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D E C I S I O N
of 21 April 2004

Case Number: T 0347/02 - 3.3.8

Application Number: 89912909.2

Publication Number: 0440744

IPC: C12N 5/00

Language of the proceedings: EN

Title of invention:
Products and methods for controlling the suppression of the neoplastic phenotype

Patentee:
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA

Opponent:
Rhône-Poulenc Rorer
INTROGEN THERAPEUTICS, INC.

Headword:
Neoplastic phenotype/UNIVERSITY OF CALIFORNIA

Relevant legal provisions:
EPC Art. 84
EPC R. 57a

Keyword:
"Allowablility of amended claim - no"
"Lack of clarity - yes"

Decisions cited:
G 0009/91

Catchword:
-

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Case Number: T 0347/02 - 3.3.8

D E C I S I O N
of the Technical Board of Appeal 3.3.8
of 21 April 2004

Appellant: (Proprietor of the patent)
THE REGENTS OF THE UNIVERSITY OF CALIFORNIA
1320 Harbor Bay Parkway
Suite 150
Alameda
California 94501 (US)

Representative:
Voelker, Ingeborg, Dipl.-Biol.
UEXKÜLL & STOLBERG
Patentanwälte
Beselerstrasse 4
D-22607 Hamburg (DE)

Respondent I: (Opponent 1)
Rhône-Poulenc Rorer
20 Avenue Raymond Aron
F-92160 Antony (FR)

Representative:
Becker, Philippe
Cabinet Becker & Associés
35, rue des Mathurins
F-75008 Paris (FR)

Respondent II: (Opponent 2)
INTROGEN THERAPEUTICS, INC.
301 Congress Avenue, Suite 1850
Austin, Texas 78701 (US)

Representative:
Bösl, Raphael, Dr. rer. nat., Dipl.-Chem.
Patentanwälte
Isenbruck Bösl Hörschler Wichmann Huhn
Postfach 860 880
D-81635 München (DE)

Decision under appeal: **Decision of the Opposition Division of the European Patent Office posted 5 February 2002 revoking European patent No. 0440744 pursuant to Article 102(1) EPC.**

Composition of the Board:

Chairman: L. Galligani
Members: F. L. Davison-Brunel
S. C. Perryman

Summary of Facts and Submissions

I. European patent No. 0 440 744 with the title "Products and methods for controlling the suppression of the neoplastic phenotype" was granted with 12 claims for all Designated Contracting States, based on the international patent application No. PCT/US89/04808.

Granted claims 1 and 6 read as follows:

"1. The use of a cancer suppressing gene or fragment thereof encoding functional cancer suppressor protein for the manufacture of a medicament comprising said cancer suppressing gene or fragment thereof encoding functional cancer suppressor protein to suppress the neoplastic phenotype of a mammalian cancer cell lacking endogenous wild type cancer suppressing protein encoded by said cancer suppressing gene."

"6. The use of a cancer suppressing gene or fragment thereof encoding functional cancer suppressor protein according to any preceding claims, wherein the cancer suppressor gene is the wild type human retinoblastoma gene."

Claims 2 to 5 concerned further embodiments of the use according to claim 1. Independent claim 7 and claims 8 to 12 which were directly or indirectly dependent on claim 7 related to medicaments comprising the cancer suppressing gene or fragment thereof.

II. Two oppositions were filed under Article 100(a) to (c) EPC. The Opposition Division revoked the patent by decision dated 5 February 2002 because it considered

that claims 1 and 6 of the main request (claims as granted) and claim 1 of the auxiliary requests I and II did not meet the requirements of Articles 56 and 83 EPC.

III. The Appellants (Patentees) filed a notice of appeal, paid the appeal fee and submitted a statement of grounds of appeal together with one new main request and five auxiliary requests.

IV. Respondents I (Opponents 1) and Respondents II (Opponents 2) answered to the grounds of appeal.

V. The Board sent a communication pursuant to Article 11(1) of the Rules of Procedure of the Boards of Appeal indicating its preliminary, non-binding opinion.

VI. Respondents II and the Appellants answered to this communication. The Appellants filed a new main request and one auxiliary request in replacement of all preceding requests.

VII. At oral proceedings, which took place on 21 April 2004, the Appellants withdrew the auxiliary request. The sole remaining request for consideration by the Board comprised five claims.

Claim 1 read as follows:

"1. The use of the wild-type human retinoblastoma gene or fragment thereof encoding functional retinoblastoma protein for the manufacture of a medicament comprising said retinoblastoma gene or fragment thereof encoding functional retinoblastoma protein to suppress the neoplastic phenotype, **including the tumorigenicity**, of

a mammalian cancer cell lacking endogenous wild-type retinoblastoma protein encoded by said retinoblastoma gene." (emphasis added by the Board).

Claims 2 to 5 were directly or indirectly dependent on claim 1 and related to further embodiments of the use according to claim 1.

VIII. The Appellants' arguments which are relevant to the present decision may be summarized as follows:

The term "including the tumorigenicity" was introduced in claim 1, corresponding to granted claim 6, to take into account the Respondents' allegations that the expression "to suppress the neoplastic phenotype" was to be understood as meaning "to suppress cell growth" and that, consequently, the claimed subject-matter lacked novelty. The amendment was, thus, allowable under Rule 57a EPC.

The patent specification (page 22, lines 28 to 31 and page 21, lines 46 to 49) showed that loss of tumorigenicity was the most important validation for the suppression of the neoplastic phenotype. The *in vivo* assay in nude mice was the test of choice well known to the skilled person. What was meant by suppression of tumorigenicity was clear: it was the suppression of the capability of cells lacking the RB gene to form tumors in nude mice as was obtained by the introduction of the RB gene in said cells. This effect which had been demonstrated for the first time by the Appellants went beyond the mere prevention of tumor formation in susceptible cells, the latter being linked to suppression of cell growth.

IX. The Respondents' arguments which are relevant to the present decision may be summarized as follows:

The neoplastic phenotype was defined in the patent specification as a combination of features, one of them being tumorigenicity. Thus, the granted claim wording: "to suppress the neoplastic phenotype" included suppression of tumorigenicity. For this reason, the amendment which consisted in adding the expression "including tumorigenicity" did not change the claimed subject-matter and was not allowable under Rule 57a EPC.

Alternatively, if the expression "including tumorigenicity" was meant to add an hitherto undisclosed feature to the claimed subject-matter, then it could only be that tumorigenicity alone was now used to define the neoplastic phenotype, rather than the above mentioned combination of features. This amounted to added subject-matter and the requirements of Article 123(2) EPC were not fulfilled. In addition, what was meant by "including tumorigenicity" was unclear in the absence of further definition of how tumorigenicity was to be measured (Article 84 EPC).

For these reasons, the claim request had to be rejected under Rule 57a EPC or as not fulfilling the requirements of Article 123(2) EPC and of Article 84 EPC.

X. The Appellants requested that the decision under appeal be set aside and that a patent be granted on the basis of the main request filed on 17 March 2004.

The Respondents requested that the appeal be dismissed.

Reasons for the decision

Rule 57a EPC; Article 84 EPC

1. Claim 1 corresponds to granted claim 6 when dependent on granted claim 1, with the addition of the feature "including tumorigenicity" to further characterize the expression "to suppress the neoplastic phenotype of a mammalian cancer cell".

2. In accordance with Rule 57a EPC, the claims may be amended provided that the amendments are occasioned by grounds of opposition even if the respective ground has not been invoked by the opponent. Furthermore, in accordance with the Enlarged Board of Appeal's decision G 9/91 (OJ EPO 1993, 408, point 19 of the decision), amendments to a claim in the course of appeal proceedings are to be fully examined as to their compatibility with the requirements of the EPC.

3. On page 21, lines 47 and 48 of the granted patent, it is mentioned: *"..., loss of tumorigenicity is the most important validation for suppression of the neoplastic phenotype by the RB gene.*". In the same manner, it is taught on page 22, lines 28 to 31: "*Suppression of the neoplastic phenotype was observed both by in vitro indices, such as soft agar colony formation, and by an in vivo assay, that of tumorigenicity in nude mice.*"

4. Since claim 1 as granted refers to the suppression of "the neoplastic phenotype of a **mammalian cancer cell**" (emphasis added), it is readily apparent that the purpose of the medicament the manufacture of which is claimed, is to "undo" the neoplastic behaviour of an **actual** cancerous cell, which includes its oncogenicity, ie its capability to form malignant tumors in vivo. Thus, the wording of the said claim does not address the prevention of the appearance of a neoplastic phenotype in susceptible precursor cells, ie cells which are only potentially cancerous.

5. In the board's judgement, the introduction into claim 1 of the feature "including tumorigenicity" serves no clear purpose and is puzzling because:

(i) The said feature puts emphasis on one of the characteristics of the neoplastic phenotype which was already in the claim thereby leaving the reader in doubt whether the proposed amendment has a limiting or merely a clarifying purpose;

(ii) It was not clearly indicated which prior art citation renders necessary its introduction in response to which substantive objection. The appellants merely pointed out that the inclusion of the amendment in the granted claim avoids equating the neoplastic phenotype with one of the characteristics which in combination define the neoplastic phenotype, in particular with cell growth in vitro ;

(iii) The said feature was introduced in the claim without any reference to a method for the assessment of "tumorigenicity", whereas the description specifically refers to "tumorigenicity in nude mice" which in the Appellants' submission is the "gold standard" for the said assessment. However, as the claim does not refer to this standard and leaves the test for tumorigenicity open both in quantitative (complete or partial loss of malignancy?) and qualitative (temporary inhibition or permanent reversion of malignancy?) terms, the reader is left in doubt as to the real significance of the amendment.

(iv) Although the Appellants insisted that the amendment was meant as a limitation to those cells in which replacement of the Rb gene not only stopped or slowed down tumor formation, but caused a reversion to "a more normal behaviour", the said limitation cannot be derived from the wording of the feature as suppression of tumorigenicity does not necessarily imply a reversion of the cell to a normal phenotype. As a matter of fact, the patent specification presents "suppress" and "revert" as two alternatives (cf page 22, line 24).

6. Thus, in consideration of the fact that Rule 57a EPC, while allowing amendments as a reaction to a ground for opposition, does not allow merely tidying up, clarifying or improving the claims, and also in view of

the fact that the amendment per se is not clear (Article 84 EPC), the Board concludes that the only request on file cannot be allowed under the EPC.

7. The appellants refrained from putting forward further requests, thus the following order is issued:

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar: The Chairman:

A. Wolinski L. Galligani