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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte ANASTASIA KHVOROVA, ANGELA REYNOLDS,
DEVIN LEAKE, WILLIAM MARSHALL,
STEVEN READ, and STEPHEN SCARINGE

Appeal 2012-010359
Application 10/940,892
Technology Center 1600

Before DONALD E. ADAMS, JEFFREY N. FREDMAN, and
JACQUELINE T. HARLOW, *Administrative Patent Judges*.

FREDMAN, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal¹ under 35 U.S.C. § 134 involving claims to a method for obtaining a siRNA sequence for a target gene. The Examiner rejected the claims as directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

¹ Appellants identify the Real Party in Interest as Dharmacon, Inc., a subsidiary of Thermo Fisher Scientific Inc. (*see* App. Br. 3).

Statement of the Case

Background

“[I]t has been shown that when short (18–30 bp) RNA duplexes are introduced into mammalian cells in culture, sequence-specific inhibition of target mRNA can be realized without inducing an interferon response” (Spec. 2: 6–8). “Certain of these short dsRNAs, referred to as small inhibitory RNAs (‘siRNAs’), can act catalytically at sub-molar concentrations to cleave greater than 95% of the target mRNA in the cell” (*id.* at ll. 8–11). “One of the most contentious issues in RNAi [RNA interference] is the question of the necessity of siRNA design, *i.e.*, considering the sequence of the siRNA used” (*id.* at 3: 16–17). “Unfortunately, none of the reported methods have provided a satisfactory scheme for reliably selecting siRNA with acceptable levels of functionality. Accordingly, there is a need to develop rational criteria by which to select siRNA with an acceptable level of functionality” (*id.* at 3:33–4: 2).

The Claims

Claims 85, 87, and 88 are on appeal. Claim 85 is representative and reads as follows:

85. A method for obtaining an siRNA sequence for a target gene, wherein said siRNA sequence comprises 19 - 30 nucleotide bases, said method comprising the steps:
- (a) selecting a target gene;
 - (b) generating a set of candidate siRNA sequences that are between 19 and 30 bases in length, wherein each of said candidate siRNA sequences comprises a sense region of 19 – 30 bases, wherein said sense region comprises a sense sequence of 19 bases that is at least 79% similar to a region of the target gene;

(c) applying an algorithm to said set of candidate siRNA sequences, wherein said algorithm comprises a set of at least four variables, wherein each variable has a value that is determined by a binary condition that is defined by the presence or absence of a base at a position within the sense sequence, and within said algorithm each variable is multiplied by a coefficient;

(d) determining a predicted relative functionality of at least two siRNA sequences within said set of candidate siRNA sequences, wherein said predicted relative functionality is measured by applying said algorithm to compute a value based on an application of said algorithm;

(e) selecting from said set of at least two candidate siRNA sequences, an siRNA sequence for gene silencing based on said predicted relative functionality, wherein a higher value generated by said formula is indicative of greater predicted functionality and said siRNA for gene silencing that is selected has the highest value from within said set of at least two siRNA sequences; and

(f) generating an output comprising said siRNA sequence for gene silencing that is selected, wherein said output is in a form that is readable by a user, thereby obtaining said siRNA sequence for gene silencing.

The Issue

The Examiner rejected claims 85, 87, and 88 under 35 U.S.C. § 101 as directed to non-statutory subject matter (Ans. 4–6).

The Examiner finds that

The claimed subject matter is not limited to use a particular apparatus or machine in the steps of the method. . . . The claimed subject matter does not require that the steps of the method are performed on a computer. The claimed process does not transform or modify polynucleotides. . . .

Therefore the claimed subject matter does not require use of

a machine or produce a transformation of an article to a different state or thing.

(Ans. 5). The Examiner finds that the “claimed process does not include a patentable application of a law of nature” (*id.*). The Examiner finds that the “claimed process uses a set of rules that determines subsets of a target sequence that are likely to be effective as siRNA compared to subsets of the target sequence that are not chosen by the claimed process” (*id.*).

The issue with respect to this rejection is: Does the evidence of record support the Examiner’s conclusion that the claims are directed to non-statutory subject matter?

Findings of Fact

1. The Specification teaches that “it has been shown that when short (18-30 bp) RNA duplexes are introduced into mammalian cells in culture, sequence-specific inhibition of target mRNA can be realized without inducing an interferon response” (Spec. 2: 6–8).

2. The Specification teaches that a “description of the mechanisms for siRNA activity, as well as some of its applications are described in [the prior art]” (*id.* at ll. 11–13).

3. The Specification teaches that:

The interference effect can be long lasting and may be detectable after many cell divisions. Moreover, RNAi exhibits sequence specificity. . . . Thus, the RNAi machinery can specifically knock down one type of transcript, while not affecting closely related mRNA. These properties make siRNA a potentially valuable tool for

inhibiting gene expression and studying gene function and drug target validation.

(*Id.* at 3: 4–10).

4. The Specification teaches that “others in the field have begun to explore the possibility that RNAi can be made more efficient by paying attention to the design of the siRNA” (*id.* at ll. 31–33).

5. The Specification teaches “determining improved functionality by the presence or absence of at least one variable selected from the group consisting of the presence or absence of a particular nucleotide at a particular position” (*id.* at 24: 23–26).

Principles of Law

[T]he claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.

Mayo Collaborative Services v. Prometheus Laboratories, Inc., 132 S.Ct. 1289, 1298 (2012).

Analysis

“Phenomena of nature . . . , mental processes, and abstract intellectual concepts are not patentable.” *Mayo* at 1293. To transform such a nonpatentable phenomenon, process, or concept into a patent-eligible application, one must do more than simply state the phenomenon, process, or concept “while adding the words ‘apply it.’” *Id.* at 1294.

On this record, Appellants' claimed invention involves (1) generating data related to candidate sequences based on a target gene for siRNA; (2) applying an algorithm to the data; and (3) determining, based on the result, whether a particular siRNA will result in gene silencing (*see, e.g.*, Claim 85). Unlike the claims at issue in *Diehr*, Appellants' claims do not involve the transformation of an article into a different state or thing. *See Diamond v. Diehr*, 450 U.S. 175, 184 (1981).

Instead, Appellants' claims purport to apply natural laws describing the relationship between siRNA sequence data and gene silencing to predict the likelihood that a particular siRNA sequence will result in gene silencing. *Cf. Mayo*, 132 S.Ct. at 1294, 1302 (“The laws of nature at issue . . . tell a treating doctor to measure metabolite levels and to consider the resulting measurements in light of the statistical relationships they describe”); *In re Meyer*, 688 F.2d 789, 794 (CCPA 1982) (“The process recited is an attempt to patent a mathematical algorithm rather than a process for producing a product as in [*Diehr*]”); *CyberSource Corp. v. Retail Decisions, Inc.*, 654 F.3d 1366, 1375 (Fed. Cir. 2011) (“[t]he mere manipulation or reorganization of data . . . does not satisfy the transformation prong”).

We follow the analytical framework set forth in *Mayo* and applied in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, ___ F.3d ____, 2015 WL 3634649 (Fed. Cir. 2015). “[W]e determine whether the claims at issue are directed to a patent-ineligible concept. . . . If the answer is yes, then we next consider the elements of each claim both individually and ‘as an ordered combination’ to determine whether additional elements ‘transform the nature of the claim’ into a patent-eligible application.” *Id* at 3.

Consistent with *Ariosa*, because the ability of siRNA sequences to silence genes is “directed to naturally occurring phenomena, we turn to the second step of *Mayo*’s framework. In the second step, we examine the elements of the claim to determine whether the claim contains an inventive concept sufficient to ‘transform’ the claimed naturally occurring phenomenon into a patent-eligible application.” *Id.* at 4.

Here, as in *Mayo*, the algorithm instructions set forth in Appellants’ claims “add nothing specific to the laws of nature other than what is well-understood, routine, conventional activity, previously engaged in by those in the field.” *Mayo*, 132 S.Ct. at 1299. At the time of Appellants’ claimed invention, the analysis of gene sequences to allow researchers to predict whether a siRNA would silence genes was known in the art (*see* FF 1, 2, 4). The difference is that while the prior art recognized that sequence data can be analyzed to identify siRNAs, the prior art methods do not utilize the same algorithm as that disclosed in the Specification to manipulate the sequence data (FF 4). *Cf. Parker v. Flook*, 437 U.S. 584, 585 (1978) (“[t]he only novel feature of the method is a mathematical formula”).

Thus, the notion that sequence data relating to siRNA can be manipulated to allow an artisan to predict whether a particular siRNA will function to silence genes was “‘well known,’ to the point where, putting the formula to the side, there was no ‘inventive concept’ in the claimed application of the formula.” *Mayo*, 132 S.Ct. at 1299, *citing Parker v. Flook*, 95 U.S. 594.

Appellants contend that “all processes use general concepts, and use of a general concept does not render a claim ineligible for patent protection

if the claim is directed to more than the abstract idea or general concept” (App. Br. 15).

We find this unpersuasive because a “basic mathematical equation, like a law of nature, . . . [is] not patentable.” *Mayo*, 132 S.Ct. at 1299. The “prohibition against patenting abstract ideas ‘cannot be circumvented by attempting to limit the use of the formula to a particular technological environment.’” *Id.* at 1297, citing *Bilski v. Kappos*, 130 S.Ct. 3218, 3230 (2010); see also *Parker v. Flook*, 95 U.S. at 595 n. 18 (“a claim for an improved method of calculation, even when tied to a specific end use, is unpatentable subject matter under § 101”).

Appellants contend that the “invention is not directed to any natural law or natural phenomena or to any direct application of a natural law or natural phenomenon as those phrases are used by the Supreme Court in *Mayo*” (Reply Br. 2). Appellants contend that:

there is nothing in nature that evaluates the functionality of short interfering ribonucleic acid sequences based on “a set of at least four variables, wherein each variable has a value that is determined by a binary condition that is defined by the presence or absence of a base at a position within the sense sequence, and within said algorithm each variable is multiplied by a coefficient” as recited in the claims on appeal and then calls for selection based on this predicted functionality.

(Reply Br. 4). We are not persuaded.

Claim 85 does not recite a specific algorithm, and preempts any algorithm for designing siRNA sequences. The claim limitation recited by Appellants regarding the four asserted “variables” can simply represent the presence or absence of the four alternative bases possible in siRNA, adenine,

guanine, cytosine, and uracil (FF 5). The claim requires no particular coefficient for the algorithm, nor does the claim impose any specific metric to identify improved gene silencing. *Ariosa* notes that “patent claims should not prevent the use of the basic building blocks of technology—abstract ideas, naturally occurring phenomena, and natural laws.” *Ariosa* at 7. Instant claim 85, by failing to recite any specific elements of the claimed algorithm, specifically attempts to fully preempt any process for designing siRNA.

In sum, we find that Appellants’ claims are directed to nonstatutory subject matter.

Conclusion of Law

The evidence of record supports the Examiner’s conclusion that the claims are directed to non-statutory subject matter.

SUMMARY

In summary, we affirm the rejection of claim 85 under 35 U.S.C. § 101 as directed to non-statutory subject matter. Because they are not separately argued claims 87 and 88 fall with claim 85.

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

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