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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

JAY M. SHORT,
Junior Party

(Patent 6,605,449),

v.

PHILLIP A. PATTEN and WILLEM P.C. STEMMER
Senior Party

(Application 10/646,221)

Patent Interference 105,532
(Technology Center 1600)

Before: FRED E. McKELVEY, *Senior Administrative Patent Judge*, and RICHARD TORCZON and SALLY GARDNER LANE, *Administrative Patent Judges*.

LANE, *Administrative Patent Judge*.

Decision – Interlocutory Motion – Bd.R. 125(b)

Short moved for judgment on the basis of no interference-in-fact (Paper 23) and unpatentability of Patten's claims for lack of written description (Paper 24).[1] We deny both of these motions. In addition with a third motion, Short moved to exclude evidence (Paper 43). We dismiss Short's third motion.

I. Introduction

Both parties claim a method of producing a library of polynucleotide sequences that are assembled from smaller "nucleic acid building blocks" (Short claim 1) or "polynucleotide segments" (Patten claim 275). Short asserts that these claims do not interfere and, given a specific claim construction, are unpatentable to Patten due to a lack of written description under 35 U.S.C. § 112, first paragraph.

II. Findings of Fact

Short

1. The involved Short US patent 6,605,449 ("the Short patent") was filed 14 June 2000, and issued 12 April 2003.

2. Short was accorded an earlier constructive reduction to practice, i.e., benefit for the purpose of priority, of US application 09/332,835, filed 14 June 1999, which subsequently issued as patent 6,537,776, on 25 March 2003. (Paper 1 at p. 4).

3. The Short patent is entitled "Synthetic Ligation Reassembly in Directed Evolution."

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[1] Oral argument was heard on 13 December 2007, before a court reporter. Mr. Daniel Pereira, and Mr. Chico Gholz argued for Short. Mr. R. Danny Huntington argued for Patten.

4. The named inventor of the involved Short patent is Jay M. Short.

5. The real party-in-interest of the Short patent is said to be Diversa Corporation. (Paper 4).

Patten

6. Patten's involved US application 10/646,221 ("the Patten application"), was filed 22 August 2003.

7. The involved Patten application was accorded an earlier constructive reduction to practice, i.e., benefit for the purpose of priority, of (1) US application 09/559,671, filed 27 April 2000, which issued as patent 6,613,514 on 2 September 2003, and (2) US application 08/769,062, filed 18 December 1996, which issued as patent 6,335,160, on 01 January 2002. (Paper 1 at 5).

8. The Patten application is entitled "Methods and Compositions for Polypeptide Engineering."

9. The named inventor of the Patten application is Phillip A. Patten.

10. The real parties-in-interest of record for the Patten application are said to be Maxygen, Inc., Codexis, Inc., and Pioneer Hi-Bred International, Inc. (Paper 9).

Count and Corresponding Claims

11. The Count is claim 1 of the Short patent or claim 275 of the Patten application.

12. Claim 1 of the Short patent recites:

> A method of producing a progeny library comprised of chimerized but pre-determined polynucleotide sequences each of which is comprised of a

pre-determined number of building block sequences that are assembled in non-random order, the method comprising:

(a) generating a plurality of pre-determined nucleic acid building block sequences comprised of sequences delineated by demarcation points selected from aligned progenitor nucleic acid sequences; and

(b) non-stochastically assembling said nucleic acid building block sequences to produce said chimerized but pre-determined polynucleotide sequences, such that a designed overall assembly order is achieved for each of said chimerized but pre-determined polynucleotide sequence.

13. Claim 275 of the Patten application recites:

A method of producing a library comprised of chimerized, defined polynucleotide sequences each of which is comprised of a defined number of polynucleotide segments that are assembled in an ordered fashion, the method comprising:

a) generating a plurality of defined polynucleotide segments selected from aligned substrate nucleic acid sequences, wherein said substrate nucleic acids encode full-length enzymes, and wherein boundaries defining the polynucleotide segments are selected from the aligned substrate nucleic acid sequences; and

b) reassembling said defined polynucleotide segments in order thereby producing the library of chimerized, defined polynucleotide sequences, such that said segments are reassembled in an ordered fashion to produce each chimerized, defined polynucleotide sequence

encoding a full-length enzyme, each of which is comprised of a defined number of polynucleotide segments that are reassembled in an ordered fashion.

14. Short claims 1-12, all of Short's patent claims, were designated as corresponding to the Count. (Paper 1 at 4).

15. Patten claim 275, Patten's only pending claim, was designated as corresponding to the Count. (Paper 1 at 4).

<u>Subject Matter Claimed</u>

16. Short claim 1 recites "non-stochastically assembling said nucleic acid building block sequences . . . ."

17. Short claim 1 further recites "such that a designed overall assembly order is achieved . . . ."

18. Short's witness, K. Dane Wittrup, Ph.D., testified that "Short's claim 1 recites a process which is carried out in a non-stochastic manner, whereas Patten's claim 275 recites a process which is carried out in a random or stochastic manner." (Exh. 2001 at ¶ 50).

19. Dr. Wittrup refers to Figure 4 of the Short patent specification to explain the difference between (1) a non-stochastic process and (2) a random or stochastic process. (Exh. 2001 at ¶¶ 51-53).

20. Figure 4A of the Short patent is reproduced below:

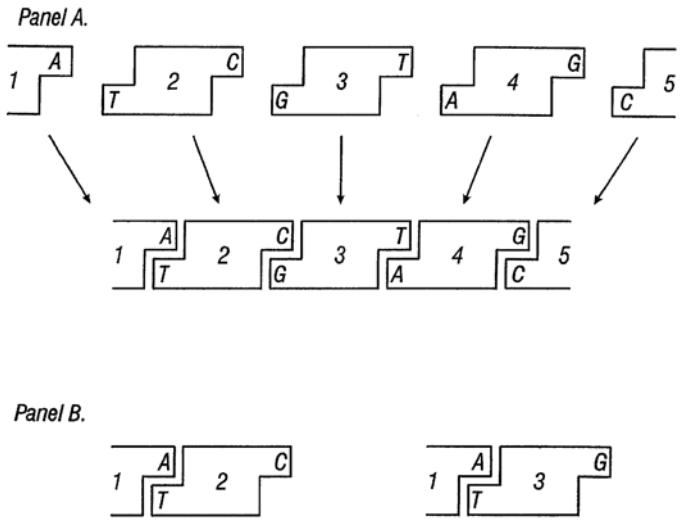

FIG. 4A

Figure 4A is a picture of an assembly scheme for coupling nucleic acid building blocks.

21. Figure 4B of the Short patent is reproduced below:

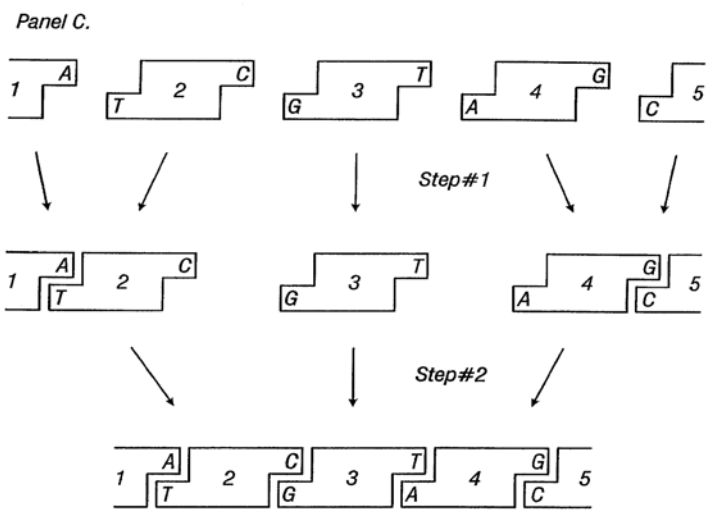

FIG. 4B

Figure 4B is a picture of an assembly scheme for coupling nucleic acid building blocks.

22. The specification of the Short patent describes the nucleic acid assembly in Figure 4A, whereby:

> In FIG, 4A Panel B, degeneracy in the overall assembly order of the 5 nucleic acid building blocks would be present if the assembly process were carried out in one step. For example, building block #2 and building block #*3* could both couple to building block #1 as shown.

(Short patent at col. 12, ll. 12-17).

23. Dr. Wittrup explains that Figure 4A, Panel B, and its description

> describe that an ordered product could be achieved as a subset of products even in a random process (see Panel A of FIG. 4A). Ex. 2025. However, when performing the process in a random or stochastic manner, it is typically the case that one would also achieve a degenerate misassembly represented by the misjoining of segments 1 and 3 in Panel B of FIG. 4A where segment 3 "flips" to improperly join with segment 1. This is an undesirable situation.

(Exh. 2001 at ¶ 51).

24. In response to this undesirable situation, Dr. Wittrup explained that the Short patent describes a “non-stochastic” process, which “puts the user in control of the assembly steps.” (Exh. 2001 at ¶ 52).

25. In support of this alternative “non-stochastic” process, Dr. Wittrup cites the following passages of the Short patent specification:

> . . . the knowledge, particularly the predictive knowledge, of the designer of an experimental process is a determinant of whether the process is stochastic or non-stochastic. Col. 2, ll. 35-38, Ex. 2025.
>
> FIG. 4, Panel C illustrates an exemplary assembly process comprised of 2 sequential steps to achieve a designed (nonstochastic) overall assembly order for five nucleic acid building blocks. In a preferred embodiment of this invention, the annealed building pieces are treated with an enzyme, such as a ligase (e.g. T4 DNA ligase), achieve covalent bonding of the building pieces. Col. 50, ll. 46-52, Ex. 2025.

> At the same time, in a particularly preferred embodiment, the assembly order (i.e. the order of assembly of each building block in the 5' to 3' sequence of each finalized chimeric nucleic acid) in each combination is by **design for non-stochastic).** Because of the non-stochastic nature of this invention, the possibility of unwanted side products is greatly reduced. Col. 53, ll. 11-17, Ex. 2025 (emphasis added).
>
> Contained within an exemplary experimental design for achieving an ordered assembly according to this invention are:
>
> 1) The design of specific nucleic acid building blocks.
> 2) The design of specific ligatable ends on each nucleic acid building block.
> 3) The design of a particular order of assembly of the nucleic acid building blocks. Col. 57, l. 62 through col. 58, l. 2, Ex. 2025.

(Exh. 2001 at ¶ 53).

26. Patten claim 275 recites “reassembling said defined polynucleotide segments in order. . . .”

27. Patten claim 275 recites “such that said segments are reassembled in an ordered fashion . . . .” . .” (Exh. 1001 at ¶ 17).

28. According to Dr. Wittrup, “Patten's specification clearly indicates that Patten's process is stochastic-whereby at best only a subset of products obtained by the process are the desired ordered product (much like that depicted in Short's '449 patent, FIG. 4A, Ex. 2025).” (Exh. 2001 at ¶ 57).

29. According to Dr. Wittrup, the specification of the Patten application teaches ordered assembly using three different methods: “(A) restriction endonuclease fragmentation in which the various segments generated are reassembled in a single reaction . . . ; (B) specially designed primers for one type of polymerase chain reaction based method . . . ; or (C) specially designed

primers for a different type of polymerase chain reaction based method . . . ." (Exh. 2001 at ¶ 63).

30. Dr. Wittrup testified that Patten's methods "must mean that the reassembly process occurs randomly while achieving, as a subset of products, an 'ordered product.'" (Exh. 2001, at ¶ 64).

31. (Exh. 2036 at ¶ 8). In regard to obviousness, Short argued:

> Patten's stochastic reassembly process would not have suggested to a person of ordinary skill in the relevant field in the December 1996 timeframe to utilize the non-stochastic or sequential assembly process as recited in claim 1 of the '449 patent. SF 29. This is so because Patten did not identify the shortcomings of the stochastic reassembly process in that at best only a subset of reaction products would be ordered. SF 30. A person of ordinary skill in the relevant field in the December 1996 timeframe would not have been motivated to perform a non-stochastic assembly process to obtain a higher proportion of correctly ordered products. SF 30. In fact, such a person would have been biased against doing a non-stochastic assembly process because of the extra work and expense of sequentially assembling the building blocks as compared to the stochastic process in Patten's claim 275. SF 30.

(Paper 23 at p. 11, ll. 4-13).

32. Short relies on Dr. Wittrup's testimony in support of its non-obviousness contentions. (*See* MFs 29-30; Exh. 2001 at ¶¶ 66-67).

33. Dr. Wittrup testified: "Patten's stochastic reassembly process would not have suggested to a person of ordinary skill in the relevant field in the December 1996 timeframe to utilize the non-stochastic or sequential assembly process as recited in claim 1 of the '449 patent." (Exh. 2001 at ¶ 66).

34. Dr. Wittrup also testified:

> Patten did not identify the shortcomings of the stochastic reassembly process in that at best only a subset of reaction products would be ordered. A person of ordinary skill in the

> relevant field in the December 1996 timeframe would not have been motivated to perform a nonstochastic assembly process to obtain a higher proportion of correctly ordered products. In fact, such a person would have been biased against doing a non-stochastic assembly process because of the extra work and expense of sequentially assembling the building blocks as compared to the stochastic process in Patten's claim 275.

(Exh. 2001 at ¶ 67).

35. Dr. Wittrup does not cite to underlying facts or data in support of the testimony in ¶ 67 of his testimony. (*Id.*).

36. Dr. Wittrup does not cite to any specific passages of the specification of the Patten application in support of his testimony.

37. Dr. Wittrup provides a thorough discussion of the knowledge of those in the art at the time of Short's filing. (Exh. 2001 at ¶¶ 23-40).

38. Dr. Wittrup does not, though, provide specific examples of the knowledge of those in the art at the time of Short's filing that would contribute to a lack of reason for performing a non-stochastic or sequential assembly process or for obtaining a higher proportion of correctly ordered products.

39. Dr. Wittrup does not tell us whether he knows of any other prior art that, when combined with the subject matter claimed by Patten, would have rendered Short's claimed subject matter obvious.

40. Dr. Wittrup does not refer to any evidence to show that there would have been "extra work and expense of sequentially assembling the building blocks as compared to the stochastic process in Patten's claim 275." (Exh. 2001 at ¶ 67).

41. In regard to its Motion 2, Short stated:

> Here, for much the same reasons as are discussed in Short's accompanying threshold motion requesting a judgment of no interference-in-fact, should Patten's claim be broadly interpreted to define the same as Short's "non-stochastically assembling" process, Patten's claim is not patentable for at least the reason that Patten does not describe a non-stochastic assembling process in the patent application.
>
> Thus, the key issue in this motion is contingent on the Board's holding in Short's accompanying motion requesting a judgment of no interference-in-fact that there is an interference-in-fact. Should the Board decide that Patten's claim is properly interpreted to be limited to a stochastic assembly process, then it need not further consider this motion. However, if Patten was in possession of a non-stochastic assembly process as in Short's claim 1, then Patten's specification must disclose that. For the reasons discussed below, Patten's specification does not.

(Paper 24, at p. 3, ll. 11-22).

III. Legal Principles

"The party filing the motion has the burden of proof to establish that it is entitled to the requested relief." 37 C.F.R. § 41.121(b). In this case, Short has the burden of showing that there is no interference-in-fact. "An interference exists if the subject matter of a claim of one party would, if prior art, have anticipated or rendered obvious the subject matter of a claim of the opposing party and vice versa." 37 C.F.R. § 41.203(a). Thus, to prevail, Short must show that none of Patten's claims anticipate or render obvious any of Short's claims, or vice versa.

To show a lack of anticipation, Short must show that either it or Patten has not claimed each and every limitation of the subject matter claimed by the other. *See Atlas Powder Co. v. IRECO, Inc.*, 190 F.3d 1342, 1346 (Fed. Cir. 1999). The analysis does not stop there, though, because Short must also show that the

same party's claimed subject matter would not be rendered obvious by what the other claimed.

Obviousness is a question of law, determined on several factual inquiries, including:

> the scope and content of the prior art are to be determined; differences between the prior art and the claims at issue are to be ascertained; and the level of ordinary skill in the pertinent art resolved. . . . Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented.

Graham v. John Deere Co. of Kansas City, 383 U.S. 1, 17-18 (1966). Thus, even if Short and Patten claim different methods of producing libraries of polynucleotides, Short must provide factual evidence that its method does not render Patten's method obvious, or vice versa, to prevail on its motion for no interference-in-fact. *Medichem,S.A. v. Rolabo, S.L.*, 353 F.3d 928, 935 (Fed. Cir. 2003) ("Although obviousness is a question of law, it is based on underlying factual determinations. [citation omitted] ").

We recognize that Short's burden is to prove a negative. It must show that those in the art would not have been led to Short's claimed method after learning of Patten's claimed method. Short must also allege that it is not aware of any prior art that when combined with the other's claims would have rendered the first's claimed subject matter obvious. *See In re Mayne*, 104 F.3d 1339, 1342 (Fed. Cir. 1997). A party might overcome its burden by showing, in light of the *Graham* factors, those in the art would not have developed the subject matter claimed using common sense and the knowledge available and motivated by

needs and problems faced at the time. *See KSR Int'l v. Teleflex, Inc.,* 127 S.Ct. 1727, 1741-42 (2007). Such a showing often comes in the form of witness testimony about what those in the art did or did not know. Alternatively, a party might show that there was prior art that taught away from any modifications of the subject matter. *See In re Gurley*, 27 F.3d 551 (Fed. Cir. 1994). In any case, if a party presents opinion testimony from a witness, the testimony must be supported with factual evidence. *Cf. UpJohn Co. v. Mova Pharm. Corp*., 225 F.3d 1306, 1311 (Fed. Cir. 2000) ("At this critical point in the determination of obviousness, there must be factual support for an expert's conclusory opinion."). Thus, Short's burden can only be met by presenting factual evidence of what those in the art would or would not have done given the knowledge of Patten's claimed subject matter and any other relevant prior art.

IV. Analysis

A. No interference-in-fact

To prevail in its motion, Short must show at least one way distinctness, that is Short must show either that the subject matter of Patten's claims would not anticipate or render obvious the Short claims, or vice versa. Short attempts to show that Patten's claims would not anticipate or render obvious the Short claims.

Short argues that the way it "generates a diverse library of chimeric polynucleotide sequences as set forth in claim 1 of the '449 patent is fundamentally different than how Patten generates diversity as set forth in claim 275 of the '221 application." (Short Motion 1 at p. 4, ll. 15-17). However, even

assuming Short has shown that there is a difference between the Short and Patten claims, the showing of a difference is not sufficient to show that there is no interference-in-fact. *Cf. Dann v. Johnston*, 425 U.S. 219, 230 (1976) (the mere existence of differences between the prior art and an invention does not establish the invention's non-obviousness). Short must show that the subject matter of the Patten claims would not have rendered obvious the subject matter of the Short claims.

Short argues that "Patten's stochastic reassembly process would not have suggested to a person of ordinary skill in the relevant field in the December 1996 timeframe to utilize the non-stochastic or sequential assembly process as recited in claim 1 of the '449 patent," (Short Motion 1 at p. 11, ll. 4-6; FF 31), but it does not provide any factual evidence in support. Short's witness, Dr. Wittrup, reiterates Short's contentions (FF 37), but fails to point to any factual evidence of the specific knowledge of those in the art indicating they would not have been able to, or would not have had reason to, perform Short's claimed process, knowing of Patten's claimed process. *Cf. Rohm and Haas Co. v. Brotech Corp.*, 127 F.3d 1089, 1092 (Fed. Cir. 1997) (nothing in the Federal Rules of Evidence or Federal Circuit jurisprudence requires the fact finder to credit the unsupported assertions of an expert witness).

Dr. Wittrup does not even assert that there is no other prior art that could be combined with the subject matter of Patten's claims to render Short's claimed subject matter obvious. (Exh. 2001 at ¶ 67; FF 35-40).

Instead Dr. Wittrup testified that Short's claimed process would have required "extra work and expense." (FF 34; Short Motion 1 at p. 11, l. 12). Dr. Wittrup does not point to factual evidence in support of this contention, however, common sense tells us that this is probably true. Common sense also tells us, and Short admits, that the ordered product (as would be consistently obtained by a non-stochastically assembly process) would have been a more desirable product than a non-ordered product. (Paper 32 (Transcript) at 13-14). We do not know, and have not been directed to evidence showing, how much extra work and expense would be required to practice the Short method. A reasonable amount of extra time and expense would not have dissuaded one skilled in the art from using a process that results in a better product. Thus, on the record before us, Short has not shown that the extra time and expense required would have negated the reason one skilled in the art would have had for selecting the Short process (in view of the Patten process), i.e., to get a better product.

We determine that Short has failed to establish a prima facie case of a lack of obviousness. Short has not shown that the subject matter of the Patten claims would not have rendered obvious the subject matter of the Short claims. Short has not argued that its claims would not have anticipated or rendered obvious the Patten claims (*See* Bd. R. 203(a)). Accordingly, Short has not shown that there is no interference-in-fact. We deny Short Motion 1

B. Written Description

Short argues that its Motion 2, for lack of written description support, is contingent on a finding of interference-in-fact. (Short Motion 2, Paper 24, at p. 3, ll. 16-18; FF 41) ("Thus, the key issue in this motion is contingent on the Board's holding in Short's accompanying motion requesting a judgment of no interference-in-fact that there is an interference."). We deny the motion for judgment of no interference-in-fact, though not because Patten claim 275 is broadly construed (Short Motion 2, Paper 24, at p. 3, ll. 18-19). Instead we hold that Short has failed to meet its burden to show non-obviousness under any construction, including a construction where the Patten claims are limited to a stochastic assembly process. Short admits that Patten's claims have written description support, at least under this "limited" construction, *id.* ("Should the Board decide that Patten's claim is properly interpreted to be limited to a stochastic assembly process, then it need not further consider this motion."). Accordingly, we deny Short Motion 2.

C. Exclusion of Evidence

In its Miscellaneous Motion 3, Short asks us to exclude page 62, line 2, through page 64, line 11, of the transcript of the cross-examination transcript of Short's witness, Dr. Wittrup. (Short Motion 3 at p. 2, ll. 2-3). Short argues that the questions posed during this part of the transcript go beyond the scope of the previous examination and, therefore, were improper. (*Id.* at p. 2, ll. 19-22). Because we deny Short's Motion 1 and Motion 2 without considering this evidence, we dismiss this motion.

V. ORDER

Upon consideration of the record and for reasons given, it is

ORDERED that Short's motion for judgment of no interference-in-fact is DENIED;

FURTHER ORDERED that Short's motion for judgment of unpatentability for lack of written description is DENIED, and

FURTHER ORDERED that Short's motion to exclude evidence is DISMISSED.

cc (via electronic filing):

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