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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte N. ALICE YAMADA and PETER TSANG

Appeal 2016-000485
Application 12/541,008
Technology Center 1600

Before JEFFREY N. FREDMAN, ULRIKE W. JENKS, and RACHEL H. TOWNSEND, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[1] under 35 U.S.C. § 134 involving claims to a computer-implemented method for providing a set of FISH probe oligonucleotide sequences. The Examiner rejected the claims as directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b). We affirm but designate our affirmance as a New Grounds of Rejection.

Statement of the Case

Background

"Fluorescence in situ hybridization (FISH) . . . allows for the detection of the presence or absence of specific DNA sequences on chromosomes by using fluorescent probes that bind to only those parts of the

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[1] Appellants identify the Real Party in Interest as Agilent Technologies, Inc. (*see* App. Br. 3).

chromosome with which they show a high degree of complementarity" (Spec. 1:27–30). However, "since [these] probes are generated from large pieces of DNA," FISH has "limited resolution." (Spec. 2:1–3.) And "[b]ecause these probes are generated over very large regions of the genome, microtranslocations and microinversions cannot be resolved by current method" (Spec. 2:3–5). "Thus, there has been an increasing need to understand more subtle chromosomal defects with substantially improved resolution, and without a priori knowledge of their location" (Spec. 2:8–10).

The Claims

Claims 1, 3, 4, 21, and 22 are on appeal. Independent claim 1 is representative and reads as follows:

> 1. A computer-implemented method for providing a set of FISH probe oligonucleotide sequences, said method comprising:
>
> (a) providing a plurality of overlapping tiled candidate fluorescence in situ hybridization (FISH) probe oligonucleotide sequences, wherein said overlapping tiled candidate FISH probe oligonucleotide sequences are complementary to non-repeat sequences of a genome of interest and are preselected based on at least one probe property;
>
> (b) sorting said plurality of overlapping tiled candidate FISH probe oligonucleotide sequences from smallest genomic distance to largest genomic distance between neighboring overlapping tiled candidate FISH probe oligonucleotide sequences to produce a sorted plurality of overlapping tiled candidate FISH probe oligonucleotide sequences;
>
> (c) evaluating a probe property value for a neighboring pair of overlapping tiled candidate FISH probe oligonucleotide sequences from said sorted plurality to identify a first member

of said neighboring pair with a more desirable probe property value than a second pair member of said neighboring pair;

(d) removing said second pair member from said plurality;

(e) reiterating said sorting, evaluating and removing steps at least once to produce said set of FISH probe oligonucleotide sequences; and

(f) outputting said set of FISH probe oligonucleotide sequences, wherein said method is performed by a computer that is specifically programmed to perform said method.

The Issue[2]

The Examiner rejected claims 1, 3, 4, 21, and 22 under 35 U.S.C. § 101 as being directed to non-statutory subject matter (Ans. 4–8).

The Examiner finds all of the claims on appeal under 35 U.S.C. § 101 as being directed to patent-ineligible subject matter because the "claim elements both individually and in combination, do not amount to significantly more than an abstract idea" (Ans. 6). The Examiner finds the claims directed to "abstract ideas" combined with "recitation of generic computer structure that serves to perform generic computer functions that are well-understood, routine, and conventional activities" (*id.* at 7). The Examiner reached this conclusion by applying the test set out in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. 66 (2012) (Ans. 5–6) based on the two-step *Alice* framework. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014).

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[2] We note that the Examiner has withdrawn rejections under 35 U.S.C. § 112(b), 35 U.S.C. § 101 utility, 35 U.S.C. § 112(a), and 35 U.S.C. § 103(a) (*see* Ans. 3).

Appellants "submit that the subject claims are not directed to a patent ineligible abstract idea and clearly do not seek to tie up any fundamental truth/principle or building block of human ingenuity" (App. Br. 5). Appellants contend the "subject method of providing a set of oligonucleotide sequences is a method of designing FISH probes that may be used to detect chromosomal abnormalities related to cancer, aneuploidy and the like. Therefore, it is clear that the claimed methods are drawn to 'improvements to another technology or technical field'" (*id.*). Appellants contend the "FISH probe sequences that are recited in the claims and that are complementary to non-repeat sequences of a genome of interest are a representation of the oligonucleotide molecule that have the sequence of nucleotides specified by the FISH probe sequence" (*id.* at 6).

Appellants also contend

> the claims recite meaningful limitations that apply the abstract idea to probe design for FISH assays. . . . The specification shows, e.g., in the Example section, that the design of overlapping FISH probes results in improved FISH signals compared to signals obtained from end-to-end tiled probes. Thus, the specification of overlapping tiled FISH probe sequences is a meaningful limitation to the claimed method.

(App. Br. 6).

To determine whether a claim is invalid under § 101, we employ the two-step *Alice* framework. In step one, we ask whether the claims are directed to a patent ineligible concept, such as an abstract idea or law of nature. *Alice*, 134 S.Ct. at 2355; *Mayo*, 566 U.S. at 75–77; *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1375 (Fed. Cir. 2015). While method claims are generally eligible subject matter, method claims

that are directed only to natural phenomena are directed to a patent ineligible concept. *Ariosa*, 788 F.3d at 1376.

Alice Step One

Claim 1 of the instant application is directed to a multistep process of sorting oligonucleotide probe sequences into a desirable set that specifically bind target sequences. That process is directed to both a law of nature and an abstract idea. In particular, the law of nature/natural phenomenon is the probe set. A probe "refers to a polynucleotide which can specifically hybridize to a target polynucleotide" (Spec. 12:9–10). That function of specific hybridization is a consequence of a natural process, i.e., it results from a high degree of complementarity.

In addition, the recited steps of sorting, evaluating, and removing and outputting a desired set involve categorizing and/or analyzing information. Our reviewing Court has explained that "[i]nformation as such is an intangible" and "that collecting information, including when limited to particular content (which does not change its character as information)," analyzing it, and presenting the results of the collection and analysis without more are patent ineligible abstract concepts. *See, e.g*, *Electric Power Group, LLC v. Alstom S.A.*, 830 F.3d 1350, 1353–54 (Fed. Cir. 2016).

The claimed invention therefore is drawn to using a computer to obtain desirable oligonucleotide probe sets that specifically bind target sequences using known, prior art standard computer processes, a relationship that is a patent-ineligible abstract idea. *Mayo*, 566 U.S. at 77.

Because the claims are directed to an abstract idea/natural law, we turn to the second step of the *Alice* framework.

Alice Step Two

In *Alice* step two, we examine the elements of the claims to determine whether they contain an inventive concept sufficient to transform the claimed naturally occurring phenomena into a patent-eligible application. *Mayo*, 566 U.S. at 71–72 (quoting *Alice*, 134 S.Ct. at 2355). We must consider the elements of the claims both individually and as an ordered combination to determine whether additional elements transform the nature of the claims into a patent-eligible concept. *Ariosa*, 788 F.3d at 1375.

The Specification teaches prior art methods for the first step of providing probes "complementary to non-repeat sequences" include "a process called RepeatMasking . . . In certain embodiments, a repeat masking tool called WindowMasker may be used to mask repetitive sequences. WindowMasker is well known in literature" (Spec. 19:23–27).

The Specification also teaches that analysis of oligonucleotides for probe property values was known in the prior art, teaching that the parameters of "length, melting temperature (Tm), non-homology with other regions of the genome, hybridization signal intensities, kinetic properties under hybridization conditions" were disclosed in "U.S. Patent No. 6,251,588" (*see* Spec. 20:1–3).

The steps of sorting, removing (eliminating), reiterating, and outputting data about oligonucleotide information are also found in the prior art. Bondarenko,[3] cited by the Examiner in the withdrawn obviousness rejection, teaches "software tools for filtering and sorting GeneChip® array data" (Bondarenko 3:50–51). Bondarenko teaches: "There are software

[3] Bondarenko, A., US 7,269,517 B2, issued Sept. 11, 2007.

tools available in the art for storing and manipulating data derived from various experiments in biotechnology, or for performing some statistical analysis of the data" (Bondarenko 3:25–28).

The steps in the "claims (e.g., arranging, storing, retrieving, sorting, eliminating, determining) are conventional, routine, and well-known. They involve the normal, basic functions of a computer." *Versata Development Group, Inc. v. SAP America, Inc.*, 793 F.3d 1306, 1335 (Fed. Cir. 2015). "In order for the addition of a machine to impose a meaningful limit on the scope of a claim, it must play a significant part in permitting the claimed method to be performed, rather than function solely as an obvious mechanism for permitting a solution to be achieved more quickly, i.e., through the utilization of a computer for performing calculations." *SiRF Tech., Inc. v. Int'l Trade Comm'n*, 601 F.3d 1319, 1333 (Fed.Cir. 2010).

We conclude that the practice of the method claims does not result in an inventive concept that transforms the abstract idea/natural phenomena of obtaining desirable oligonucleotide probe sets that specifically bind target sequences into a patentable invention. *Mayo* and *Ariosa* make clear that transforming claims that are directed to a law of nature requires more than simply stating the law of nature while adding the words "apply it." *Mayo*, 566 U.S. at 72; *Ariosa*, 788 F.3d at 1377.

In *Ariosa*, the challenged claims involved a method that was a general instruction to doctors to apply routine, conventional techniques when seeking to detect paternally inherited cell-free fetal DNA in the blood serum of a pregnant woman. *Ariosa*, 788 F.3d at 1377. The same is true here. The claims contain steps that require using a computer to obtain non-repeat

sequences using known techniques and evaluating those sequences based on standard, well-known probe properties to identify desirable probes. Appellants cannot purport to have invented providing non-repeat sequences (*see* Spec. 19:22–29), sorting nucleic acid information (*see* Bondarenko 3:50–51), evaluating probe properties such as melting temperature, length, or GC content (*see* Spec. 20:1–9), or performing routine data manipulation steps such as removing, repeating, and outputting data regarding oligonucleotides. No specific element is identified as inventive in the Specification.

Therefore, as in *Cleveland Clinic*, the claims identify oligonucleotide probes based on probe property values using conventional methods and "compare those values to predetermined or control values derived from conventional statistical methods." *Cleveland Clinic Foundation v. True Health Diagnostics LLC*, 859 F.3d 1352, 1362 (Fed. Cir. 2017).

We find unpersuasive Appellants' argument that "the design of overlapping FISH probes results in improved FISH signals compared to signals obtained from end-to-end tiled probes. Thus, the specification of overlapping tiled FISH probe sequences is a meaningful limitation to the claimed method" (App. Br. 6).

The particular probes' selection from which to cull those with more desirable properties simply represents an abstract idea embodied by a law of nature that is further defined by the recited mathematical relationship in claim 22, i.e., a percentage of overlap with another probe. However, a "claim directed to an abstract idea does not automatically become eligible merely by adding a mathematical formula." *RecogniCorp, LLC v. Nintendo*

Co., Ltd., 855 F.3d 1322, 1328 (Fed. Cir. 2017). The addition of the mathematical formula determined using standard regression techniques based on a natural correlation and changing raw data levels into calculated data levels "simply changes the data into other forms of data [that] cannot save [the claims]." *Id.* The claims, whether considered limitation-by-limitation or as a whole, do not sufficiently transform the abstract idea/natural phenomena of obtaining desirable oligonucleotide probe sets that specifically bind target sequences into a patentable invention.

We also find unpersuasive, Appellants' contention that because the evaluating step implements a specific method of selecting an optimal set of FISH probes from candidate probe sequences, it is a meaningful limitation that applies any alleged abstract idea. (App. Br. 6–7). As already discussed, these steps are routine and conventional. These claims simply call "on a computer to do nothing that is even arguably an advance in physical implementations of routine mental information-comparison and rule-application processes." *SmartGene, Inc. v. Advanced Biological Laboratories, SA*, 555 Fed. Appx. 950, 955 (Fed. Cir. 2014). As our reviewing Court in SmartGene noted, under similar circumstances, in such a context, "the concern about preempting public use of certain kinds of knowledge, emphasized in *Mayo*, is a grave one." *Id.*

We therefore conclude that Supreme Court and Federal Circuit precedent constrains us to conclude that all of the claims on appeal are directed to patent-ineligible subject matter.

Because our reasoning differs from that of the Examiner, and because we rely upon the Bondarenko reference and portions of the Specification that

were not relied upon by the Examiner in the § 101 rejection, we designate our affirmance as a New Grounds of Rejection to provide Appellants with a fair opportunity to respond to this new position.

SUMMARY

In summary, we affirm the rejection of claims 1, 3, 4, 21, and 22 under 35 U.S.C. § 101, as being directed to non-statutory subject matter.

We designate our affirmance as a new ground pursuant to 37 C.F.R. § 41.50(b). Section 41.50(b) provides "[a] new ground of rejection pursuant to this paragraph shall not be considered final for judicial review." Section 41.50(b) also provides:

> When the Board enters such a non-final decision, the appellant, within two months from the date of the decision, must exercise one of the following two options with respect to the new ground of rejection to avoid termination of the appeal as to the rejected claims:
>
> (1) Reopen prosecution. Submit an appropriate amendment of the claims so rejected or new Evidence relating to the claims so rejected, or both, and have the matter reconsidered by the examiner, in which event the prosecution will be remanded to the examiner. The new ground of rejection is binding upon the examiner unless an amendment or new Evidence not previously of Record is made which, in the opinion of the examiner, overcomes the new ground of rejection designated in the decision. Should the examiner reject the claims, appellant may again appeal to the Board pursuant to this subpart.
>
> (2) Request rehearing. Request that the proceeding be reheard under § 41.52 by the Board upon the same Record. The request for rehearing must address any new ground of rejection and state with particularity the points believed to have been

> misapprehended or overlooked in entering the new ground of rejection and also state all other grounds upon which rehearing is sought.

Further guidance on responding to a new ground of rejection can be found in the Manual of Patent Examining Procedure § 1214.01.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED; 37 C.F.R. § 41.50(b)