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Datasheet for the decision of 1 December 2025

Case Number: T 1350/24 - 3.3.08

Application Number: 17722542.2

Publication Number: 3446119

IPC: G01N33/569

Language of the proceedings: EN

Title of invention:
Improved HLA epitope prediction

Applicants:
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Massachusetts Institute of Technology
President and Fellows of Harvard College
Dana-Farber Cancer Institute, Inc.
The General Hospital Corporation
Carr, Steven A.
Hacohen, Nir
Wu, Catherine, Ju-ying
Abelin, Jennifer, G.
Sarkizova, Siranush
Keskin, Derin, B.
Clauser, Karl, R.
Rooney, Michael, S.

Headword:
HLA epitope prediction/THE BROAD INSTITUTE et al.

Relevant legal provisions:
EPC Art. 84
RPBA 2020 Art. 11

Keyword:
Claims - essential features (yes)
Remittal (yes)

Decisions cited:

Catchword:
-

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Beschwerdekammern

Boards of Appeal

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Case Number: T 1350/24 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 1 December 2025

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Decision under appeal:	**Decision of the Examining Division of the European Patent Office posted on 8 July 2024 refusing European patent application No. 17722542.2 pursuant to Article 97(2) EPC**

Composition of the Board:

Chair	T. Sommerfeld
Members:	B. Claes
	L. Bühler

Summary of Facts and Submissions

I. The appeal of the applicants (appellants) lies from the decision of the examining division refusing European patent application No 17 722 542.2, which was filed under the PCT as an international patent application and published as WO 2017/184590 ("the application"). The title of the application is "*Improved HLA epitope prediction*".

II. The examining division refused the application on the grounds that claims 1, 6 and 17 of the main request filed on 24 May 2024 and the claims of the pending auxiliary requests failed to meet the requirements of Article 84 EPC since they lacked essential features.

Independent claims 1, 6 and 17 of the main request read as follows.

"1. A method for generating a prediction algorithm for identifying HLA- allele [*sic*] specific binding neoantigen-comprising peptides for inclusion in an immunogenic composition capable of inducing a tumor specific immune response, the method comprising:

training a machine with an HLA class I - allele specific binding peptide sequence database obtained by a method comprising:

(a) providing a population of dendritic cells or B cells expressing a single class I HLA allele;

(b) isolating HLA-peptide complexes from said cells;

(c) isolating peptides from said HLA-peptide complexes; and

(d) sequencing said peptides, wherein said sequencing is performed by mass spectrometry;

wherein variables used to train the machine comprise peptide sequence, and the expression level of the source protein of peptides within the population of cells,

thereby generating the prediction algorithm."

"6. A method for identifying HLA- allele [*sic*] specific binding neoantigen-comprising peptides for inclusion in an immunogenic composition capable of inducing a tumor specific immune response, the method comprising analyzing the sequence of a peptide from a tumor-specific mutation which alters the amino acid sequence of a genome encoded protein with a machine which has been trained with an HLA class I - allele specific binding peptide sequence database obtained by a method comprising:

(a) providing a population of dendritic cells or B cells expressing a single class I HLA allele;

(b) isolating HLA-peptide complexes from said cells;

(c) isolating peptides from said HLA-peptide complexes; and

(d) sequencing said peptides, wherein said sequencing is performed by mass spectrometry,

wherein the method further comprises determining the expression level of the source protein of the peptide within a cell; and wherein peptide sequence and the expression level of the source protein of peptides within the population of cells are predictive variables used by the machine."

"17. A method of identifying a plurality of subject-specific neoantigen-comprising peptides for preparing a subject-specific immunogenic composition, wherein the subject has a tumor and the subject-specific peptides

are specific to the subject and the subject's tumor, said method comprising:

(a) whole genome or whole exome nucleic acid sequencing of a sample of the subject's tumor and a non-tumor sample of the subject;

(b) determining based on the whole genome or whole exome nucleic acid sequencing:

(i) non-silent mutations present in the genome of cancer cells of the subject but not in normal tissue from the subject, and

(ii) the HLA genotype of the subject,

wherein the non-silent mutations comprise a point, splice-site, frameshift, read-through, neoORF or gene-fusion mutation; and

(c) selecting from the identified non-silent mutations the plurality of subject-specific peptides, each having a different tumor neo-epitope that is an epitope specific to the tumor of the subject and each having a predictive score indicative of binding an HLA protein of the subject,

wherein said predictive score is determined by analyzing the sequence of peptides derived from the non-silent mutations by carrying out the method of any one of the claims 6-16."

III. With their statement of grounds of appeal, the appellants resubmitted their main request and argued, *inter alia*, that the examining division had incorrectly decided on the claims of the main request under Article 84 EPC. They also submitted a declaration by a technical expert (document D10).

IV. The board issued a communication under Article 15(1) RPBA.

V. In this decision, reference is made to the following documents.

D3: US 2011/0257890

D6: M. Bassani-Sternberg *et al.*, Molecular & Cellular Proteomics 14(3), 2015, pages 658-673

D10: Declaration by Morten Nielsen

VI. The appellants' submissions and arguments on appeal, insofar as they are relevant for the decision, are taken into consideration in the Reasons for the Decision set out below.

VII. The appellants have requested that the decision under appeal be set aside and that the case be remitted to the examining division for further prosecution on the basis of the set of claims of the main request or one of the auxiliary requests filed with the statement of grounds of appeal.

The appellants have also requested that document D10, which was also filed with the statement of grounds of appeal, be admitted into the proceedings.

Reasons for the Decision

Main request - lack of clarity (Article 84 EPC)

Claims 1 and 6 - essential features

1. According to the established case law of the boards of appeal, Article 84 EPC is to be interpreted as meaning

not only that a claim must be comprehensible from a technical point of view, but also that it must define the object of the invention by clearly indicating all the essential features thereof. Independent claims should explicitly specify all the essential features that are needed to define the invention. All features that are necessary for solving the technical problem with which the application is concerned are to be regarded as essential features, and it is necessary to indicate all the essential features in the claim in order to meet the clarity requirement. The essential features should comprise, in particular, those features which distinguish the invention from the state of the art (Case Law of the Boards of Appeal, 11th edition, 2025, "CLBA", II.A.3.3).

The decision under appeal

2. The examining division gave the following reasons for its conclusion that claims 1 and 6 lacked essential features and hence failed to meet the requirements of Article 84 EPC.

2.1 According to the examining division, it was essential to the claimed invention that the prediction algorithm recited in the claims performed better than known algorithms. Hence, since the purpose of the prediction algorithm generated according to the claim was defined as a result to be achieved ("for identifying HLA-allele specific binding neoantigen-comprising peptides for inclusion in an immunogenic composition capable of inducing a tumor specific immune response"), "*the database used to train the machine as well* [sic] *the variables chosen have to be so defined that a skilled person would arrive at an algorithm performing better*

without any undue burden" (see the decision under appeal, point 13.9, emphasis added by the board).

2.2 Claim 1 covered many databases which could be used for training the machine and "*all the other steps related to peptide identification are standard in the art*" (see the decision under appeal, point 13.10). Furthermore, "*at least D3 and D6 use the same approach for proteome analysis of HLA-binding peptides, so the database set cannot be the reason for alleging a different effect*" (see the decision under appeal, point 13.13, emphasis added by the board).

2.3 Moreover, since the claim did not explain how the expression level of the source protein and the peptide sequence "*are to be read in the context of the algorithm*", they "*do not suffice to clearly define the invention*" (see the decision under appeal, point 13.15). Hence, "*the data set and variables used to train the machine are loosely defined and do not serve to unambiguously explain the different performance of the claimed algorithm*" (see the decision under appeal, point 13.17, emphasis added by the board).

2.4 The examining division concluded, therefore, that "*someone reading the claim and trying to repeat the invention would be lost trying to figure out how to obtain an algorithm that satisfies the requirements of the invention*" and that "*the claims lack essential features defining the claim in such a manner that the skilled reader would know when or not working within the scope of the claim*" (see the decision under appeal, point 13.14, emphasis added by the board).

2.5 Furthermore, it was "*not clear from the claims alone or read in light of the description that it suffices to train a machine with a loosely defined database and two (or more) variables*", and "*the mathematical methods (algorithm) and the training datasets are disclosed in insufficient detail to reproduce the technical effect over the whole range claimed*". The claim required the skilled person "*to define the required database among the wide range of different possibilities and correspondly train the machine with different variables in order to seek for an algorithm that might fulfil the requirements in the claim*". This amounted to "*more than trial and error experimentation*" and was thus "*an invitation to a research programme*" (see the decision under appeal, point 13.16, emphasis added by the board).

3. From the above summary of the reasoning of the examining division it is reasonable to conclude that the presupposition that the prediction algorithm generated by the method of claim 1 and the predictive variables used by the machine used in method claim 6 are required to perform *better* than known algorithms is pivotal to the examining division's reasoning. It was with this presupposition in mind that the examining division deemed it an undue burden for the skilled person to define the database and the variables for training the machine *a priori* in order to achieve better prediction performance.

Claim construction

4. The method of claim 1 (see section II. above) is for generating a prediction algorithm by training a machine with an HLA class I allele-specific binding peptide sequence database obtained from a population of

dendritic cells or B cells expressing a single class I HLA allele,
- wherein the variables used to train the machine include the peptide sequence and the expression level of the source protein of peptides within the population of cells and
- the resulting prediction algorithm is useful for identifying HLA allele-specific binding neoantigen-comprising peptides and can be included in an immunogenic composition capable of inducing a tumour-specific immune response.

5. Similarly, the method of claim 6 (see section II. above) is for identifying HLA allele-specific binding neoantigen-comprising peptides for inclusion in an immunogenic composition useful in inducing a tumour-specific immune response, by analysing the sequence of a peptide from a tumour-specific mutation which alters the amino-acid sequence of a genome-encoded protein with a machine trained with an HLA class I allele-specific binding peptide sequence database obtained from a population of dendritic cells or B cells expressing a single class I HLA allele and wherein the peptide sequence and the expression level of the source protein of peptides within the population of cells are predictive variables used by the machine.

6. However, contrary to the presupposition adhered to by the examining division, these claims do *not* require the resulting prediction algorithm (claim 1) or the identification method (claim 6) to outperform known prediction algorithms or identification methods in any aspect or predictive characteristic. Therefore, the examining division's reasoning that the claims lack essential features, as summarised in point 2. above, is in fact based on an incorrect presupposition and is

therefore neither persuasive nor pertinent for this reason alone.

7. Furthermore, the board notes the following with respect to the examining division's reasoning.

7.1 All of the arguments of the examining division concerning specific algorithms and databases required to achieve the presupposed technical effect, i.e. that the prediction algorithm generated by the method of claim 1 and the predictive variables used by the machine used in method claim 6 are required to perform better than known algorithms, are irrelevant to an assessment of essential features in the absence of a requirement for such a technical effect in claims 1 and 6.

7.2 The board agrees with the appellants that the description neither explicitly nor implicitly describes any features that are not recited in claim 1 as being necessary or essential for carrying out the invention.

7.3 The board also agrees with the appellants that the examining division's reasoning concerns aspects of the disclosure of the invention under Article 83 EPC rather than matters pertaining to essential features and clarity that could be relevant under Article 84 EPC.

7.4 According to the established case law of the boards of appeal (see CLBA, II.A.3.4), a broad claim *per se* is not to be equated with one lacking clarity. Here, the board is of the opinion that while the features in the claim concerning the peptide sequence database and the two variables used to train the machine may be broadly defined, they nevertheless provide, having regard to the rest of the disclosure in the application, the

detail required to fulfil the promise of the invention, in this case the essential features.

7.5 Finally, (i) the concerns of the examining division on reproducing "*the technical effect over the whole range claimed*" (see point 2.5, above) and (ii) the assessment of features in the claim in view of disclosures in the state of the art (see point 2.2 above, i.e. documents D3 and D6) relate to elements of inventive step under Articles 52(1) and 56 EPC, not clarity under Article 84 EPC.

8. In view of the above considerations, the board has not seen convincing reasons from the examining division as to why claims 1 and 6 would not comply with the clarity requirement of Article 84 EPC.

Claim 17

9. The method of claim 17 (see section II. above) implements the method of claim 6 and is for identifying subject-specific tumour antigen-comprising peptides for preparing a subject-specific immunogenic composition, comprising:
(a) sequencing the whole genome or exome of a sample of the tumour and a non-tumour sample of the subject;
(b) determining non-silent mutations in the tumour as compared to the non-tumour sample and the HLA genotype of the subject, and
(c) selecting from the identified non-silent mutations those peptides having a different epitope specific to the tumour and having a predictive score indicative of binding an HLA protein of the subject,
wherein said predictive score is determined by analysing the peptides of the non-silent mutations by carrying out the method of any one of claims 6 to 16.

10. The examining division rejected claim 17 on the grounds of a lack of clarity (Article 84 EPC). In coming to this decision, the examining division limited itself
- firstly to merely stating that the claim is "*drafted in such a manner that a skilled person trying to repeat the method would be left alone deciding which tumor sample to use, and which non-silent mutations should be determined in order to select the ones that are subject-specific peptides having the required characteristics as in step (c)"* and that "*the applicant tries to obtain protection to a plethora of methods for which no data is given in the description*" (see the decision under appeal, point 13.21, emphasis added by the board),
- secondly to noting the reference in the claim to "*the method of claim 6 which is already unclear per-se"* (see the decision under appeal, point 13.22) and
- thirdly to noting the requirement of "*the preparation of an immunogenic composition based on compounds that have first to be discovered*" (see the decision under appeal, point 13.22, emphasis added by the board).

11. The examining division then concluded that "[t]*he number of ambiguities is such that the scope of claim 17 is rendered difficult to ascertain and lacks therefore, clarity (Art. 84 EPC)*" (see the decision under appeal, point 13.23, emphasis added by the board).

12. The board notes, however, that claim 17 explicitly stipulates that "*a sample of the subject's tumor*" as well as "*a non-tumor sample of the subject*" are to be used for determining non-silent mutations in the tumour as compared to the non-tumour sample which could be selected when having a predictive score indicative of

binding to an HLA protein of the subject. Accordingly, the board does not concur with the examining division's statement that in this respect "*a skilled person trying to repeat the method would be left alone".* Furthermore, this and the further consideration of the examining division that "*the applicant tries to obtain protection to a plethora of methods for which no data is given in the description*" are matters concerning the disclosure of the invention under Article 83 EPC and/or inventive step under Articles 52(1) and 56 EPC, rather than clarity under Article 84 EPC. These arguments are, hence, not persuasive.

13. Moreover, the second reason of the examining division is not persuasive either, in view of the board's earlier finding that the examining division's reasoning under Article 84 EPC concerning claim 6 is not convincing (see point 8. above).

14. The third reason of the examining division relates to so-called "reach-through" aspects of the claim, namely the "subject-specific neoantigen-comprising peptides for preparing a subject-specific immunogenic composition" resulting from the claimed method for identifying such. While, in general, a claim that broadly covers any compound identified using a certain method might under certain circumstances be considered to infringe the requirements of Article 84 EPC for being too vague (unclear) or not sufficiently supported, the subject-matter of the claim under consideration is a method for identifying such peptides and not the totality of all possible peptides that might be discovered by that method. "Reach-through" aspects of such a method claim should be addressed under the requirements of sufficiency of disclosure of the invention (Article 83 EPC) and cannot lead to a

lack of clarity due to an uncertain scope of protection of the claim.

15. In view of the above considerations, the board has not seen convincing reasons from the examining division as to why claim 17 would not comply with the clarity requirement of Article 84 EPC, either.

Remittal to the examining division

16. The appellants have requested that in the event the appeal is allowed and the decision under appeal is set aside the case be remitted to the examining division for further prosecution on the basis of the main request (see point VII. above).

17. Pursuant to Article 111(1) EPC, the board may either exercise any power within the competence of the department responsible for the appealed decision or remit the case to that department for further prosecution.

18. It is the primary function of appeal proceedings to give a judicial decision on the correctness of the decision under appeal (Article 12(2) RPBA; see also CLBA, section V.A.1.1, second paragraph, and the decisions referred to therein).

19. Although the decision under appeal does address certain issues with respect to sufficiency of disclosure (Article 83 EPC) and inventive step (Article 56 EPC) in the context of the examining division's assessment of the clarity requirements under Article 84 EPC, there is no comprehensive examination under these requirements. Such matters were not considered in the oral proceedings, either. Not remitting the case to the

opposition division in the event that the appeal is allowed would therefore require the board to carry out an in-depth examination of the application rather than review the contested decision in a judicial manner, the latter being the primary purpose of appeal proceedings.

20. In view of these considerations, the board concludes that there are special reasons within the meaning of Article 11 RPBA for remitting the case for further prosecution, in line with the appellants' request.

Final considerations

Document D10 - admittance

21. The board has come to the above conclusions without referring to document D10, which was filed by the appellants with their statement of grounds of appeal. Under these circumstances, the question of whether this document should be admitted into the appeal proceedings under Article 12(4) RPBA does not have to be addressed.

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 on the basis of the set of claims of the main request.

The Registrar: The Chair:

C. Rodríguez Rodríguez T. Sommerfeld

Decision electronically authenticated