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Datasheet for the decision of 5 February 2020

Case Number: T 2172/15 - 3.3.08

Application Number: 10770456.1

Publication Number: 2427572

IPC: C12Q1/68, C12N15/11, C40B40/06

Language of the proceedings: EN

Title of invention:
Sequencing methods

Patent Proprietor:
Illumina, Inc.

Opponent:
Kilger, Christian

Headword:
Sequencing/ILLUMINA

Relevant legal provisions:
EPC Art. 100(b), 111(1)

Keyword:
Main request - sufficiency of disclosure - (no)
Remittal to the opposition division

Decisions cited:
T 0292/85, T 0929/92, T 0412/93, T 1543/12

Catchword:

Europäisches Patentamt
European Patent Office
Office européen des brevets

Beschwerdekammern

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Case Number: T 2172/15 - 3.3.08

D E C I S I O N
of Technical Board of Appeal 3.3.08
of 5 February 2020

Appellant: (Opponent)	Kilger, Christian Wachtelstr. 4 14195 Berlin (DE)
Representative:	CH Kilger Anwaltspartnerschaft mbB Fasanenstrasse 29 10719 Berlin (DE)
Respondent: (Patent Proprietor)	Illumina, Inc. 5200 Illumina Way San Diego, CA 92122 (US)
Representative:	Tollervey, Rebecca Mewburn Ellis LLP City Tower 40 Basinghall Street London EC2V 5DE (GB)
Decision under appeal:	**Decision of the Opposition Division of the European Patent Office posted on 13 October 2015 rejecting the opposition filed against European patent No. 2427572 pursuant to Article 101(2) EPC.**

Composition of the Board:

Chairman	B. Stolz
Members:	M. Montrone
	D. Rogers

Summary of Facts and Submissions

I. An appeal was lodged by the opponent (hereinafter the "appellant") against the decision of an opposition division to reject its opposition against the European patent No. 2 427 572, having the title "Sequencing methods".

II. With its statement of grounds of appeal, the appellant made submissions on insufficiency of disclosure, lack of novelty and inventive step against the subject-matter of the claims as granted.

III. In reply, the patent proprietor (hereinafter the "respondent") submitted eight auxiliary requests.

IV. The parties were summoned to oral proceedings. In a communication pursuant to Article 15(1) RPBA, the parties were informed of the board's provisional, non-binding opinion on some of the legal and substantive matters of the case, including sufficiency of disclosure. In reply thereto, both parties submitted arguments and counter-arguments in support of their case.

V. Oral proceedings before the board were held on 5 February 2020.

VI. Claim 1 of the main request (claims as granted) reads:

"1. A method for obtaining nucleic acid sequence information, said method comprising performing iterations of:

(a) at least one dark extension step comprising providing a dark extension sequencing reagent to a

target nucleic acid in the presence of a polymerase, said dark extension sequencing reagent comprising one or more nucleotide monomers, wherein said one or more nucleotide monomers pair with at least two nucleotide types in said target and with no more than three nucleotide types in said target, thereby forming a polynucleotide complementary to at least a portion of said target; and

(b) at least one read extension step comprising providing a read extension sequencing reagent to said target nucleic acid, said read extension sequencing reagent comprising at least one nucleotide monomer, said at least one nucleotide monomer of said read extension sequencing reagent comprising a reversibly terminating moiety, the read extension step further comprising removing unincorporated read extension sequencing reagent and removing said reversibly terminating moiety;

wherein (a) and (b) can be carried out in either order;

whereby sequence information is obtained comprising regions in which single nucleotide assignments are not made interspersed by regions comprising at least two consecutive positions that are assigned with single base resolution".

VII. The appellant's submissions, insofar as relevant to the present decision, may be summarised as follows:

Main request (claims as granted)

Sufficiency of disclosure - claim 1

The method according to claim 1 was insufficiently disclosed. Step(a) of claim 1 was directed to a dark extension step that *inter alia* required the pairing of "*one*" nucleotide monomer with three types of nucleotides in a target sequence. A monomer having these functional properties was neither disclosed in the patent, nor was it available from any of the prior art documents on file. The method could thus not be performed by the skilled person over the whole breadth of claim 1.

VIII. The respondent's submissions, insofar as relevant to the present decision, may be summarised as follows:

Main request (claims as granted)

Sufficiency of disclosure - claim 1

The patent in suit sufficiently disclosed the method according to claim 1, in particular the dark extension step as defined in step(a). Although step(a) of claim 1 specified that "*one or more nucleotide monomers pair with at least two nucleotide types in said target and with no more than three nucleotide types in said targe*t", this did not require that "*one*" monomer paired with "*no more than three nucleotide types*", or in other words that one nucleotide bound to three nucleotides in a target sequence.

Rather when read objectively, step(a) of claim 1 defined that a set or a genus of monomers collectively bound to either two or three nucleotides in a dark extension reaction. The requirements of Article 100(b) EPC were met if compounds were available that allowed the skilled person to work the method substantially across the whole of the claimed scope. The skilled person by using a set of two or three standard nucleotides, or a set of one semi-universal nucleotide and one standard nucleotide, or solely one semi-universal nucleotide, obtained a pairing with two or three types of nucleotides as required by step(a) of claim 1. This claim construction was not inconsistent with the formal wording of "*one or more*" nucleotides that pair with "*at least two*" but "*no more than three*" nucleotide types.

Furthermore, the features "*one or more nucleotide monomers*" and "*at least two nucleotide types in said target and with no more than three nucleotide types*" as recited in step(a) related to two ranges, wherein the pairing defined a functional relationship between the nucleotides in both ranges. In these circumstances the case law had established that it was sufficient for working the claimed method over its entire breadth if the invention could be performed with each value of both ranges. It was, however, not required that this was achieved by a combination of every single value in one range with each of the other range, i.e. by a pairing of one nucleotide with three types of nucleotides (see decision T 1543/12, point 4.3 of the Reasons).

Also according to established case law in relation to generic claims, the consideration of each individual embodiment or variant covered by a generic group was

not appropriate for assessing enablement (see decisions T 412/93, points 113 to 115 of the Reasons, T 292/85 point 3.2.1 of the Reasons). The correct approach rather was the assessment of whether or not the claimed subject-matter was based on a concept "*fit for generalisation*", wherein the teaching of the patent as a whole in relation to the invention was the critical factor (see decision T 929/92, points 44 to 45 of the Reasons). For this exercise the contribution of the claimed method to the art had to be taken into account. In the present case this was in essence the provision of an iterative process comprising at least one "*dark*" and one "*read*" extension step, wherein the nature of a single nucleotide was not critical, because a set of nucleotides irrespective of their nature achieved the required pairing as defined in step(a) of claim 1.

Novelty and inventive step

The claims as granted should also be assessed with regard to novelty and inventive step (Articles 54 and 56 EPC).

IX. The appellant requested that the decision under appeal be set aside and the patent be revoked, or alternatively that the case be remitted to the opposition division for further prosecution upon the basis of the first to the eighth auxiliary requests, all filed under cover of a letter dated 7 July 2016.

X. The respondent requested that the appeal be dismissed, or alternatively that the case be remitted to the opposition division for further prosecution upon the basis of the first to the eighth auxiliary requests, all filed under cover of a letter dated 7 July 2016.

Reasons for the Decision

Main request (claims as granted)

Sufficiency of disclosure - claim 1

1. The relevant issue to be assessed with regard to sufficiency of disclosure is whether or not the patent provides all the necessary information for the skilled person for performing the dark extension step specified in step(a) of claim 1 across the whole breadth of said step. In particular, whether the skilled person can readily provide a dark extension sequencing reagent comprising "*one or more nucleotide monomers wherein said one or more nucleotide monomers pair with at least two nucleotide types*" in a target nucleic acid, but "*with no more than three nucleotide types*".

2. It is established case law that the issue of whether or not the disclosure of a patent is sufficiently clear and complete for it to be carried out by a person skilled in the art must be decided by appraising the information contained in a patent as a whole in light of the common general knowledge of the skilled person at the relevant date.

   The disclosure of **one way of performing an invention** is **only** sufficient if it allows the invention to be performed substantially **within the whole range claimed.** In other words, sufficiency of disclosure presupposes that the skilled person is able to obtain substantially **all** embodiments falling within the ambit of a claim. This principle applies to any invention irrespective of the way in which it is defined, be it by way of a

functional feature or not (see Case Law of the Boards of Appeal of the EPO, 9th edition, 2019, II.C.5.4).

3. It is uncontested that nucleotides pairing with two but not more than two nucleotides were known in the art at the date of filing. It is also uncontested that the term "*more*" in "*one or more nucleotide monomers*" as referred to in step(a) of claim 1 specifies a group or a set of at least two nucleotides that pair with two or three types of nucleotides. It is however, a matter of dispute how the feature "*one or more nucleotide monomers*" that pair "*with at least two*" but "*no more than three*" nucleotide types in the dark extension reaction of step(a) of claim 1 is to be interpreted, and as a related issue, whether or not step(a) of claim 1 requires that in case of a single ("*one*") nucleotide said nucleotide pairs with two or three nucleotide types.

4. The respondent submitted that the feature "*one or more nucleotide monomers*" in step(a) of claim 1 defined a set or a generic group of nucleotides, but not a single one, that bound collectively to two or three types of nucleotides.

4.1 While the board agrees with the respondent that the dark extension step as defined in step(a) of claim 1 includes as an embodiment the use of a set or a group of nucleotides that pair collectively with two or three nucleotide types, the extension reaction is not limited thereto but comprises further embodiments. Step(a) of claim 1 literally states in the context of nucleotide monomers: "... *providing a dark extension sequencing reagent ...said ... sequencing reagent comprising one or more nucleotide monomers*". Giving the term "*one or more*" its ordinary meaning the claim explicitly

encompasses the use of a dark extension sequencing reagent comprising "*one*", i.e. a single nucleotide, while "*more*" relates to the use of any number of nucleotides greater than or equal to two.

4.2 Step(a) of claim 1 further specifies as a functional requirement that the monomers "*pair with at least two nucleotide types*" in a target sequence and "*with no more than three nucleotide types*". As stated above, step(a) of claim 1 explicitly mentions the provision of a dark extension sequencing reagent comprising "*one*", i.e. a single nucleotide. The claim thus clearly requires that not only at least two nucleotides as a group, but, in case of a single nucleotide, said single nucleotide be able to pair with two or three nucleotide types. Accordingly the respondent's argument that step(a) of claim 1 relates to a set or a generic group of nucleotides that collectively bind to two or three nucleotides only, does not convince the board.

4.3 Consequently, step(a) of claim 1 encompasses as one of its embodiments the use of of a single nucleotide monomer pairing with three types of nucleotides in a target sequence.

5. The respondent has not contested that neither the patent nor any of the cited prior art documents disclose such a nucleotide. Nor do these documents teach the skilled person how to generate a nucleotide having the functional properties defined in the claim. In these circumstances, the skilled person encounters an undue burden in carrying out the invention across substantially the whole scope of claim 1.

6. In a further line of argument under sufficiency of disclosure, the respondent submitted that the numbers

recited in step(a) of claim 1 defined two different ranges, wherein the nucleotide's ability to pair with either two or three types of nucleotides depended on the number of nucleotide monomers used for pairing. In such a situation in order for an invention to be carried out over the whole range claimed, the case law had established that each value within the ranges had to be achieved individually. There was however no need that each and every possible combination of all individual limiting values within the claimed ranges could be achieved (see decision T 1543/12 of 19 April 2016, point 4.3 of the Reasons).

6.1 The board is not convinced by this argument. In the case underlying decision T 1543/12 a method was claimed that concerned the generation of a L-lysine product. This product was *inter alia* characterised by three parameter ranges, namely a moisture content of up to 5% by weight, a L-lysine content in the final product of 40 to 85% by weight, and an equivalent ratio of anion/ L-lysine of 0.68 to 0.95. The appellant in that case submitted that it was not possible to produce products having a lysine content of 85% and an equivalent ratio of more than 0.71, although an equivalent ratio of 0.68 to 0.95 was claimed. The board in that case pointed out that the example of the appellant was technically impossible to achieve, since a product comprising 85% by weight of L-lysine could maximally comprise 15% by weight of an anion forming compound (the sum of compounds in a product obviously cannot exceed 100% by weight of that product). In such a situation is was clear that only a certain ratio of anion/L-lysine could be reached within the claimed range, since both the L-lysine content in the final product, and the achievable ratio of anion/L-lysine were dependent on each other and could not vary independently over the whole of both

ranges of the values claimed (see point 4.3 of the Reasons).

6.2 The situation in the present case, however, is different from T 1543/12, since the nucleotide monomers in step(a) of claim 1 are not characterised by certain parameters derived from different ranges, but by numerical values relating to discrete individual compounds (nucleotide monomers or nucleotide types). Moreover, nucleotide monomers pair independently from each other with different types of nucleotides. Thus, a pairing with three types of nucleotides is not limited to a set of standard nucleotides, or to a mixture of standard and semi-universal nucleotides, but could if available, also be achieved by a single nucleotide. Technical reasons preventing such a pairing by a single nucleotide are unknown to the board, and have not been submitted by the respondent.

7. In another line of argument under sufficiency of disclosure, the respondent submitted that the case law in relation to generic claims had established that not every embodiment or variant covered by a generic group of compounds had to be assessed for enablement (see decisions T 412/93 of 21 November 1994, points 113 to 115 of the Reasons, T 292/85 of 27 January 1988, point 3.2.1 of the Reasons). Rather, the provision of a concept fit for generalisation in the patent was the decisive issue to be taken into account (see decision T 929/92 of 19 February 1996, points 44 and 45 of the Reasons).

8. As set out above, step(a) of claim 1 is not limited to a set of compounds or a generic group of compounds to be used in a dark extension step, but explicitly mentions the use of a single nucleotide monomer having

certain functional properties, including the ability to pair with three types of nucleotides. However, such a monomer is neither disclosed in any of the available documents including the patent, nor is a teaching for its production. Thus, contrary to the respondent's view, there is no concept fit for generalisation allowing a person skilled in the art to perform the dark extension step across the whole breadth of step(a) of claim 1 without undue burden.

9. In light of the considerations above, the board concludes, that the patent does not provide the skilled person, taking common general knowledge into account, with all the information necessary for carrying out the claimed invention over the entire breadth of claim 1 of the main request without undue burden (Article 100(b) EPC). The decision under appeal has accordingly to be set aside.

10. Since the subject matter of the main request is insufficiently disclosed, the board sees no merit in providing a reasoned decision on novelty and inventive step, as requested by the respondent.

Remittal

11. Both parties requested a remittal of the case for further prosecution, if the main request contravened Article 100(b) EPC.

12. The essential function of an appeal in *inter partes* proceedings is to consider whether the decision which has been issued by the department of first instance is correct. Hence, a case is normally remitted, if essential questions regarding the patentability of the

claimed subject-matter have not yet been examined and decided by the department of first instance.

13. In opposition proceedings, the respondent submitted auxiliary requests identical to the present first to eighth auxiliary requests. These requests were refiled with the respondent's reply to the appellant's statement of grounds of appeal. The opposition division decided in the respondent/patent proprietor's favour on the claims as granted, hence there was no need for it to decide on the admission or allowability of the auxiliary requests. The board considers that these auxiliary requests raise issues that have not been addressed in the proceedings to date.

14. In the light of the above facts and the requests of both parties to remit the case to the opposition division for consideration of these auxiliary requests, the board considers that special reasons are present justifying a remittal.

Order

For these reasons it is decided that:

1. The decision under appeal is set aside.

2. The case is remitted to the opposition division for further prosecution upon the basis of the first to eighth auxiliary requests, all filed under cover of a letter dated 7 July 2016.

The Registrar: The Chairman:

L. Malécot-Grob B. Stolz

Decision electronically authenticated