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**Datasheet for the decision  
of 5 October 2018**

**Case Number:** T 2065/14 - 3.3.04

**Application Number:** 05722705.0

**Publication Number:** 1718767

**IPC:** A61K39/395

**Language of the proceedings:** EN

**Title of invention:**

Compositions for treating breast and pancreatic cancer

**Patent Proprietor:**

The regents of the university of Michigan

**Opponent:**

Eisai Co., Ltd.

**Headword:**

Notch signalling inhibitor/UNIVERSITY MICHIGAN

**Relevant legal provisions:**

EPC Art. 123(2)

**Keyword:**

All requests - amendments - allowable (no)

**Decisions cited:**

**Catchword:**

-



**Beschwerdekammern**

**Boards of Appeal**

**Chambres de recours**

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Case Number: T 2065/14 - 3.3.04

**D E C I S I O N**  
**of Technical Board of Appeal 3.3.04**  
**of 5 October 2018**

**Appellant:**

(Opponent)

Eisai Co., Ltd.  
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**Respondent:**

(Patent Proprietor)

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**Decision under appeal:**

**Interlocutory decision of the Opposition  
Division of the European Patent Office posted on  
12 August 2014 concerning maintenance of the  
European Patent No. 1718767 in amended form.**

**Composition of the Board:**

<b>Chairwoman</b>	G. Alt
<b>Members:</b>	B. Claes
	L. Bühler

## Summary of Facts and Submissions

- I. The opponent (hereinafter "appellant") lodged an appeal against the interlocutory decision of the opposition division concerning the maintenance of European patent No. 1 718 767 in amended form with the claims of auxiliary request 2 then on file.
- II. The patent, having the title "*Compositions for treating breast and pancreatic cancer*", was opposed under Article 100(a) EPC on the grounds of lack of novelty (Article 54 EPC) and lack of inventive step (Article 56 EPC), and under Article 100(b) and 100(c) EPC.
- III. Claim 1 of auxiliary request 2, which the opposition division considered to comply with the requirements of the EPC, read:

"1. An inhibitor of Notch signalling for use in a method of inhibiting tumorigenic cells to treat breast cancer in a subject, wherein the inhibitor is an anti-Notch antibody that inhibits proliferation of tumorigenic cells, and wherein the method comprises co-administering the inhibitor and an anticancer agent to the subject, wherein the anticancer agent is a chemotherapeutic antineoplastic."
- IV. With the statement of grounds of appeal the appellant submitted, *inter alia*, that the patent as amended in accordance with auxiliary request 2 related to subject-matter extending beyond the content of the application as filed (Article 123(2) EPC).
- V. With its reply to the statement of grounds of appeal, the patent proprietor (hereinafter "respondent")

submitted a main request (identical to auxiliary request 2 considered in the decision under appeal, see section III), auxiliary requests 1 and 2 (of which claim 1 was identical to claim 1 of the main request), auxiliary request 3, and, further, arguments to the effect that the patent as amended in accordance with the requests fulfilled the requirements of the EPC.

Claim 1 of auxiliary request 3 read:

"1. An inhibitor of Notch signalling for use in a method of preventing or reducing metastasis and inhibiting tumorigenic cells to treat breast cancer in a subject suspected of undergoing metastasis or at risk of metastasis, wherein the inhibitor is an anti-Notch antibody that inhibits proliferation of tumorigenic cells, and wherein the method comprises co-administering the inhibitor and an anticancer agent to the subject, wherein the anticancer agent is a chemotherapeutic antineoplastic." (emphasis added by the board)

- VI. With a further submission, the appellant reacted to the reply of the respondent holding, *inter alia*, that the three auxiliary requests also related to added subject-matter.
- VII. In a communication pursuant to Article 15(1) RPBA, annexed to the summons to oral proceedings, the board informed the parties, *inter alia*, of its preliminary and non-binding view that claim 1 of the main request comprised subject-matter extending beyond the content of the application as filed ("added subject-matter").
- VIII. Oral proceedings took place on 5 October 2018 in the presence of the appellant. As announced before in

writing, nobody was present on behalf of the respondent. At the end of the oral proceedings, the chair announced the decision of the board.

- IX. The appellant's arguments, submitted in writing and at the oral proceedings, in as far as they are relevant for the present decision, may be summarised as follows:

*Main request and auxiliary requests 1 and 2 - claim 1 - added subject-matter (Article 123(2) EPC)*

The passage on page 25, line 28 to page 25, line 1 was the only disclosure in the application as filed which referred to the term "anti-Notch antibody". The passage concerned, however, "a regulator of tumorigenesis" and listed in this context, *inter alia*, such antibodies, but equally Notch ligands other than antibodies, and, generally, agonists or antagonists of proteins in the Notch signal transduction/response pathway. Accordingly, the passage related to the broad concept of Notch pathway interference.

On page 28, lines 4 to 9, the application as filed listed a variety of therapeutic agents and/or techniques of which at least one could be combined with "administering a therapeutic compound of the present invention" in some embodiments of the invention. Chemotherapeutic antineoplastics were only one group of the listed wide variety of therapeutic agents and/or techniques.

In order to arrive at the combination of the specific characteristics of the therapeutic agents recited in the claim, i.e. an anti-Notch antibody and a chemotherapeutic antineoplastic, the skilled person thus had to choose from two lists of features disclosed

in the application as filed. In the absence of a clear pointer in the disclosure to the particular combination, the claimed subject-matter could not be considered clearly and unambiguously derivable from the application as filed.

The passage on page 27, lines 29 and 30, merely referred to "some embodiments of the present invention" and did not establish a clear and unambiguous pointer to a feature combination of an anti-Notch antibody and a chemotherapeutic antineoplastic in the context of the treatment of breast cancer.

The claim, which was identical in all three requests, accordingly did not comply with the requirements of Article 123(2) EPC.

*Auxiliary request 3 - claim 1 -  
added subject-matter (Article 123(2) EPC)*

Although the claim included additional features as compared to claim 1 of the main request and auxiliary requests 1 and 2, it equally related to a feature combination which constituted added subject-matter.

- X. The respondent's arguments in writing, in as far as they are relevant for the present decision, may be summarised as follows:

Claim 20 of the application as filed provided a basis for claim 1 of the main request.

Breast cancer was unambiguously disclosed in the application as filed as the preferred cancer for treatment in accordance with the invention.



The anti-tumorigenic therapeutic agent used in the methods of the invention was identified as being an anti-Notch antibody on page 18, lines 6 to 9 of the application as filed, and an anti-Notch antibody was furthermore specifically listed as a regulator of tumorigenesis "according to the present invention" on page 24, lines 28 to 30.

Antibodies were discussed at length in the application as filed on page 11, line 15 to page 12, line 24, and on page 27, lines 3 to 28. Furthermore, the application as filed singled out an anti-Notch antibody as the preferred anti-tumorigenic therapeutic agent for use according to the invention. Indeed, on page 25, lines 2, 5, 11 and 16 to 29, and page 26, lines 1 to 6, the application as filed unambiguously identified the "anti-tumorigenic therapeutic agent" as an "anti-Notch therapeutic agent" and then subsequently, e.g. on page 26, lines 22 to 23, identified this "anti-Notch therapeutic agent" as an "antibody". An anti-Notch antibody was therefore directly and unambiguously disclosed in the application as filed as the preferred anti-tumorigenic therapeutic agent to be used in accordance with the invention.

The application as filed also provided basis for the administration of the anti-Notch antibody with a further therapeutic agent which was an anti-cancer agent which in turn was a chemotherapeutic antineoplastic agent. Indeed, page 27, lines 29 to 30 of the application provided a general basis for the co-administration as claimed.

The skilled person would thus, on reading the entire specification of the application as filed, directly and unambiguously derive that chemotherapeutic

antineoplastic agents were combinable with anti-tumorigenic agents as an additional "therapeutic agent".

- XI. The appellant requested that the decision under appeal be set aside and the patent be revoked.

The respondent requested in writing that the appeal be dismissed or, alternatively, that the decision under appeal be set aside and the patent be maintained on the basis of one of the auxiliary requests 1 to 3 filed with the reply to the appellant's statement of grounds of appeal.

### **Reasons for the Decision**

1. The appeal is admissible.
2. The duly summoned respondent was not present nor represented during the oral proceedings, as announced in writing. In accordance with Rule 115(2) EPC and Article 15(3) RPBA, the board continued the proceedings in the respondent's absence and the party was treated as relying on its written submissions.

*Main request and auxiliary requests 1 and 2 - claim 1 - added subject-matter (Article 123(2) EPC)*

3. In the following, reference to the "application" is a reference to the "application as filed".
4. Claimed is an anti-Notch antibody for use in a method of inhibiting the proliferation of tumorigenic cells to treat breast cancer in a subject which comprises the co-administration of a chemotherapeutic antineoplastic

agent. In view of the appellant's case, it needs to be decided, pursuant to Article 123(2), whether or not the skilled person, objectively, would derive directly and unambiguously from the disclosure of the application, using common general knowledge, the co-administration of an anti-Notch antibody and a chemotherapeutic antineoplastic agent in a method of inhibiting the proliferation of tumorigenic cells to treat breast cancer.

5. The respondent has not referred to a literal disclosure in the application as basis for the wording of the claim, but has rather argued that the claims and several passages in the description of the application provided such a basis.
6. In a first line of argument the respondent referred to claims 16 and 20 of the application as a disclosure of the claimed subject-matter. These claims, as well as claims 21 and 22, read:

"16. A method for treating a subject having tumorigenic breast cells, comprising: a) identifying the presence of a tumorigenic breast cell in said subject; b) identifying one or more markers or properties characteristic of said tumorigenic breast cell to identify the nature of said tumorigenic breast cell; and c) selecting a therapeutic course of action based on said nature of said tumorigenic breast cell."

"20. The method of claim 16, wherein said course of action comprises co-administration of a Notch pathway inhibitor and a second anti-neoplastic agent to said subject.

21. A method of preventing or reducing metastasis, comprising: administering a Notch pathway inhibitor to a subject suspected of having metastasis.

22. The method of claim 21, wherein said Notch pathway inhibitor comprises an anti-Notch4 antibody."

7. The board considers, however, that, whereas the recited claims may - in the context of breast cancer treatment of a subject - possibly convey the co-administration of a "Notch pathway inhibitor" (i.e. any inhibitor of any compound involved in the Notch signalling pathway), or of an "anti-Notch4 antibody" (i.e. an antibody specifically recognising Notch4 as part of the Notch pathway), with a "anti-neoplastic agent", these claims do not provide a basis - in the same context - for the co-administration of an "anti-Notch antibody", i.e. an antibody recognising any Notch molecule involved in the Notch pathway, and a further "anti-neoplastic agent".
8. Indeed, the board considers that the particular generalisation by the term "anti-Notch antibody", i.e. antibodies recognising not only the Notch4 protein but also other Notch proteins such as Notch1 or Notch2, amounts to a so-called "intermediate" generalisation in between the concepts of a general "Notch pathway inhibitor" and the specific "anti-Notch4 antibody" which was not clearly and unambiguously derivable for the skilled person from the indicated claims.
9. In a second line of argument the respondent referred to page 27, lines 29 to 30 of the application as providing a general basis for the co-administration as claimed, the passage reading: "*In some embodiments of the present invention, the anti-tumorigenic therapeutic*

*agents of the present invention are co-administered with other anti-neoplastic therapies."*

10. The respondent subsequently argued that the application disclosed the "anti-Notch antibody" as the preferred anti-tumorigenic therapeutic agent of the invention as recited in the claim. The passages referred to in particular in this context were passages on page 18, lines 6 to 9: "*Inhibitors of Notch signaling (such as Numb and Numb-like; or antibodies or small molecules that block Notch activation) can be used in the methods of the present invention to inhibit tumorigenic cells. In this manner, the Notch pathway is modified to kill or inhibit the proliferation of tumorigenic cells.*"; on page 24, line 28 to page 25, line 1: "*A pharmaceutical composition containing a regulator of tumorigenesis according the present invention can be administered by any effective method. For example, a Notch ligand, an anti-Notch antibody, or other therapeutic agent that acts as an agonist or antagonist of proteins in the Notch signal transduction/response pathway can be administered by any effective method.*"; as well as passages on page 25, lines 2 to 29 and page 26, lines 1 to 6 and 22 to 23 of the application.
11. However, the board notes, firstly, that none of the passages referred to by the respondent, including the basic passage on page 27 (see point 9) are disclosures in the direct context of the treatment of breast cancer in a subject, i.e. the therapeutic context of the claim. In fact, the passage on page 27 explicitly emphasises that the co-administration only applies "*[i]n some embodiments of the present invention*" without specifying such embodiments.

12. The board notes, secondly, that the passage on page 18 (see point 10), enumerates a number of "*inhibitors of Notch signaling*" in general and on page 24 (see point 10)) exemplifies a number of "*regulators of tumorigenesis*". However, these passages do not refer to the more specific group of compounds referred to as "*anti-tumorigenic therapeutic agents*" in the basic passage on page 27. Furthermore, whereas the passages on pages 25 and 26 (see above) refer to "*anti-Notch therapeutic agents*", they do not disclose an "anti-Notch antibody" as referred to in the claim. In fact, the board notes in this context that the passage on page 26, lines 22 to 23, reading "*In some embodiments, the therapeutic agent is an antibody (e.g., an anti-Notch4 antibody).*", indeed does not refer to an "anti-Notch antibody" but specifically to "*an anti-Notch4 antibody*" (see also point 6 above).
13. The board notes, thirdly, that the third element of the combination of features defining the claimed subject-matter, i.e. "*a chemotherapeutic antineoplastic*" is mentioned solely in the passage on page 28, lines 4 to 9: "*Some embodiments of the present invention provide methods (therapeutic methods, research methods, drug screening methods) for administering a therapeutic compound of the present invention and at least one additional therapeutic agent (e.g., including, but not limited to, chemotherapeutic antineoplastics, antimicrobials, antivirals, antifungals, and anti-inflammatory agents) and/or therapeutic technique (e.g., surgical intervention, radiotherapies).*"
14. The skilled person derives from this passage that "*chemotherapeutic antineoplastics*" are only disclosed as one of several options that may be used as an additional therapeutic agent to the "therapeutic

compound of the invention", and this only in some embodiments of the invention. The passage neither discloses nor implies the particular feature "chemotherapeutic antineoplastic" to be combined with the other two specific features in the claim.

15. In view of the above findings and considerations, the board judges that the invention as claimed, in particular the combination of technical features relating to the co-administration of an anti-Notch antibody and a chemotherapeutic antineoplastic in a method of inhibiting tumorigenic cells to treat breast cancer, is not directly and unambiguously derivable for a skilled person from the disclosure in the application. The claim thus relates to subject-matter extending beyond the content of the application as filed.
16. The claim therefore does not comply with the requirements of Article 123(2) EPC.

*Auxiliary request 3 - claim 1 - added subject-matter  
(Article 123(2) EPC)*

17. The wording of this claim differs from the wording of claim 1 of the main request only by the addition of further technical features. However, since the particular feature combination found to constitute added subject-matter within the meaning of Article 123(2) EPC in the context of the main request is still present in the claim, this claim likewise relates to added subject-matter.
18. Auxiliary request 3 therefore fails *mutatis mutandis* to comply with the requirements of Article 123(2) EPC.

19. Thus, no allowable claim requests are on file.

**Order**

**For these reasons it is decided that:**

1. The decision under appeal is set aside.
2. The patent is revoked.

The Registrar:

The Chair:



S. Lichtenvort

G. Alt

Decision electronically authenticated