*having a tendency to form oligomers*" as in claim 1 of the main request (see section III). Accordingly, the same reasoning as set out above in points 5 to 18 for claim 1 of the main request applies.
20. Therefore, claim 1 of auxiliary requests 1 to 4 does not comply with the clarity requirement of Article 84 EPC.

Order

For these reasons it is decided that:

1. The appeal is dismissed.

The Registrar:

The Chair:



S. Lichtenvort

G. Alt

Decision electronically authenticated