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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte MALCOLM JAMES SIMONS

Appeal 2016-002684
Application 12/663,197[1]
Technology Center 1600

Before JOHN G. NEW, TIMOTHY G. MAJORS, and DAVID COTTA, *Administrative Patent Judges.*

NEW, *Administrative Patent Judge*.

DECISION ON APPEAL

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[1] Appellant states that the real party-in-interest is Haplomic Technologies Pty, Ltd. App. Br. 2.

SUMMARY

Appellant files this appeal under 35 U.S.C. § 134(a) from the Examiner's Final Rejection of claims 16, 20, 22, and 24–27. Specifically, claims 16, 20, 22 and 24–25 stand rejected as unpatentable under 35 U.S.C. § 102(b) as being anticipated by X. Liu et al., *Preparation of Single Rice Chromosome for Construction of a DNA Library Using a Laser Microbeam Trap*, 109 J. BIOTECH. 217–26 (2004). Claims 16, 20, 22 and 24–27 also stand rejected under 35 U.S.C.

§ 101 as being directed to nonstatutory subject matter.

We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

NATURE OF THE CLAIMED INVENTION

Appellant's invention is directed to methods for obtaining epigenetic information for a polyploid subject; specifically, determining whether any two modifications are present in *cis* on one chromosome, or in *trans* across two sister chromosomes. Abstract.

REPRESENTATIVE CLAIM

Claim 16 is representative of the claims on appeal and recites:

> 16. A method for improving methylation mapping, comprising,
>
> substantially isolating a DNA molecule from the biological sample, wherein the DNA molecule is an individual metaphase chromosome or a chromatid, or a fragment obtained therefrom;

> analyzing the DNA molecule to determine the presence or absence of one or more methylated bases in the DNA molecule and determining whether any two methylated bases are present in *cis* on the DNA molecule.

App. Br. 17.

ISSUES AND ANALYSES

We decline to adopt the Examiner's findings and conclusions that the appealed claims are anticipated by the prior art. However, we adopt the Examiner's findings and conclusions that the claims are unpatentable as being directed to nonstatutory subject matter. We address the arguments raised by Appellant below.

A. Rejection of claims 16, 20, 22 and 24–25 under 35 U.S.C. § 102(b)

Issue

Appellant argues that the Examiner erred in finding that Liu discloses the limitations of claim 16 reciting: "determin[ing] the presence or absence of one or more methylated bases in the DNA molecule" and "determin[ing] whether any two methylated bases are present in *cis* on the DNA molecule." App. Br. 4.

Analysis

The Examiner finds that Liu discloses isolation of a single chromosome, or a fragment thereof, and analyzing the DNA molecule for methylated bases. Final Act. 4. The Examiner finds that the polymerase chain reaction ("PCR") disclosed by Liu would not prevent the analysis of methylation because the claims as presented only require isolation of a

single chromosome, or a chromatid or a fragment thereof, and analyzing any two methylated bases on the DNA molecule. *Id.* The Examiner further finds that the method disclosed by Liu is within the scope of the claims as presented because Liu discloses isolating a single chromosome, or fragments thereof, and analyzing methylation of any two bases on the DNA molecule. *Id.*

Appellant argues that the only disclosure in Liu with respect to methylation of genomic DNA is at page 225, as cited by the Examiner, and which discloses:

> Mao constructed a rice chromosome 4 library by microdissection of a pair of chromosome 4 in a metaphase spread and by amplification using adaptor PCR on Sau3AI digested DNA. It was demonstrated that 58% single or low copy sequences and 42% repeat sequences were presented in their library. Sau3AI is cytosine methylation sensitive. In plants, methylation islands are clustered in regions of repeat sequences. The methylation islands were not digested by Sau3AI. Therefore using Sau3AI digested fragments of rice DNA might give rise to more unique sequences in the constructed library. The difference in the ratio of unique to repeated sequences between the two gene libraries reflects the differences in methodology.

App. Br. 4 (citing Y.W. Mao et al., *Construction of a DNA Library from Chromosome 4 of Rice (Oryza sativa) by Microdissection*, 8 Cell Res. 285–93 (1998) ("Mao")).

Appellant contends that the library disclosed by Liu was made using sonicated, T4 polymerase-filled and -trimmed DNA, and not by Sau3AI-digested DNA as the starting material. App. Br, 4. According to Appellant, Liu's reference to Mao's library is only made to compare the relative proportions of unique and repeat sequences. *Id.* at 4–5. Appellant contends

that, in the disclosure quoted *supra*, Liu suggests that Mao's library contains a higher percentage of unique sequences because clusters of methylation islands in portions of the genome that are enriched in repeat sequences in the genome are not fragmented by Sau3AI. *Id.* at 5. Therefore, Appellant asserts, despite the use of the methylation-sensitive restriction enzyme Sau3AI, a person of ordinary skill would not look to Mao's methodology or library in order to determine the methylation of genomic DNA according to the claimed method. *Id.* Rather, Appellant maintains, nothing in Liu discloses the additional steps of mapping which bases within the cloned Sau3AI fragment are methylated in the original chromosomal fragment, as recited in claim 16. *Id.*

The Examiner responds that Liu discloses obtaining a DNA molecule from an individual metaphase chromosome and characterizing the DNA molecule by analyzing the percentage of repeat sequences. Ans. 8. The Examiner finds that Liu infers from the high percentage of repeat sequences found in the DNA in their data that the repeat sequences have clustered methylated sequences, and that this anticipates the step of analyzing the DNA to determine the presence or absence of one or more methylated bases in the DNA molecule. *Id.* The Examiner finds that the high percentage of repeat sequences disclosed by Liu inherently comprises one or more methylated bases. *Id.* The Examiner further finds that the step of determining whether any two methylated bases are present in *cis* on the DNA molecule reads on a random distribution of a plurality methylated bases on a DNA sample and does not necessarily require the presence of two adjacent methylated bases. *Id.*

We are not persuaded by the Examiner's findings. Liu discloses that:

> The 200 inserts from the library established from rice chromosome 4 were blast to rice repeat database in TIGR in order to find the ratio of the repeat sequences in our library. A similarity of >70% was used as a match cutoff. One hundred and sixty-four (82%) inserts were homologous to rice repeat sequences. The repeats were unknown retrotransposon or gypsy retrotransposon elements. In general, there were 50% repetitive sequences in rice, but the repetitive sequences in our library were much higher than 50%....
>
> Repeat sequences in a genome are expected to be cloned at a higher frequency than unique sequences after PCR due to their relative abundance. This explains the high percentage of repeat sequences in our single chromosome library.

Liu 224–225. Liu then continues with the paragraph quoted by Appellant *supra*.

In comparing their results with those of Mao, Liu attempts to account for the differences between the high repeat: unique genomic sequence ratio reported in Liu, compared with those disclosed by Mao. Liu 225. Liu suggests that the difference may be a result of the fact that Mao sequenced DNA fragments after digestion with the Sau3AI enzyme, which does not digest "methylation islands," i.e., regions of the DNA that are heavily methylated and which contain many repeat sequences. *Id.* ("In plants, methylation islands are clustered in regions of repeat sequences. The methylation islands were not digested by Sau3AI. Therefore using Sau3AI digested fragments of rice DNA might give rise to more unique sequences in the constructed library"). Consequently, we find that the passages of Liu cited by the Examiner are directed to accounting for why Liu's PCR results demonstrate a higher repeat: unique genomic sequence ratio than Mao, *viz.*, because many of the repeat sequences of Mao were contained in the

undigested "methylation islands" left undigested by the Sau3AI enzyme and consequently not analyzed by Mao. However, we do not discern any disclosure of Liu that is directed to the claimed limitations of claim 16 reciting: "determin[ing] the presence or absence of one or more methylated bases in the DNA molecule" and "determin[ing] whether any two methylated bases are present in *cis* on the DNA molecule."

"For a claim to be anticipated, each claim element must be disclosed, either expressly or inherently, in a single prior art reference, and the claimed arrangement or combination of those elements must also be disclosed, either expressly or inherently, in that same prior art reference." *Therasense, Inc. v. Becton, Dickinson and Co.*, 593 F.3d 1325, 1332–33 (Fed. Cir, 2010). The Examiner does not point us to, nor do we discern, any passage of Liu that discloses "determin[ing] the presence or absence of one or more methylated bases in the DNA molecule" and "determin[ing] whether any two methylated bases are present in cis on the DNA molecule," as required by claim 16. We consequently reverse the Examiner's rejection of claims 16, 20, 22 and 24–25 on this ground.

B. Rejection of claims 16, 20, 22 and 24–27 under 35 U.S.C. § 101

Issue

Appellant argues that the Examiner erred in concluding that the claims on appeal are directed to an "abstract idea" and are therefore directed to a judicial exception to the subject matter eligible for patenting under 35 U.S.C. § 101. App. Br. 9.

Analysis

The Examiner finds that, as recited in the claims, correlating epigenetic information to the presence of any two methylated bases on a chromosome is considered a law of nature. Final Act. 2. The Examiner also finds that the additional recited steps of isolating a DNA molecule from a single metaphase chromosome in a biological sample and treating the genomic DNA with bisulfite constitute routine conventional activity and do not significantly transform the naturally existing methylated bases. *Id.* at 2–3. The Examiner further finds that the prior art of record discloses the use of microdissection or laser-mediated dissection to isolate single chromosomes — techniques used routinely in the field of molecular biology. *Id.* at 3. The Examiner concludes that application of routine conventional activity does not add anything significant to the naturally-existing methylated chromosome and does not modify the arrangement of nucleotide bases on a chromosome. *Id.*

Appellant argues that isolating a DNA molecule is a step that can only occur in the real, physical world and, as such, is not merely "an abstract idea." App. Br. 11. Appellant asserts that, although one might argue that "analyzing" data represents merely abstract thought, in the claims, the "analyzing" step is one that requires identification of specific methylated sites on a DNA molecule, and that such identification requires real-world manipulation of the DNA. *Id.* Therefore, Appellant argues that, reviewed as a whole, the claims are not directed to an abstract idea (or any other judicial exception). *Id.*

Appellant argues further that if, *arguendo*, the claims are determined to be directed to a judicially-created exception, then the claims also provide "significantly more" than the judicial exception, so as to render the claim

eligible for patenting. App. Br. 11. Appellant asserts that the method recited in claim 16 improves the art of DNA methylation mapping. *Id.* at 12. Pointing to the Specification, Appellant contends that it discloses that a significant improvement over the prior art is achieved by using isolated haploid genetic material, i.e., an isolated single chromosome as recited in the claim, as the starting material for analysis of methylation sites along the DNA molecule. *Id.* According to Appellant, this technical improvement resolves ambiguity with respect to the phasing of methylation tags among the two copies of any one chromosome in a diploid cell — a perceived problem of techniques disclosed in the prior art. *Id.* Therefore, Appellant contends, the claims on appeal recite "significantly more" than the judicial exception and are therefore directed to patent-eligible subject matter. *Id.*

Appellant further points to our reviewing court's holding in *DDR Holdings, LLC v. Hotels.com et al.*, 773 F.3d 1245, 1258–59 (Fed. Cir. 2014) as supporting their argument. App. Br. 14. According to Appellant, the field of DNA methylation analysis at the time of the claimed invention was burdened by a problem of unambiguously determining the phase of any two methylation marks identified in a DNA methylation analysis, i.e., whether said two marks resided on the same chromosome or whether one was present on a paternal copy of the chromosome and the other was present on a maternal copy of the chromosome. *Id.* (citing, e.g., Spec. 5). Appellant asserts that the claims on appeal recite a solution to this problem, i.e., first isolating a DNA molecule and then studying it for its methylated bases. *Id.* Therefore, Appellant argues, the claims recite "a concept for resolving this particular DNA methylation analysis-centric problem," rendering the claims patent-eligible. *Id.* (citing *DDR Holdings*, 773 F.3d at 1266; also citing

Messaging Gateway Solutions, LLC v. Amdocs, Inc., Civil Action No. 14–732–RGA, 2015 WL 1744343, at *4 (D. Del. Apr. 15, 2015) (holding that a claim may be patent eligible if it provides a solution "tethered to the technology that created the problem" and specifies how claim elements interact to achieve a "desired result which overrides conventional practice")). Appellant concludes that the claims on appeal are not directed to any isolated DNA molecule itself, and so do not include any natural product as a judicial exception. App. Br. 14. Furthermore, Appellant concludes, even if the claims are directed to a judicial exception, the presently claimed invention adds "significantly more" to the judicial exception, insofar as it constitutes an improvement in the technical art of chromosomal methylation mapping. *Id.*

The Examiner responds that the claims recite a method and are therefore directed to a statutory category, i.e., a process. Ans. 9. The Examiner finds, however, that the claims are directed to determining the presence or absence of one or more methylated bases on the DNA and determining whether any two methylated bases are present in *cis* on the DNA molecule, and, as such, are directed towards a phenomenon of nature. *Id.* (*see* Final Act. 2). The Examiner finds that the claims, when analyzed as a whole, do not particularly point out any non-naturally occurring differences between the claimed method and an abstract idea, and that the additional steps recited (obtaining a DNA molecule or obtaining the DNA molecule by laser mediated dissection) do not transform or modify the DNA molecule. *Id.* at 9–10. Therefore, the Examiner concludes, the claimed method does not recite "significantly more" than a judicial exception to Section 101. *Id.* at 10.

We are not persuaded by Appellant's arguments. Section 101 states that: "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101. However, the Supreme Court has long held that there are exceptions to this statute, *viz.*, laws of nature, natural phenomena, and abstract ideas. *Alice Corp. v. CLS Bank Int'l*, 134 S.Ct. 2347, 2354 (2014) (collecting cases).

The analytical framework under Section 101 set forth by the Supreme Court in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S.Ct. 1289 (2012) has been summarized by our reviewing court in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015):

> First, we 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....
> The Supreme Court has described the second step of this analysis as a search for an "inventive concept"—i.e., an element or combination of elements that is "sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself."

Ariosa, 788 F.3d at 1375 (citing *Mayo*, 132 S.Ct. at 1297–98, 1294).

Appellant's independent claim 16 recites a method of "substantially isolating a DNA molecule from the biological sample... [and] analyzing the DNA molecule to determine the presence or absence of one or more methylated bases in the DNA molecule and determining whether any two

methylated bases are present in *cis* on the DNA molecule." Appellant's claim recites a method of isolating and describing the location of methylated sites on DNA isolated from an individual chromosome or chromatid and determining whether any two of the methylated sites are present in cis, i.e., both located on the maternal or paternal chromosome from which it was isolated. *See* Spec. 5. As such, Appellant's claims are directed to a method of describing the location of methylated sites that are already present in the chromosomal DNA within the cell. Appellant's claims do not, explicitly or inherently, require any alteration of the methylation sites in the isolated DNA, merely a description of whether two methylated sites are *cis* (i.e., located on the same chromosome) or *trans* (located on sister chromosomes). *See* Spec. 5. Nor are Appellant's claims of detecting methylation sites linked to any particular location on a particular chromosome, chromatid, of fragment thereof.

Appellant's Specification further shows that the invention is for the purpose of detecting whether methylated sites are *cis* or *trans* without significantly altering the nature or location of the site:

> [T]he present invention provides a method for obtaining epigenetic information for a polyploid subject, the method including the steps of obtaining a biological sample from the subject, the sample containing: (i) at least one paternally-derived DNA molecule and/or associated protein and/or, (ii) at least one maternally-derived DNA molecule and/or associated protein, analyzing any one or more of the paternally- or maternally-derived DNA molecules or associated proteins for the presence or absence of modifications [i.e., methylation], wherein the step of analyzing determines whether any two modifications are present in *cis* on one chromosome, or in *trans* across two sister chromosomes

Spec. 5*; see also* Spec. 3–5; 12–13. Finally, Appellant's claims do not unconventional method for isolating sample material or detecting methylated bases.

We agree with the Examiner that claim 1 is directed to one of the judicially-created exceptions to Section 101, *viz.*, a phenomenon of nature. This finding is consonant with the holdings of our reviewing court. *See, e.g., Ariosa*, 788 F.3d at 1376 (holding that claims directed to a method for detecting a naturally-occurring, paternally inherited nucleic acid in a maternal blood sample were patent ineligible because they were directed to "detecting the presence of a naturally occurring thing or a natural phenomenon"); *Genetic Techs. Ltd. v. Merial L.L.C.*, 818 F.3d 1369, 1376 (2016) (holding that claims directed to a method of detecting a coding region of a genome by amplifying and analyzing a linked non-coding region of that person's genome were directed to a natural phenomenon); *Rapid Litig. Mgmt Ltd. v. CellzDirect, Inc.,* 827 F.3d 1042, 1048 (Fed. Cir. 2016) ("In recent cases, we found claims 'directed to' a patent-ineligible concept when they amounted to nothing more than observing or identifying the ineligible concept itself.").

We therefore proceed to the second step of the *Mayo* analysis, which requires that "we must examine the elements of the claim to determine whether it contains an inventive concept sufficient to transform the claimed abstract idea [or law of nature] into a patent-eligible application." *Alice*, 134 S.Ct. at 2357 (internal quotation marks omitted) (citing *Mayo*, 132 S.Ct. at 1294, 1298). "The question ... is whether the claims do significantly more than simply describe [a] natural relation[ ]." *Mayo*, 132 S.Ct. at 1297. The inventive concept necessary at step two of the *Mayo/Alice* analysis must not

be furnished by the unpatentable law of nature (or natural phenomenon or abstract idea) itself. That is, under the *Mayo/Alice* analytical framework:

> [A] claim directed to a newly discovered law of nature (or natural phenomenon or abstract idea) cannot rely on the novelty of that discovery for the inventive concept necessary for patent eligibility; instead, the application must provide something inventive, beyond mere "well-understood, routine, conventional activity." *Mayo*, 132 S.Ct. at 1294; *see also Association for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S.Ct. 2107, 2117 (2013); *Ariosa*, 788 F.3d at 1379. "[S]imply appending conventional steps, specified at a high level of generality, to laws of nature, natural phenomena, and abstract ideas cannot make those laws, phenomena, and ideas patentable." *Mayo*, 132 S.Ct. at 1300. Claims directed to laws of nature are ineligible for patent protection when, "(apart from the natural laws themselves) [they] involve well-understood, routine, conventional activity previously engaged in by researchers in the field." *Mayo*, 132 S.Ct. at 1294.

Genetic Techs., 818 F.3d at 1376.

Claim 16 broadly claims any and all methods of determining the location (*cis* or *trans*) of methylated sites on isolated cellular DNA. The claim does not require any particular method of analysis, not does Appellant argue that the actual localization and identification of the sites relies on a novel, heretofore undescribed (and unrecited by the claim) method. Indeed, Appellant contends that their claims are directed to "a concept for resolving this particular DNA methylation analysis-centric problem." *See* App. Br. 14.

Claim 26 depends upon claim 16 and recites:

> The method according to claim 16, wherein the analyzing includes a method selected from the group consisting of DNA sequencing using bisulfite treatment, restriction landmark

genomic scanning, methylation-sensitive arbitrarily primed PCR, Southern analysis using a methylation-sensitive restriction enzyme, methylation-specific PCR, restriction enzyme digestion of PCR products amplified from bisulfite-converted DNA, and combinations thereof.

Claim 26, which similarly depends from claim 16, is more specific:

> The method according to claim 16, wherein where the analyzing includes DNA sequencing using bisulphite treatment, the analyzing includes:
>
> (a) reacting the DNA with sodium bisulfite to convert unmethylated cytosine residues to uracil residues while leaving any 5-methylcytosine residues unchanged to create an exposed bisulfite-converted DNA sample having binding sites for primers specific for the bisulfite-converted DNA sample;
>
> (b) performing a PCR amplification procedure using top strand or bottom strand specific primers;
>
> (c) isolating the PCR amplification products;
>
> (d) performing a primer extension reaction using a methylation-sensitive single nucleotide primer extension (Ms-SNuPE) primer, dNTPs and Taq polymerase, wherein the Ms-SNuPE primer comprises from about a 15-mer to about a 22-mer length primer sequence that is complementary to the bisulfite-converted DNA sample and terminates immediately 5' of the cytosine residue of the one or more CpG dinucleotide sequences to be assayed; and
>
> (e) determining the methylation state of the one or more CpG dinucleotide sequences by determining the identity of the first primer-extended base.

Appellant contends that these more particularized methods of analysis further remove the subject matter claimed in claims 25–27 from the realm of "abstract ideas." App. Br. 15. Nevertheless, the Examiner finds, and Appellant does not dispute, that these methods were all well-understood, routine, conventional activity, and well-known in the prior art. Ans. 10.

We conclude, with the guidance provided by our reviewing court in, for example, *Genetic Techs.*, that the additional steps of Appellant's claims fail to recite an inventive concept beyond "well-understood, routine, conventional activity previously engaged in by researchers in the field." *Genetic Techs.*, 818 F.3d at 1376 (quoting *Mayo*, 132 S.Ct. at 1294). Rather, Appellant's claims "simply append[ ] conventional steps, specified at a high level of generality, to […] natural phenomena […] [which] cannot make those laws, phenomena, and ideas patentable." *Id.* (quoting *Mayo*, 132 S.Ct. at 1300). We therefore conclude that the claims fail to add "significantly more" to the isolation and identification of naturally-occurring methylated DNA sites as being either *cis* or *trans*. Consequently, the claims are unpatentable under 35 U.S.C. § 101. *See Mayo*, 132 S.Ct. at 1294.

In this instance, however, Appellant's claim 16 is directed to no specific or new laboratory technique, but rather claims any and all techniques extant for the determination of localizing methylation sites on isolated cellular DNA. The Examiner finds, and Appellant does not dispute, that the methods recited in claims 25–27 are well-known in the art. Appellant does not claim any new technique for the localization of methylated sites, but only the employment of well-known techniques to describe a phenomenon of nature already present in the cells. As such, we

determine that the claims fall within the judicial exception to Section 101 as impermissibly being directed to a phenomenon of nature.

Alternatively, we find that the claims are directed to another judicially-created exception to Section 101. Appellant disputes the Examiner's finding that the claims require a "correlation step. *See* App. Br. 12–13. However, claim 16 (and by incorporation its dependent claims) requires localizing methylated sites on the isolated cellular DNA and "determining whether any two methylated bases are present in *cis* [or inferentially *trans*] on the DNA molecule." In other words, claim 16 is directed to isolating and localizing, by any and all methods, methylated sites naturally occurring in cellular DNA and then making a mental assessment as to whether the localized methylated sites are *cis* or *trans*. This latter step require only a mental comparison step, *viz.*, a comparison of the attained results, to determine whether two methylated sites are either *cis* or *trans*. As such, we conclude that this step is directed to a patent-ineligible abstract idea. In this regard, we find the Federal Circuit's holding in *In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation*, 774 F.3d 755 (Fed. Cir. 2014) instructive. In *BRCA*, the Federal Circuit held that method claims directed to the comparison of wild-type genetic sequences with a subject's genetic sequence were directed to the patent-ineligible abstract idea of comparing BRCA sequences and determining the existence of alterations. *BRCA*, 774 F.3d at 763. The Federal Circuit found, in this regard, that:

> The methods, directed to identification of alterations of the gene, require merely comparing the patient's gene with the wild-type and identifying any differences that arise. The number of covered comparisons is unlimited. The covered comparisons are

> not restricted by the purpose of the comparison or the alteration being detected.

Id. (internal reference omitted); *see also Myriad*, 133 S.Ct. at 2116.

In the appeal before us, the claims require comparing identified and naturally-occurring methylation sites on isolated DNA and mentally determining whether the methylated sites are either *cis* or *trans*. The methods of identification and localization are acknowledged as encompassing any method (claim 16) or methods that were well known in the art at the time of invention (claims 26–27) and, in the required second step of the *Mayo* analysis, do not add, as we have explained *supra*, "significantly more" to the claims. The mental step of making a determination of whether two methylated sites are *cis* or *trans* therefore constitutes an abstract idea, another judicially-created exception to Section 101, and is an additional reason why Appellant's claims are not patent eligible. We consequently find that Appellant's claims are unpatentable under 35 U.S.C. § 101 on this basis.

We have already explained why we find that the claims are directed to a phenomenon of nature or, alternatively, an abstract idea. Appellant's claim 16 permits the user to employ any and all methods of analysis to describe this phenomenon and/or idea. As such, they also preempt any possibility of determining the *cis* or *trans* location of methylated sites by any method, extant or yet to be invented. The prohibition of such preemption is a central concern of the judicially-created exceptions to Section 101. *See Alice*, 134 S.Ct. at 2354. Similarly, dependent claims 25–27 encompass the use of technologies well known in the art to similarly achieve this end. "Where a patent's claims are deemed only to disclose patent ineligible

subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot." *Ariosa*, 788 F.3d at 1379.

We therefore affirm the Examiner's rejection of claims 16, 20, 22 and 24–27 as being directed to non-statutory subject matter under 35 U.S.C. § 101.

DECISION

The Examiner's rejection of claims 16, 20, 22 and 24–25 as unpatentable under 35 U.S.C. § 102(b) is reversed.

The Examiner's rejection of claims 16, 20, 22 and 24–27 as unpatentable under 35 U.S.C. § 101 is affirmed.

AFFIRMED