

Internal distribution code:

- (A) Publication in OJ
(B) To Chairmen and Members
(C) To Chairmen
(D) No distribution

**Datasheet for the decision
of 8 November 2012**

Case Number: T 1648/11 - 3.3.08

Application Number: 98202403.6

Publication Number: 885971

IPC: C12Q 1/68

Language of the proceedings: EN

Title of invention:

Methods and compositions for chromosome-specific staining

Patent Proprietor:

REGENTS OF THE UNIVERSITY OF CALIFORNIA

Opponents:

Dako Denmark A/S
Kreatech Biotechnology B.V.

Headword:

Chromosome-specific staining/UNIVERSITY OF CALIFORNIA

Relevant legal provisions:

EPC Art. 123(2)
RPBA Art. 12(4), 13(1)(3)

Keyword:

"Main request and auxiliary request 1 - added matter (yes)"
"Auxiliary requests 2 and 3 - not admitted into the
proceedings"

Decisions cited:

T 0328/87, T 0296/96, T 0823/96

Catchword:

-



Case Number: T 1648/11 - 3.3.08

DECISION
of the Technical Board of Appeal 3.3.08
of 8 November 2012

Appellants:
(Patent Proprietors) Regents of the
University of California
1111 Franklin Street
12th Floor
Oakland
California 94607 (US)

Representative: Fisher, Adrian John
Carpmaels & Ransford
One Southampton Row
London WC1B 5HA (GB)

Respondent I:
(Opponent 1) Dako Denmark A/S
Produktionsvej 42
DK-2600 Glostrup (DK)

Respondent II:
(Opponent 2) Kreatech Biotechnology B.V.
Vlierweg 20
NL-1032 Amsterdam (NL)

Representative: Zimmer, Franz-Josef
Grünecker Kinkeldey
Stockmair & Schwanhäusser
Anwaltssozietät
Leopoldstrasse 4
D-80802 München (DE)

Decision under appeal: **Decision of the Opposition Division of the
European Patent Office posted 17 May 2011
revoking European patent No. 885971 pursuant to
Article 101(3) (b) EPC.**

Composition of the Board:

Chairman: M. Wieser
Members: M. R. Vega Laso
J. Geschwind

Summary of Facts and Submissions

- I. European patent No. 0 885 971 with the title "Methods and compositions for chromosome-specific staining" was granted on European patent application No. 98202403.6, published as EP 0 885 971. The application was filed with 11 claims as a divisional application of the earlier European patent application No. 90308718.7 in accordance with Article 76 EPC 1973. References to the "application as filed" in the present decision apply to the original application documents.

- II. The patent was granted with 25 claims directed to methods of staining target chromosomal DNA to detect a chromosomal amplification or deletion (claims 1 to 17), and test kits for staining chromosomal DNA to detect a chromosomal amplification or deletion (claims 18 to 25).

- III. An opposition to the grant of the patent was filed on the grounds for opposition of Article 100(a), (b) and (c) EPC, in particular that the claimed subject-matter lacked either novelty (Article 54 EPC) or an inventive step (Article 56 EPC), that the claimed invention was not sufficiently disclosed in the patent, and that the subject-matter of the patent extended beyond the content of the application as filed. During the opposition proceedings an intervention based on the same grounds for opposition was filed.

- IV. By a decision posted on 17 May 2011, the opposition division revoked the patent under Article 101(2) and 101(3) (b) EPC, on the grounds that the amendments introduced into the claims according to each of the requests on file (main request and first to seventh

auxiliary requests) contravened Article 123(2) EPC. The claims according to the main request and the third to seventh auxiliary requests had been filed by letter dated 21 January 2011, and those of the first and second auxiliary requests were submitted during the oral proceedings before the opposition division.

- V. The patent proprietors (appellants) lodged an appeal against the decision of the opposition division and requested that the appeal proceedings be expedited on the grounds that the opposed patent was the subject of infringement proceedings in Germany. As a subsidiary request, oral proceedings were requested.
- VI. Together with their statement of grounds of appeal, the appellants filed eight sets of claims (main request and auxiliary requests 1 to 7) which were identical to those underlying the decision under appeal.
- VII. Claim 1 of the main request reads as follows:

"1. A method of staining target chromosomal DNA to detect a chromosomal amplification or deletion comprising:

(a) providing a first probe which is a heterogeneous mixture of labeled nucleic acid fragments that includes unique sequences which are substantially complementary to a first portion of a chromosome for which detection is desired, wherein the labeled nucleic acid fragments are labeled with a first label and have a complexity of from 50 kilobases to 10 Mb;

(b) employing the probe and target chromosomal DNA in in situ hybridization to permit detection of probe which is hybridized to target chromosomal DNA, wherein the target chromosomal DNA is interphase DNA and wherein the target chromosomal DNA is present in a morphologically identifiable cell nucleus during the in situ hybridization; and

(c) detecting signal from the first label and signal from a second label hybridized to a second portion of a chromosome to determine whether an amplification or deletion is present in the target chromosomal DNA, wherein the second label is different from the first label, and the second portion is different from the first portion." Dependent claims 2 to 15 relate to variations of the method according to claim 1. Claims 16 to 22 are directed to test kits for staining chromosomal DNA to detect a chromosomal amplification or deletion.

VIII. The sole claim of auxiliary request 2 differed from claim 1 of the main request essentially in that the feature "*..., wherein the first and second portions are portions of the same chromosome*" had been introduced at the end of step (c), and that in the preamble and in step (c) the wording "*amplification or*" had been deleted.

IX. Respondent I (opponent 01) and respondent II (opponent 02) replied to the statement of grounds of appeal. Together with its reply, respondent I submitted an expert opinion as additional evidence.

- X. The parties were summoned to oral proceedings on 8 November 2012. In a communication pursuant to Article 15(1) of the Rules of Procedure of the Boards of Appeal (RPBA), the board expressed its provisional opinion on some of the issues concerning Article 123(2) EPC that intended to discuss during the oral proceedings. With regard to the evidence filed in appeal proceedings, the board drew attention to Article 12(4) RPBA.
- XI. In response to the board's communication the appellants filed eight sets of claims as new main request and auxiliary requests 1 to 7, as well as new evidence in support of their line of argument on Article 83 EPC. They requested that the new requests be admitted into the proceedings and stated that, if the new requests were to be deemed admissible, the requests filed together with the statement of grounds of appeal would be withdrawn.
- XII. Both respondents submitted observations on the appellants' reply and objected to the admission of the new sets of claims into the proceedings.
- XIII. Three days before the scheduled oral proceedings the appellants submitted arguments in support of their request for admission of the new requests into the proceedings.
- XIV. During the oral proceedings, which were held on 8 November 2012, the appellants withdrew the auxiliary requests 1 and 3 to 7 filed together with the statement of grounds of appeal, and the main request and auxiliary requests 1 to 5 filed with letter of

1 October 2012. The claims according to the auxiliary request 2 filed with the statement became their new auxiliary request 1. Auxiliary requests 6 and 7 filed with letter of 1 October 2012 became their new auxiliary requests 2 and 3, respectively.

XV. The following document is referred to in the present decision:

Declaration of Dr. Mary E. Harper, dated 16 January 2011.

XVI. The submissions made by the appellants may be summarized as follows:

Main request - Article 123(2) EPC

The application as filed disclosed that the invention included the detection of amplifications and deletions, and that two or more different labels could be used in the methods of the invention. An explicit disclosure of the combination of these two features was not necessary because it was generally implicit to the skilled person that the features disclosed in the application could be combined unless they were clearly incompatible. This principle had been recognised by the boards of appeal in decisions T 328/87 (see point 2.2 of the reasons) and T 296/96 (see point 3.1 of the reasons).

The skilled person would seriously contemplate the use of two different labels for the detection of amplifications and deletions, because the specification included examples of such use (page 112, lines 20 to 24 for amplifications, and page 33, lines 9 to 13 for

deletions). These passages provided indirect support for claim 1, especially when considered in the light of the general teachings regarding detection of amplifications and deletions and the use of two or more different labels.

Auxiliary request 1 - Article 123(2) EPC

The first auxiliary request was limited to the detection of deletions and to the use of two labels which hybridized to different portions of the same chromosome. Claim 1 thus represented the embodiment disclosed in Figure 11F and described on page 33, lines 9 to 13. It was not necessary to specify in the claim that the labels were of different "colours", or that the second label targeted "flanking sequences". The use of coloured labels was not an essential feature of the method illustrated in Figure 11F and the specification was replete with references to labels other than coloured labels. Moreover, it could not reasonably be said to be necessary to use a second label which targets two "flanking" sequences. The relevant passage of the description was on page 33, lines 9 to 13. This passage explicitly contemplated either none or two controls for hybridization. It would be self-evident to the skilled reader that a single control could alternatively be used.

There was no justification for the opposition division's assumption that the regions bound by the control probe had to be in the immediate vicinity of the deleted sequence. Although the drawings in Figure 11F showed these regions to be relatively close

to the deleted region, the drawings were merely schematic.

Auxiliary requests 2 and 3 - Admission into the proceedings

The auxiliary requests 2 and 3 could not have been filed in the proceedings before the opposition division. In the written stage of the opposition proceedings, the opposed patent had been defended by filing several requests, and at the oral proceedings further requests addressing issues under Article 123(2) EPC were filed. Thus, the proprietors had done everything to ensure fair and reliable proceedings in line with their obligation to exercise due care in the proceedings.

Since at the oral proceedings in opposition the opposition division had not given detailed reasons for its finding that claim 1 contravened Article 123(2) EPC, the proprietors did not fully understand which of the elements of step (c) in claim 1 was at stake. In addition, at the oral proceedings there had been very little time to consider and propose amendments to attempt to overcome the objections and a very limited opportunity to respond to the opposition division's view on the amendments. Therefore, the proprietor could not have anticipated how step c) of claim 1 should be amended to successfully overcome the objections right away.

Until receipt of the board's communication, the appellants had no reason for believing that the various claim requests then on file did not fully address the opposition division's objections under

Article 123(2) EPC. Thus, the late filing of the new requests was justified as a prompt and good-faith attempt to respond to concerns raised by the board.

It could not be the intention of Article 12(4) RPBA to force the proprietor of a patent to anticipate and file any possible options of amended claim sets during the first instance-procedure in order to avoid the risk of preclusion in appeal proceedings.

The second and third auxiliary requests were not *prima facie* unallowable but found a clear basis in the application as filed. The new requests were based on a combination of Figure 11F with the disclosure on pages 31, 32 and 33 of the application as filed.

Article 13(1) RPBA mentioned the complexity of the new subject-matter submitted, the current state of the proceedings and the need for procedural economy as factors to be considered by the board when exercising its discretion. However, Article 13(1) RPBA did not preclude the consideration of factors such as the relevance of the submission, including the existence or absence of grounds justifying late submission and the request's prospects of success.

Although the new requests had been filed at a relatively late stage in the appeal proceedings, they did not necessitate a postponement or remittal of the case and, thus, did not unduly delay the termination of the appeal procedure.

The non-admission of the new requests in appeal proceedings would be contrary to the essential

principle of procedural fairness. It unduly disadvantaged the appellants who would be restricted to defend claims which the board had already indicated (in its provisional opinion) to be non-allowable.

The principle of the right to be heard (Article 113(1) EPC) required that the appellants were given the chance to make further amendments to the opposed patent. If the board were not to allow the new requests into the proceedings, this would constitute a violation of this fundamental principle.

XVII. The submissions made by the respondents were essentially as follows:

Main request - Article 123(2) EPC

Amended claim 1 encompassed subject-matter that extended beyond the content of the application as filed. In the context of Article 123(2) EPC, the decisive question was whether or not a person skilled in the art could derive the claimed subject-matter, clearly and unambiguously, from the application as filed. The standard taken by the appellants, i.e. what was obvious to a skilled person, was not the correct standard.

Auxiliary request 1 - Article 123(2) EPC

The opposition division correctly decided that page 33, lines 9 to 13 and the corresponding Figure 11F of the application as filed were not an adequate basis for the method of claim 1.

Auxiliary requests 2 and 3 - Admission into the proceedings

Auxiliary requests 2 and 3 were late filed and run counter basic procedural requirements as laid down in Article 12(4) RPBA. They could have been presented already in opposition proceedings because the issues concerning step (c) of the method of claim 1 had been discussed already in the provisional opinion sent by the opposition division in preparation of the oral proceedings. During the discussion at the oral proceedings before the opposition division it was entirely clear that the opposition division could not find a basis in the application as filed for this step (see page 2, second paragraph of the minutes dated 17 May 2011).

Although the decisive reasons were apparent from the decision under appeal, the new requests had not been filed together with the statement of grounds of appeal. However, only six weeks before the oral proceedings, an entirely new case was presented. It was *prima facie* clear that there was neither an explicit nor an implicit basis for the amendments in the specification or in Figure 11F.

XVIII. The appellants requested that the decision under appeal be set aside and that the patent be maintained on the basis the main request (filed with the statement of grounds of appeal on 14 September 2011) or on the basis of auxiliary request 1 (filed as auxiliary request 2 with the statement of grounds of appeal on 14 September 2011), or on the basis of auxiliary requests 2 or 3

(filed as auxiliary requests 6 and 7 with letter of 1 October 2012).

XIX. Respondents I and II requested that the appeal be dismissed.

Reasons for the Decision

Main request - Article 123(2) EPC

1. The present main request is identical to the main request underlying the decision under appeal. In its decision, the opposition division found that there was no general disclosure in the application as filed for a method in which the signal from a first labeled probe and a second label were used to determine the presence of a deletion or amplification. The passage on page 33, lines 9 to 13 and Figure 11F were not regarded as an appropriate basis because i) they related only to a deletion (not to an amplification as specified in the claim), ii) the portions to which the labeled probes hybridized, namely the deletion itself and its flanking regions, were - other than in the claim - narrowly defined, and iii) the labeled portions belonged to the same chromosome, a feature which was not included in the claim (see paragraph 2.3.5 of the decision under appeal).

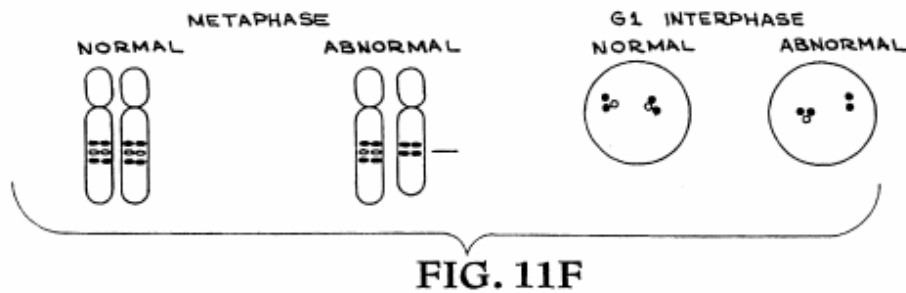
2. The board shares the view of the opposition division. While it is true that the detection of chromosomal amplification by staining targeted chromosomal material is mentioned in the application as filed (see, for instance, page 17, lines 10 to 13), and that

combinations of labels are disclosed in different passages of the application as filed (see, *inter alia*, page 12, lines 19 to 22; passage from page 31, second full paragraph to page 32, end of first paragraph; page 37, lines 6 to 8; and page 48, lines 2 to 8), there is no specific disclosure in the application as filed for the use of two differently labeled probes for detecting chromosomal amplification. Contrary to appellants' view, the passage on page 112, second paragraph, which relates to the detection of a BCR-ABL fusion (see heading on page 105, lines 5 and 6) using a labeled probe specific for BCR and a differently labeled probe specific for ABL, cannot be accepted as an appropriate basis.

3. As regards the detection of chromosomal deletions, the sole specific disclosure of the use of differently labeled probes is found in the passage on page 33, lines 9 to 13 of the application as filed, in which Figure 11F is described. This passage reads:

"f. Section f) represents a staining pattern useful in the detection of a deletion. A deletion could also be detected with a probe that stains only the deleted region; however, lack of probe binding may be due to reasons other than deletion of the target sequence. The flanking regions stained a different "color" serve as controls for hybridization."

Figure 11F of the application as filed is as follows:



4. It is apparent from the Figure that three different probes and two different labels are used, one probe binding to the portion which is deleted in the abnormal cells, and the other two probes, which have a different label than the first probe, binding to the flanking regions, i.e. the regions flanking the deletion.
5. However, apart from requiring that the first and second portion of the chromosome to which the, respectively, first and second label hybridize, are different, claim 1 does not identify the specific portions as the portions flanking the deletion. Moreover, the claim does not even specify that the portions are on the same chromosome, but seems to encompass also methods in which the controls for hybridization may hybridize to a different chromosome.
6. In view of the above, the board judges that claim 1 represents a generalization of the disclosure on page 33 and Figure 11F, which a person skilled in the art could not derive, directly and unambiguously, either from a combination of the passage quoted above and Figure 11F, or from the application as filed taken as whole.
7. The statements in decision T 296/96 of 12 January 2000 cited by the appellants do not support their line of

argument, but rather run counter it. It is stated in this decision:

"The content of a document must not be considered to be a reservoir from which features pertaining to separate embodiments could be combined in order to artificially create a particular embodiment" (see paragraph 3.1 of the reasons).

This is precisely what claim 1 is directed to: an artificially created method of staining chromosomal DNA which results from the combination of some features of the specific embodiment of Figure 11F with other features disclosed in the application as filed in a different context.

8. Since a basis in the application as filed for the feature *"... detecting signal from the first label and signal from a second label hybridized to a second portion of a chromosome to determine whether an amplification or deletion is present ..."* in the context of a method according to claim 1 cannot be acknowledged, Article 123(2) EPC is contravened.

Auxiliary request 1 - Article 123(2) EPC

9. The present auxiliary request 1 is identical to the auxiliary request 2 underlying the decision under appeal. The sole claim of this request differs from claim 1 of the main request in that the claimed method has been restricted to the detection of a chromosomal deletion, and that the feature *"... wherein the first and second portions are portions of the same chromosome ..."* has been included in step (c).

10. As basis for the amended claim the appellants relied on the same passage and figure of the application as filed as for the main request. However, like the opposition division, the board considers that the wording of claim 1 does not define what a person skilled in the art would derive from the disclosure in the application as filed indicated by the appellants. It is clearly stated on page 33, lines 12 and 13 (see paragraph 3 above) that the flanking regions are stained with a different "color", and it is apparent from Figure 11F that, in addition to the probe hybridizing to a portion which is deleted in abnormal cells, two further probes that hybridize to the flanking regions and are labeled with a different label than the first probe are used. By omitting these features, the appellants have introduced subject-matter which is not immediately apparent to skilled person reading the application as filed.

11. Contrary to appellants' line of argument relying on the expert evidence provided by Dr. Mary Harper, the board observes that whether or not a person skilled in the art could possibly think of other approaches for providing controls for hybridization, is immaterial in the context of assessing compliance with Article 123(2) EPC. The question of what may be rendered obvious to a skilled person by the disclosure in the application as filed in the light of the common general knowledge, is not relevant to the assessment of the actual disclosure content of the application (see decision T 823/96 of 28 January 1997; paragraph 4.5 of the reasons).

12. The board thus concludes that also the first auxiliary request offends against Article 123(2) EPC.

Auxiliary requests 2 and 3 - Admission into the proceedings

13. According to Article 12(4) RPBA, the boards are empowered to hold inadmissible facts, evidence or requests which could have been presented in the first instance proceedings. Moreover, any amendment to a party's case made after it has filed its grounds of appeal may be admitted and considered at the board's discretion (see Article 13(1) RPBA). If the amendment is sought to be made after oral proceedings have been arranged, it shall not be admitted if it raises issues which the board or the other party or parties cannot reasonably be expected to deal without adjournment of the oral proceedings (Article 13(3) EPC).
14. In the present case, auxiliary requests 2 and 3 were filed more than one year after the appellants' statement setting out their grounds of appeal, and after oral proceedings have been arranged. Auxiliary request 2 differed from auxiliary request 1 in that the claim specified a second probe labeled with a second label as a control probe and that "*... the first portion to which the first probe hybridizes is the deletion region and the second portion to which the second probe hybridizes is a flanking region of the deletion region*". Additionally, the complexity specified in step (a) had been restricted to "*from 50 kilobases to 1 Mb*". In auxiliary request 3 the claim specified a second label and a third label of a second probe and a third probe serving as control probes, and that "*... the second and third labels are different*

- from the first label, and the first, second and third portions are different from each other, and wherein the first portion to which the first probe hybridizes is the deletion region and the second and third portions to which the second and third probes hybridize are flanking regions of the deletion region".*
15. In spite of appellant's contention, there is no doubt that such requests could have been filed in opposition proceedings as the relevant objections were already discussed in opposition proceedings (see paragraph 2.10 of the opposition division's communication attached to the summons to oral proceedings dated 21 October 2010). Exactly in that situation it is the purpose and aim of Article 12(4) RPBA to provide the board with the discretion not to allow the introduction of new requests into the appeal procedure which could have been filed already in opposition procedure. The board does not see therein any violation of the principle of procedural fairness.
16. It should be noted that, although the reasons for the opposition division's adverse finding on Article 123(2) EPC were clearly apparent from the decision under appeal, the appellants did not file the new requests together with the statement of grounds of appeal. Thus, the new requests must be regarded as an amendment to their case within the meaning of Article 13(1) RPBA, the admission of which is at the board's discretion.
17. The amendments introduced into the claims of the new requests, which the appellant argues to be an attempt to overcome the objections under Article 123(2) EPC,

not only fail to solve all outstanding issues, but even raise new ones. The claim of auxiliary request 2 specifies only two - instead of three - probes and fails, therefore, to mirror the embodiment disclosed in Figure 11F. The claim of auxiliary request 3 specifies a third probe labeled with a third label. This third label may or may not be the same as the second label. However, a third label different from the second has no basis in Figure 11F of the application as filed.

18. Thus, auxiliary requests 2 and 3, which have been filed very late in the proceedings, add to the complexity of the case. In view of the kind of amendments contained in the claims of these requests, it can reasonably be expected that they cannot be dealt with without an adjournment of the oral proceedings, which runs counter to procedural economy.
19. Therefore, the board, exercising its discretion under Articles 12(4) and 13(1) and in accordance with Article 13(3) RPBA, does not admit auxiliary requests 2 and 3 into the proceedings.
20. The board is convinced that the requirements of Article 113(1) EPC are satisfied. Contrary to the interpretation of the appellants (see paragraph XVI above), Article 113(1) EPC does not require that the appellants be given yet another chance to make further amendments to the opposed patent, but that decisions may only be based on grounds or evidence on which the parties have had an opportunity to present their comments.

Conclusion

21. In view of the submissions made by the appellants,
their requests cannot be granted.

Order

For these reasons it is decided that:

The appeal is dismissed.

The Registrar:

The Chairman:

A. Wolinski

M. Wieser