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**Datasheet for the decision
of 6 November 2025**

Case Number: T 0085/23 - 3.3.04

Application Number: 15737995.9

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Language of the proceedings: EN

Title of invention:
Expansion of lymphocytes with a cytokine composition for
active cellular immunotherapy

Patent Proprietor:
polybiocept GmbH

Opponents:
STRAWMAN LIMITED
Margaret Dixon Limited

Headword:
Expansion of lymphocytes/POLYBIOCEPT

Relevant legal provisions:
EPC Art. 123(2)

Keyword:

Amendments - added subject-matter (yes)



Beschwerdekammern

Boards of Appeal

Chambres de recours

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Case Number: T 0085/23 - 3.3.04

D E C I S I O N
of Technical Board of Appeal 3.3.04
of 6 November 2025

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Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted on 8 November 2022
revoking European patent No. 3 154 567 pursuant
to Article 101(3) (b) EPC**

Composition of the Board:

Chairwoman D. Luis Alves
Members: B. Rutz
 R. Romandini

Summary of Facts and Submissions

- I. The appeal by the patent proprietor (appellant) lies from the opposition division's decision to revoke European patent No. 3 154 567, which is based on European patent application No. 15 737 995.9, published under the PCT as international application WO 2015/189357.
- II. The patent had been opposed on the grounds of Article 100(a) EPC, in relation to novelty (Article 54 EPC) and inventive step (Article 56 EPC), and of Article 100(b) and (c) EPC.
- III. In the decision under appeal, the opposition division held that claim 1 of the main request was not clear (Article 84 EPC) and related to subject-matter which extended beyond the content of the application as filed (Article 123(2) EPC). Auxiliary requests 1 to 5, all filed on 14 October 2022, as well as auxiliary request 5a, filed at the oral proceedings, were not admitted into the opposition proceedings.
- IV. With the statement setting out the grounds of appeal, the appellant filed sets of claims of auxiliary requests 2 to 5.
- V. Respondents I and II filed replies to the appeal.
- VI. The board summoned the parties to oral proceedings and informed them of its preliminary opinion in a communication pursuant to Article 15(1) RPBA.
- VII. In that communication, the board indicated, *inter alia*, that it preliminarily found that several claims of all

the requests were not clear and that the subject-matter of several claims of all the requests extended beyond the content of the application as filed.

VIII. By letter dated 4 February 2025, the appellant informed the board that it would not be attending the oral proceedings.

IX. By letter dated 7 March 2025, respondent II (opponent 2) informed the board that it would not be attending the oral proceedings.

X. The board cancelled the oral proceedings.

XI. Claims 1 to 4 of auxiliary request 2 read as follows:

"1. Use of a composition for in vitro expanding tumor infiltrating lymphocytes comprising interleukin 2 (IL-2), interleukin 15 (IL-15) and interleukin 21 (IL-21), wherein the composition is in liquid form, the concentration of IL-2 in the liquid composition is 1000 U/ml, the concentration of IL-15 10 ng/ml and wherein the concentration of IL-21 is 10 ng/ml.

2. A method of preparing a population of clinically relevant tumor infiltrating lymphocytes, comprising the steps of:

- providing a body sample obtained from a mammal, in particular a tissue sample or body liquid sample, comprising at least one tumor infiltrating lymphocyte and optionally separating the cells in the body sample;
- culturing the body sample in-vitro to expand and/or stimulate tumor infiltrating lymphocytes in the sample wherein the culturing comprises using IL-2, IL-15 and IL-21; wherein the concentration of IL-2 in the culture is in the range of 500 to 2000 U/ml; the concentration

of IL-15 is in the range of 0.1 to 100 ng/ml and the concentration of IL-21 is in the range of 0.1 to 100 ng/ml;

- and optionally determining the presence of clinically relevant tumor infiltrating lymphocyte in the cultured sample; wherein the in-vitro culturing comprises a first expansion step comprising an incubation in culture medium comprising IL-2, IL-15 and IL-21 until tumor infiltrating lymphocytes become detectable, and wherein the in-vitro culturing comprises a second expansion step comprising an incubation in culture medium comprising feeder cells and/or an antibody against CD3 in addition to IL-2, IL-15 and IL-21.

3. The method according to claim 2, wherein the clinically relevant tumor infiltrating lymphocytes are selected from tumor-reactive lymphocytes, pathogen reactive lymphocytes and autoimmune reactive lymphocytes, preferably tumor-reactive lymphocytes.

4. The method according to claim 2 or 3, wherein the body sample is selected from the group consisting of peripheral blood, cord blood, bone marrow, lymph nodes liver, [sic] pleural effusion, thorax, abdominal cavity, synovial fluid, peritoneum, retroperitoneal space, thymus, and tumor, preferably peripheral blood or tumor."

Auxiliary request 3 differs from auxiliary request 2 in that "tumor infiltrating lymphocytes" in all the claims is replaced by "tumor infiltrating T-cells".

Auxiliary request 4 differs from auxiliary request 2 in that claim 1 ("use of a composition") has been deleted.

Auxiliary request 5 differs from auxiliary request 4 in that "tumor infiltrating lymphocytes" in all the claims is replaced by "tumor infiltrating T-cells".

XII. The appellant's submissions are summarised as follows:

Auxiliary requests 2 to 5

Added subject-matter (Article 123(2) EPC)

The application as filed on page 23, lines 9 to 12, contained the definition of tumor infiltrating lymphocytes (TIL): "*A lymphocyte sample derived from tumor is also referred as tumor infiltrating lymphocytes (TIL)*". The explanation in lines 11 and 12 of page 23 that "*TIL is any kind of lymphocyte that is located in, on or around a tumor*" indicated a particular embodiment which did not have to be incorporated into claim 1 to comply with Article 123(2) EPC. The feature "*located in, on or around a tumor*" was not inextricably linked to the term "*tumor infiltrating lymphocyte*" in the application as filed. The inclusion of tumor infiltrating lymphocytes in claim 1 was therefore not an unallowable intermediate generalisation.

The term "*clinically relevant lymphocytes*" was described on page 14, lines 26 to 31 of the application as filed: "*Clinically relevant lymphocytes are also referred to as antigen-edited lymphocytes ... Particularly preferred clinically relevant lymphocytes are clinically relevant T-cells or antigen-edited T-cells.*"

This meant that clinically relevant tumor infiltrating lymphocytes were antigen-edited tumor infiltrating

lymphocytes, such as antigen-edited tumor infiltrating T-cells.

Examples 3, 8 to 14, 16, 19 and 20 described expansion of tumor infiltrating lymphocytes from peripheral blood mononuclear cells (PBMC), and Examples 27, 28 and 31-41 described expansion of tumor infiltrating lymphocytes from a tumor sample.

XIII. Respondents I and II's submissions are summarised as follows:

Auxiliary requests 2 and 4

Added subject-matter (Article 123(2) EPC)

The disclosure on page 23, lines 9 to 17 of the application as filed was not a direct and unambiguous basis for the amendment because it referred to the expansion of tumor-reactive lymphocytes, not necessarily TILs. According to page 23, lines 9 and 10, TILs were a lymphocyte sample derived from tumor. However, tumor-reactive lymphocytes could be expanded from PBMC without taking a tumor sample (see e.g. page 3, lines 1 to 3 and Example 9 of the application as filed). Therefore an expansion of TILs was not directly and unambiguously derivable from the disclosure on page 23 of the application as filed. The amendment specifying that lymphocytes were tumor infiltrating lymphocytes added matter and contravened the requirements of Article 123(2) EPC.

The amended claims did not require the lymphocyte sample to be derived from a tumor, as required by page 23, lines 9 to 16 cited as the basis for the original amendment. Dependent claims 3 and 4 cast doubt on the scope of the claims. For example, dependent

claim 3 implied that clinically relevant TILs could be selected from tumor-reactive, pathogen-reactive and autoimmune-reactive lymphocytes. The application as filed defined these cell types as distinctive lymphocyte groups (see page 14, line 23 to page 15, line 4 of the application as filed). The appellant had argued that lymphocytes derived from a tumor might also be pathogen-reactive or autoimmune-reactive. However, (i) the claims made no reference to the TILs being derived from a tumor and (ii) pathogen-reactive and autoimmune-reactive lymphocytes were presented as alternatives to tumor-reactive lymphocytes in both the list presented in claim 3 and the description. Similarly, dependent claim 4 provided a list of sources of the body sample which were not limited to tumor samples or even derived from patients with a tumor. The amendment to the claims to refer to "*tumor infiltrating lymphocytes*" was an intermediate generalisation of the disclosure in the application as filed, and resulted in the subject-matter extending beyond the application as filed, contrary to Article 123(2) EPC.

Auxiliary requests 3 and 5

Added subject-matter (Article 123(2) EPC)

The basis in the application as filed proposed by the patent proprietor for amending "*tumor-infiltrating lymphocytes*" to "*tumor-infiltrating T-cells*" stated that "[1]lymphocytes include B-cells, NK-cells and T-cells" (see page 33, line 25). This disclosure was not a direct and unambiguous basis for the amendment because T-cells were mentioned only as part of a list of lymphocytes given by way of example. In fact, the text on page 33, lines 25 to 27 focused on B-cells and NK-cells rather than on T-cells; in one embodiment, the lymphocyte was a B-cell, and in another embodiment it

was an NK-cell. Moreover, the description of lymphocytes provided on page 33 was not about tumor infiltrating lymphocytes, and therefore did not disclose a tumor infiltrating T-cell. A lymphocyte that was a tumor infiltrating T-cell was therefore not directly and unambiguously derivable from the disclosure on page 33 of the application as filed, let alone the expansion thereof.

The amendment to tumor infiltrating T-cells appeared to be based on the selection from multiple lists, namely the limitation of the composition/method to expand lymphocytes to TILs and then the further limitation of TILs to tumor infiltrating T-cells. This specific type of cell was never disclosed as being or even implied to be a preferred embodiment of the invention. Nor was this type of cell disclosed in combination with the selection of features of the claimed composition/method, e.g. the selected concentration of interleukins.

In conclusion, there was no disclosure in the application as filed of tumor infiltrating T-cells in combination with the use and method as claimed, and the amendment extended the subject-matter beyond the content of the application as filed, contrary to Article 123(2) EPC.

XIV. The appellant requested that the decision under appeal be set aside and the case be remitted to the opposition division to deal with the grounds for opposition under Article 100(a) and (b) EPC, on the basis of the set of claims of auxiliary request 2, filed with the appeal; alternatively, that the case be remitted to the opposition division to deal with the grounds for opposition under Article 100(a) and (b) EPC, on the

basis of any of the sets of claims of auxiliary requests 3 to 5, filed with the appeal. The board understands the appellant's request to be that the board deal with the objections under Articles 84 and 123(2) EPC. Further, reimbursement of the appeal fee was requested, due to a substantial procedural violation.

Respondents I and II requested that the appeal be dismissed and the decision under appeal to revoke the patent be upheld. Respondent II further requested that none of auxiliary requests 2 to 5 be admitted into the appeal proceedings.

Reasons for the Decision

Admissibility of the appeal

1. Respondent II argued that the fact that there was no "*main request*" meant that the appeal was inadmissible because "*there is no text on the basis of which PP [patent proprietor] seeks maintenance of the patent*". The board disagrees, and considers the appeal admissible because the labelling of the appellant's requests as auxiliary requests 2 to 5, and not main request and auxiliary requests 1 to 3, has no substantive impact on the fact that the appellant requests that the patent be maintained in amended form based on the sets of claims of these requests. The order of the requests is also clear from their numbering.

Substantial procedural violation

2. The appellant submitted that the opposition division had committed a substantial procedural violation on the grounds that (i) it had not exercised its discretion properly in not admitting auxiliary requests 2 to 5 into the opposition proceedings, and that (ii) in reaching the decision not to admit the auxiliary requests it had based the decision in part on a lack of clarity of the term "*lymphocytes*", in contradiction to decision G 3/14 of the Enlarged Board of Appeal, since said term was already present in the claims as granted.

3. The issue of a procedural violation would become relevant only if the appeal were deemed allowable, i.e. if the board, on the basis of one of the claim requests by the appellant, were to set aside the decision of the opposition division. Since this is not the case (see below), the board is not required to decide on this issue.

Auxiliary requests 2 to 5 (as filed in appeal)

Admittance (Article 12(4) and (6) RPBA)

4. The board admits the requests for reasons of procedural efficiency in order to consider them on substance. As the requests are not allowable (see below) the respondents are not adversely affected by this decision.

Auxiliary request 2

Amendments (Article 123(2) EPC)

Claims 2 to 4

5. Claim 2 defines a method of preparing a population of clinically relevant tumor infiltrating lymphocytes.

Claims 3 and 4 are dependent on claim 2 and list specific embodiments of tumor infiltrating lymphocytes and of body samples.

6. The application as filed, however, does not disclose that "*tumor infiltrating lymphocytes*" may be selected from the cell types in claim 3, for example "*pathogen reactive lymphocytes*" or "*autoimmune reactive lymphocytes*", or that they may be expanded from a body sample as defined in claim 4, for example "*peripheral blood, cord blood, bone marrow, lymph nodes liver, [sic] pleural effusion, thorax, abdominal cavity, synovial fluid, peritoneum, retroperitoneal space, thymus*".

7. Rather, the application as filed links "*tumor infiltrating lymphocytes*" to tumors in terms of their origin and their localisation (page 23, lines 9 to 12):

"A lymphocyte sample derived from tumor is also referred as tumor infiltrating lymphocytes (TIL). 'TIL' as used herein is short for 'tumor infiltrating lymphocytes'. TIL is any kind of lymphocyte that is located in, on or around a tumor. TIL is any kind of lymphocyte that is located in and around a tumor."

8. The appellant argued that tumor infiltrating lymphocytes may migrate from the tumor to other body tissues or body fluids. This is, however, not what the application as filed discloses (see quote above: "*in, on or around a tumor*"). The appellant has also not provided evidence that this understanding would be part of the common general knowledge.

9. The appellant further argued that expansion of tumor-reactive T-cells from peripheral blood was preferred in the application as filed (see Examples 9 and 10). This provided an example that tumor infiltrating cells could migrate from the tumor to other body fluids.

10. The board does not agree. The application as filed makes a distinction between tumor infiltrating lymphocytes and tumor-reactive T-cells (see page 2, last two lines, and page 3, lines 1 to 3). This is also apparent from the examples, which show that tumor-reactive T-cells can also be generated from healthy donors by priming with tumor antigens, e.g. NY-ESO-1 (see Example 1). In contrast, tumor infiltrating lymphocytes, as defined in the application as filed (see page 23, lines 9 to 12), are required to be derived from or located in, on or around a tumor.

11. The application as filed limits TIL to lymphocytes derived from tumor and to lymphocytes located in, on or around a tumor. The reference to other cell types and to being expandable from other body samples than tumor results in added subject-matter in claims 2 to 4, contrary to the requirements of Article 123(2) EPC.

Auxiliary request 3

12. In the claims of this request the term "*tumor infiltrating lymphocytes*" is replaced by "*tumor infiltrating T-cells*". "*Tumor infiltrating T-cells*" are not explicitly mentioned in the application as filed and are also not directly and unambiguously derivable from it using common general knowledge. T-cells are mentioned in several instances, but they are not disclosed in combination with tumor infiltration. Rather, they are disclosed as an alternative, for

example on page 2, lines 30 to 32: "*harvesting of tumor infiltrating lymphocytes (TIL) from tumor lesions or T-cells from peripheral blood*", and on page 3, lines 1 to 3: "*protocols on the expansion of tumor reactive T-cells from peripheral blood and TILs*". The examples in the application as filed relate to TIL generated from tumor tissue samples (Examples 27, 28, 31 to 41), while tumor-reactive T-cells or antigen-specific T-cells are derived from PBMCs (Examples 1 to 26).

13. Other passages of the application as filed, such as page 6, lines 19 to 21, state that "*the clinically relevant lymphocyte is selected from a B-cell, an NK cell and T-cell*", but make no link to tumor infiltration.
14. Page 14, lines 20 to 21 of the application as filed states "*the composition of a combination of at least two types of cytokines selected from IL-2, IL-15 and IL-21 specifically favors the generation of lymphocytes, in particular T-cells, which are clinically relevant*". However, this disclosure is not linked to tumor infiltration.
15. In conclusion, the term "*tumor infiltrating T-cells*" in the claims extends the subject-matter beyond the content of the application as filed (Article 123(2) EPC).

Auxiliary requests 4 and 5

16. The conclusions for auxiliary request 2 also apply to auxiliary request 4, and the conclusions for auxiliary request 3 also apply to auxiliary request 5.

Conclusion

17. All the claim requests extend the subject-matter beyond the content of the application as filed, contrary to the requirements of Article 123(2) EPC.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairwoman:



I. Aperribay

D. Luis Alves

Decision electronically authenticated