IN THE UNITED STATES DISTRICT COURT

FOR THE DISTRICT OF DELAWARE

LADATECH, LLC,	)	
	)	
Plaintiff,	)	
	)	
v.	)	Civ. No. 09-627-SLR
	)	
ILLUMINA, INC. and SOLEXA, INC.,	)	
	)	
Defendants.	)	

MEMORANDUM ORDER

At Wilmington this 24th day of January, 2012, consistent with the memorandum opinion issued this same date and with the tenets of claim construction set forth by the United States Court of Appeals for the Federal Circuit in *Phillips v. AWH Corp.*, 415 F.3d 1303 (Fed. Cir. 2005);

IT IS ORDERED that the disputed claim language of the patent in suit, U.S. Patent No. 6,107,023 ("the '023 patent"), shall be construed as follows:

1. "**A method of amplifying a mixture of different sequence duplex DNA fragments, comprising**:" The preamble is limiting, in that each of the steps of the method claim must be performed on fragments in a mixture. Not only is this result consistent with its plain language,[1] but with the prosecution history[2] and with the

[1]The term "mixture of different sequence duplex DNA fragments" provides an antecedent basis for the term "the fragments" in the first two operative steps of the method.

[2]The applicants relied on the method being directed toward the amplification of a mixture to distinguish the prior art. (JA-90-91)

understanding of one of ordinary skill in the art.[3] It is not inconsistent with the specification, as figure 1, cited by defendants, is a flow diagram of the amplification process, with "Duplex DNA Fragments" as the starting point.

2. A "**linker**" is a short piece of DNA having a known sequence and of sufficient length to bind at least one primer. This construction is consistent with how the term was used in the specification[4] and to those of ordinary skill in the art at the time of the invention.[5] The court agrees with plaintiff that, in distinguishing Helfman during the examination process, plaintiff did not expressly disclaim the ordinary meaning of the term "linker;" plaintiff only argued that the linkers in the prior art did not play the same role as they do in the invention of the '023 patent and, therefore, their structure was different. The only requirement for the prior art connecting linkers was that "one end must be capable of ligating to an end of the DNA fragment to be amplified, and the other end must be capable of ligating to an open end of the cleaved plasmid. The structure of the connector linkers between the two ends is irrelevant, except that it should be short. In contrast, the structure of the priming linkers of the '023 patent must be substantially completely defined from end to end so that complementary primers can be designed that are able to hybridize to them." (JA-855) The distinguishing characteristic was not length, but known sequence.

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[3]Defendants' expert, Dr. Silverstein, testified at his deposition that each of the steps of claim 12 were performed on a mixture of different sequence duplex DNA fragments. (D.I. 112, ex. A at 66:21-67:6)

[4]('023 patent at 5:44-46, 6:33-39)

[5](D.I. 112, exs. A at 27:6-11; B at 21:22-22:12; D-G)

3. A "**double-stranded linker**" is a linker with two strands that are sufficiently hybridized to maintain the linker's double-stranded nature. This construction is consistent with the specification[6] and not inconsistent with the prosecution history.[7]

4. "**Both strands of the fragments, at both fragment ends**" means that both strands of a fragment are attached to double-stranded linkers at their 5' and 3' ends. Defendants argue that their proposed construction ("a linker is attached to both ends **of every fragment** in the mixture of DNA fragments") does not require 100% biochemical efficiency, but only suggests that the court should require that the linkers be attached **directly** to both ends of both DNA strands (as opposed to allowing the linker to first be attached only to one end of a DNA fragment, followed by cleaving the fragment to generate a sub-fragment and attaching the second linker to the end of the sub-fragment). (D.I. 123 at 19-20) The '023 patent describes double-strand linkers with noncomplementary ends ("tails").[8] According to plaintiff (and not specifically disputed by defendants), it was well understood in the art that a primer with a 5'-noncomplementary end ("tail") can introduce a sequence to the linker and that, in subsequent reaction steps, a primer may bind to both the original sequence and the

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[6]('023 patent, figure 2 (showing linkers having single-stranded (i.e., not hybridized) "overhangs"; *id.* at col. 5:51-55)

[7]*See* JA-102 and JA-134. The examiner characterized Van de Sande as disclosing "'universal' sequencing primer-linkers comprised of two strands that are at least partially complementary." In response, the applicants did not disagree with the examiner's characterization of the linkers in Van de Sande; instead, the applicants distinguished Van de Sande as not teaching or suggesting "using such universal primers in any method involving mixed populations of DNA."

[8]('023 patent, figs. 2 and 3; 6:5-8)

sequences introduced to the linker from the tail. (D.I. 112 at 28; D.I. 132 at 14) Although this discussion related to the limitation "linker region," it occurs to the court that defendants were really addressing this scenario in connection with the limitation "at both fragment ends."

5. "**Single fragment strand**" shall be given its ordinary meaning.

6. "**Primer**" refers to a short piece of DNA that serves as a starting point for copying DNA. This construction is consistent with both the exemplary primers described in the specification and with the understanding of one of ordinary skill in the art.[9]

7. "**A primer**" means one or more primers. This construction is consistent with Federal Circuit precedent,[10] as well as with the specification.[11] Although plaintiff distinguished Mullis in the examination process, it did so on the basis of Mullis' requirement for two sequence-specific primers. There is no clear and unambiguous language in either the prosecution history or the specification that limits claim 12 to the use of one primer, especially in light of dependent claim 15 which requires that the linkers be the same (and, thus, the primer be the same). Claim 12 must have been

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[9]('023 patent, col. 6:49, 65-67; 12:1-5; D.I. 112, ex. K at col. 6:31-37)

[10]*See Baldwin Graphic Sys., Inc. v. Siebert, Inc.*, 512 F.3d 1338, 1342-43 (Fed. Cir. 2008). The Federal Circuit's decision in *Harari v. Lee*, 656 F.3d 1331 (Fed. Cir. 2011), is clearly distinguishable due to the specific language used in the claim at issue. There is no such language at bar.

[11]('023 patent, col. 8:11-16 ("by addition of primer"); 9:41-44 ("Alternatively, the hybridization mixture may contain a large molar excess of primer oligonucleotides effective to hybridize"); 16:17-21 (standard language not limiting invention to the particular embodiments disclosed))

broad enough to allow the addition of this new dependent claim upon reexamination.

8. "**Whose sequence is complementary to a linker region on each fragment strand**" means that the primer is sufficiently complementary to a linker region to allow for copying of DNA. This construction is consistent with the specification,[12] the prosecution history,[13] and to those of ordinary skill in the art at the time.[14]

9. "**Linker region**" means the region of the fragment strands where the linker has been added, and is not limited to sequences present on the original linker ligated to the fragments. This construction is consistent with the court's recognition that the double-stranded linkers can have noncomplementary ends that can bind to the primer which, in the subsequent primer extension step, would synthesize a sequence complementary to the tail which was not present on the "original" linker.

10. "**Each fragment strand**" shall be given its ordinary meaning. Defendants argue that the limitation should be construed to require that the primer be "'complementary' to 'each' fragment strand, rather than half of the fragment strands." (D.I. 123 at 29) The court disagrees, based on the reasoning supplied above.

11. "**Repeating said denaturing, hybridizing, and converting steps until a desired degree of amplification is achieved**" means that the steps of denaturing,

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[12]('023 patent, col. 4:24-5:11; 6:51-65)

[13](JA-78-79, JA-91)

[14](D.I. 112, ex. K at col. 6:56-65 ("The primers herein to be selected are 'substantially' complementary to the different strands of each specific sequence to be amplified.")) Once again, the applicants did not distinguish Mullis based on the degree of "complementarity" of the primers, but rather on the fact that Mullis required prior knowledge of the specific sequence to be amplified. (JA-91)

hybridizing, and converting are repeated as desired. Defendants' argument that the claim requires that a "final exponential level of amplification is achieved" has no support in the intrinsic evidence, and it was recognized in the art that no reaction has 100% biochemical efficiency (meaning that the efficiency will be less than two-fold in each cycle).

United States District Judge