UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
13/691,048	11/30/2012	Craig S. Atwood	1256-01823	5579

81391 7590 08/16/2016

Andrus Intellectual Property Law, LLP
100 East Wisconsin Avenue
Suite 1100
Milwaukee, WI 53202-4178

EXAMINER	
POHNERT, STEVEN C	

ART UNIT	PAPER NUMBER
1634	

MAIL DATE	DELIVERY MODE
08/16/2016	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CRAIG S. ATWOOD

Appeal 2015-001611
Application 13/691,048
Technology Center 1600

Before DONALD E. ADAMS, RICHARD J. SMITH, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This appeal under 35 U.S.C. § 134(a) involves claims 26–28, 30–32, 42, 44, 45, and 47–49 (App. Br. 22; *see* Final Rej. 2).[2] Examiner entered rejections under 35 U.S.C. § 101, 35 U.S.C. § 102(b), and 35 U.S.C. § 103(a). We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

---

[1] Appellant identifies the Real Party in Interest as the "Wisconsin Alumni Research Foundation" (App. Br. 1).

[2] "Claim[s] 41, 43, 50–53, and 55 [stand] withdrawn from examination" (App. Br. 22). Examiner failed to present a rejection of Claim 54, therefore, we do not include Claim 54 in our deliberations.

STATEMENT OF THE CASE

Appellant's independent claims 26 and 42 are representative and reproduced below with the non-elected species of the claimed invention ellipted[3]:

26. A method comprising administering treatment to a patient at risk for developing Alzheimer's disease (AD) or a patient diagnosed with AD, wherein the patient is homozygous or heterozygous for an Apolipoprotein E4 (*APOE4*) allele, and the patient has a single nucleotide polymorphism (SNP) . . . rs4073366, wherein the patient is homozygous for the cytosine allele (C-allele) or the patient is homozygous for the guanine allele (G-allele) at the polymorphic position of rs4073366. . . .

42. A method for administering treatment to a patient at risk for developing Alzheimer's disease (AD) or a patient diagnosed with AD, wherein the patient is homozygous or heterozygous for an Apolipoprotein E4 (*APOE4*) allele, the method comprising:

(a) treating a sample from the patient with reagents that detect a single nucleotide polymorphism (SNP) . . . consisting of . . . rs4073366 . . .; and

(b) administering AD treatment to the patient if . . . the patient is determined to be homozygous for the cytosine allele (C-allele) or the patient is determined to be homozygous for the guanine allele (G-allele) at the polymorphic position of rs4073366 . . . .

[3] Due to a restriction requirement and species election, we limit the scope of our review to Appellant's elected invention (*see* Examiner's February 5, 2013 Restriction Requirement and Appellant's June 3, 2013 Response to Restriction Requirement; *see also* App. Br. 7: n. 1). *See Ex parte Ohsaka*, 2 USPQ2d 1460, 1461 (BPAI 1987).

Claims 26–28, 30–32, 42, 44, 45, and 47–49 stand rejected under 35 U.S.C. § 101.[4]

Claims 26–28 and 30 stand rejected under 35 U.S.C. § 102(b) as anticipated by Sano[5] as evidenced by Wragg[6] and dbSNP rs4073366.[7]

Claims 26–28 and 30 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Sano, Wragg, and dbSNP rs4073366.

Claims 31 and 32 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Sano, Wragg, dbSNP rs4073366, and Mattson.[8]

Anticipation:

ISSUE

Does the preponderance of evidence on this record support Examiner's finding that Sano teaches Appellant's claimed invention, as evidenced by Wragg and dbSNP rs4073366?

---

[4] Examiner's statement of the rejection includes canceled claims 29 and 46 (*see generally* App. Br. 22 and 24; Final Rej. 2). In addition, Examiner's statement of the rejection includes claim 41, which stands withdrawn from consideration (*see* App. Br. 22; Final Rej. 2). Claims 29, 41, and 46 were not included in our deliberations.

[5] Sano et al., *A controlled trial of selegiline, alpha tocopherol, or both as treatment for Alzheimer's disease*, 336 The New England Journal of Medicine 1216–1222 (1997).

[6] Wragg et al., *Genetic association between intronic polymorphism in presenilin-1 gene and late-onset Alzheimer's disease*, 347 Lancet 509–512 (1996).

[7] NCBI dbSNP Short Genetic Variations Cluster Report: rs4073366, http://www.ncbi.nlm.nih.gov/projects/SNP/snp_ref.cgi?rs=4073366, accessed Jan. 6, 2014.

[8] Mattson, *Pathways towards and away from Alzheimer's disease*, 430 Nature 631–639 (2004).

FACTUAL FINDINGS (FF)

FF 1. Appellant discloses that "[t]he *APOE4* allele (ε4) . . . [is] a risk factor for late-onset AD," but, "the risk for AD imparted by one or two ε4 alleles is only partially penetrant: ~50% of AD patients do not carry an ε4 allele" (Spec. ¶ 3).

FF 2. Appellant discloses methods "to determine that a patient has an increased risk for developing AD (*e.g.*, a risk greater than about 99%) where: (i) the patient has at least one *APOE4* allele; (ii) the patient is female; and (iii) the patient is homozygous for the C-allele or the G-allele for rs4073366" or "(*e.g.*, a[] risk greater than about 85%) where: (i) the patient has at least one *APOE4* allele; (ii) the patient is homozygous for the C-allele or the G-allele for rs4073366" (Spec. ¶ 16; *see generally* Ans. 9–10).

FF 3. Sano discloses the treatment "of patients with Alzheimer's disease [] with selegiline or alpha-tocopherol or both was beneficial in delaying the primary outcome of disease progression" (Sano 1220; *see* Ans. 8; *see also* Sano 1218: Table 1 (identifying the number of male and females in the population)).

FF 4. Examiner relies on dbSNP rs4073366 to establish that the homozygous G allele at the polymorphic position of SNP rs4073366 occurs in "over 75% of people assayed in populations greater than 44," therefore, Examiner finds that the population of AD patients treated according to Sano's methodology, "would inherently encompass th[e] [rs4073366] genotype" required by Appellant's claimed invention (Ans. 9).

FF 5. Wragg discloses that "[a]s much as 40-50% of the risk for late-onset [Alzheimer's] disease is attributable to alleles at the ApoE locus," wherein "ApoE4 is thought to increase risk of Alzheimer's disease in a dose-

dependent manner" (Wragg 509; Ans. 9; *see also* Wragg 509 (discussing "DNA sequence analysis" and sample populations that include male and female patients "blood samples from 208 [] cases of dementia of the Alzheimer type and from 185 age-matched controls (. . .; 58% female in each series))).

ANALYSIS

Examiner finds that Sano's method of treating Alzheimer's subjects "inherently anticipates claim 26 as one subject would have the required genotype" (Ans. 10). We are not persuaded.

As Appellant explains,

> the Office appears to be arguing that because 40-50% of the risk for late-onset disease is attributable to alleles at the ApoE locus, and because over 75% of people assayed in populations greater than 44 are homozygous for the G-allele of dbSNP rs4073366, it is highly probable that Sano's method of treating [] Alzheimer's subjects would have included treating a patient that is positive for the ApoE-allele and the G-allele of dbSNP rs4073366.

(App. Br. 8–9; *cf.* Ans. 8–10; FF 3–5.) Similarly, with respect to Examiner's discussion of Appellant's Specification, Appellant contends that

> the Office appears to be arguing that because patients having AD have been treated in the prior art, and because the genetic markers that the present inventor has identified are indicative of a high risk for AD, then statistically patients having the inventor's identified genetic markers must have been administered treatment for AD in the prior art.

(App. Br. 9; *cf.* Ans. 9–10; FF 1–5.) "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *In re*

Robertson, 169 F.3d 743, 745 (Fed. Cir. 1999) (citations and internal quotation marks omitted).

As Appellant explains, "the mere fact that at least one of Sano's Alzheimer subjects may have had the genotype recited in the present claims based on statistics is not sufficient to establish inherent anticipation" (App. Br. 10). We agree. We recognize, but are not persuaded by, Examiner's assertion that Appellant's "claims require a single active step of administering a treatment to a patient with AD or risk of AD" and Appellant's "response has provided no arguments that the prior art does not anticipate the single positive active step of the claims" (Ans. 16 and 17).[9] As Appellant explains, Examiner's interpretation of Appellant's claimed invention fails to account for all the limitations of Appellant's claimed invention. *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) ("A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.").

[9] We recognize, as does Appellant, that in response to Appellant's arguments concerning the prior art rejections, Examiner refers to "Haasl (BMC Medical Genetics (2008) volume 9, page 37)" to support Examiner's assertion that "it is unclear if APOE4 positive and CC genotype as claimed is correlated with AD as asserted" (*see* Ans. 14–15; *cf.* Reply Br. 2). Examiner, however, failed to rely upon Haasl in any statement of rejection before this panel, therefore, we decline to consider Haasl. *In re Hoch*, 428 F.2d 1341, 1342 n.3 (CCPA 1970).

CONCLUSION OF LAW

The preponderance of evidence on this record fails to support Examiner's finding that Sano teaches Appellant's claimed invention, as evidenced by Wragg and dbSNP rs4073366.

The rejection of claims 26–28 and 30 under 35 U.S.C. § 102(b) as anticipated by Sano as evidenced by Wragg and dbSNP rs4073366 is reversed.

Obviousness:

ISSUE

Does the preponderance of evidence relied upon by Examiner support a conclusion of obviousness?

FACTUAL FINDINGS (FF)

FF 6. Examiner relies on Sano, dbSNP rs4073366, Wragg, and Appellant's Specification as discussed above (*see* FF 1–5; Ans. 11–13).

FF 7. Examiner finds that the combination of Sano, dbSNP rs4073366, and Wragg fails to suggest "treating subjects with diet or lifestyle" and relies on Mattson to disclose "that behavior, diet, and environmental factors affect the risk of AD," wherein Mattson "suggests increasing exercise and changing diet as potential methods of reducing Alzheimer disease and slowing progression" (Ans. 13–14; *see* Mattson 631 ("interventions for the prevention and treatment of AD [] range from changes in diet and lifestyle, to vaccines and drugs")).

ANALYSIS

The rejection over the combination of Sano, Wragg, and dbSNP rs4073366:

Based on the combination of Sano, Wragg, and dbSNP rs4073366, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious to treat Alzheimer subjects as disclosed by Sano, wherein "at least one Alzheimer patient ha[s] the required genotype being treated" (Ans. 13). In this regard, Examiner finds that Sano "is merely treating a population that must statistical[ly] have one subject with the required genotype" (*id.*). We are not persuaded.

For the reasons discussed above, the evidence of record fails to support Examiner's conclusion (*see* App. Br. 8–10). "[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006). In this regard, Examiner's conclusion that Sano might possibly treat at least one individual with AD fails to provide a sufficient evidentiary basis to support Examiner's conclusion that the combination of Sano, Wragg, and dbSNP rs4073366 makes obvious Appellant's claimed invention.

The rejection over the combination of Sano, Wragg, dbSNP rs4073366, and Mattson:

Based on the combination of Sano, Wragg, dbSNP rs4073366, and Mattson, Examiner concludes that, at the time Appellant's invention was made, it would have been prima facie obvious "to treat subjects in the method [suggested by the combination] of Sano, Wragg, and dbSNP

[rs4073366] by chang[ing] [the subjects'] diet and/or lifestyle" (Ans. 14). We are not persuaded. Examiner failed to establish that Mattson makes up for the deficiency in the combination of Sano, Wragg, and dbSNP rs4073366 discussed above.

CONCLUSION OF LAW

The preponderance of evidence relied upon by Examiner fails to support a conclusion of obviousness.

The rejection of claims 26–28 and 30 under 35 U.S.C. § 103(a) as unpatentable over the combination of Sano, Wragg, and dbSNP rs4073366 is reversed.

The rejection of claims 31 and 32 under 35 U.S.C. § 103(a) as unpatentable over the combination of Sano, Wragg, dbSNP rs4073366, and Mattson is reversed.

Patent-eligible Subject Matter:

ISSUE

Does the evidence of record support Examiner's finding that Appellant's claimed invention is not directed to patent-eligible subject matter?

ANALYSIS

Examiner finds that Appellant's claimed invention is directed to a "method" that involves "a naturally recurring correlation of APOE[4], rs407336 . . . and risk or diagnosis of AD" (Ans. 3–4). *See Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. 1289, 1296–97 (2012). Examiner finds that Appellant's "claims do not provide additional elements" that would establish that Appellant's claims would do

"more than [apply] the natural principle" (Ans. 5). *Mayo*, 132 S. Ct. at 1297. In sum, Examiner finds that Appellant's claimed invention "merely requires the detection of [a] naturally occurring sequence that is correlated with AD risk or diagnosis and administration of therapy claimed with a high degree of generality," which "are not patent eligible" (Ans. 5). We agree.

For the reasons set forth herein, we are not persuaded by Appellant's contention that Appellant's "claims do recite statutory subject matter because the claims are narrowly drawn to [a] specific SNP[] and include a practical step of administering treatment to a patient that has the specific SNP[]" (App. Br. 11; *see* Reply Br. 4–6).

> We recognize, but are not persuaded by, Appellant's contention that if the Office were to define the "natural principle" encompassed by [Appellant's] claims more broadly and commensurate with the inventor's finding that a plurality of genes that encode gene products that function in the steroidogenic pathway are associated with the risk of AD, then the claims would not be viewed as reciting steps with a "high degree of generality."

(App. Br. 12.) The method of Appellant's claim 26 comprises administering *any* treatment to a patient at risk for developing, or diagnosed with, AD (*see* Appellant's claim 26). Similarly, the method for administering treatment to a patient at risk for developing, or diagnosed with, AD, set forth in Appellant's claim 42, requires the administration of *any* AD treatment to the patient (*see* Appellant's claim 42). Methods comprising the administration of treatment to a patient at risk for developing, or diagnosed with, AD were known in the art at the time of Appellant's claimed invention (*see* FF 3 and 7; *see* Ans. 19 (Appellant's "claims encompass the use of any treatment. [Appellant's] dependent claims require the administration of lifestyle or diet

changes, [which were known in the art,] but do[] not limit diet or life style changes in any fashion")).

Appellant's claimed invention requires a patient that is homozygous or heterozygous for an *APOE4* allele, which was, at the time of Appellant's claimed invention, "thought to increase risk of Alzheimer's disease in a dose-dependent manner" (*see* Appellant's claims 26 and 42; *cf.* FF 5; *see* Ans. 19 ("The APOE4 genotype and presence of APOE4 allele are naturally occurring as is there correlation with AD or risk of AD")). The rs4073366 SNP was also known in the art at the time of Appellant's claimed invention (*see* FF 4).

Moreover, Appellant's claimed method is not transformed into patent-eligible subject matter because it further requires identifying a protein or a mutation. To the contrary, the claims merely apply well-understood, routine methods to identify a subpopulation of patients with, or at risk of developing, AD that are homozygous or heterozygous for the *APOE4* allele and homozygous for the C-allele or G-allele at a polymorphic position of the rs4073366 SNP (*see, e.g.*, Appellant's independent claims 26 and 42). *Cf. In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litig.*, 774 F.3d 755, 759 (Fed. Cir. 2014) ("The two method claims now on appeal involve comparisons between the wild-type BRCA sequences with the patient's BRCA sequences"). Comparing two sequences to detect alterations is a patent-ineligible "abstract mental process." *Id.* at 763.

Therefore, the question before this panel distills down to the same question presented in *Mayo*: Do Appellant's "claims add *enough* to [Appellant's] statements of the correlations to allow the process [Appellant] describe[s] to qualify as [a] patent-eligible process[] that *appl*[*ies*] natural

laws?" *Mayo*, 132 S. Ct. at 1297. On this record, as in *Mayo*, we find "that the answer to this question is no." *See id.*

We recognize, but are not persuaded by, Appellant's contention that "[t]he present claims do recite statutory subject matter because the claims are narrowly drawn to [a] specific SNP[] and include a practical step of administering [any] treatment to a patient that has the specific SNP[]" (App. Br. 11; *see id.* at 12; *see* Reply Br. 4–6). Notwithstanding Appellant's contention to the contrary, it is not sufficient for a claim to "simply recite a law of nature and then add the instruction 'apply the law.'" *See Mayo*, 132 S. Ct. at 1297. As discussed above, the administration step of Appellant's claimed invention was known in the art prior to the date of Appellant's claimed invention (*see* FF 3 and 7). *Cf. Mayo*, 132 S. Ct. at 1297. Nevertheless, "the 'prohibition against patenting abstract ideas 'cannot be circumvented by attempting to limit the use of the formula[, abstract mental process, or natural law,] to a particular technological environment.'" *Id.* (citing *Bilski v. Kappos*, 130 S. Ct. 3218, 3230 (2010)).

There is no requirement in Appellant's claimed invention that the art recognized "treatment" regimens already provided to patients with, or at risk of developing, AD is changed in any way by detecting *APOE4* and rs4073366 SNP alleles, or otherwise subdividing the foregoing patient population (*see* Ans. 20 (Appellant's "claims are not limited to any . . . specific treatment); Ans. 22; *cf.* App. Br. 14 (Appellant's "claims do require an active step of administering therapy based on an identified correlation"); *see also id.* at 14–15 (Appellant "has identified a novel and non-obvious class of patients that will benefit from treatment for AD and the claims recite

an active step of administering therapy to the identified class of patients"; *id.* at 19; *see* Reply Br. 6–11).

The "wherein" clauses of Appellant's claimed invention, as in *Mayo*, "simply tell a doctor about the relevant natural laws . . . while trusting them to use those laws appropriately where they are relevant to their decisionmaking." *Mayo*, 132 S. Ct at 1297.

While Appellant's claims do not recite determining steps, in *haec verba*, determining steps are implied by the requirement of Appellant's claim 26 that the patient is homozygous or heterozygous for an *APOE4* allele and homozygous for the C-allele or G-allele at the polymorphic position of the rs4073366 SNP (*see* Appellant's claim 26; *cf.* Ans. 20 (Appellant's "[c]laim 26 . . . does not provide a positive active step in which the genotype is determined"). A determining step is also implied by the requirement of Appellant's claim 42 that requires that the patient is homozygous or heterozygous for an *APOE4* allele and the step of treating a sample from the patient with reagents that detect a SNP rs4073366 polymorphism (*see* Appellant's claim 42; *cf.* Ans. 20 (Appellant's "claims are not limited to any specific method of detection[or] any specific reagent for detecting")). Here, however, as in *Ariosa*, the detection of *APOE4* and rs4073366 SNP alleles–"natural phenomen[a]– . . . add[] no inventive concept to the limitations of" Appellant's claimed invention. *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1378 (Fed. Cir. 2015); *see In re BRCA1*, 774 F.3d at 763 (Comparing two sequences to detect alterations is a patent-ineligible "abstract mental process.").

As discussed above, Appellant's claimed method does no more than identify a sub-population of patients with, or at risk of developing, AD and

then *administer exactly the same treatment* to those patients as was done in the prior art for the entire population of patients with, or at risk of developing, AD. Therefore, we are not persuaded by Appellant's contention that "[i]n contrast to the claims at issue in *Mayo*, [Appellant's] claims do require an active step of administering therapy based on an identified correlation" (App. Br. 14). Notwithstanding Appellant's contention to the contrary, Appellant's therapy administration step is *not* based on any identified correlation, because patients are administered exactly the same treatment regimen suggested by the prior art for *any* AD patient. We are, also, not persuaded by Appellant's unsupported contention that the medical community would not appreciate that a treatment regimen that can be applied to the *entire genus* of AD patients – can also be applied to a *sub-genus* of those AD patients (*see* App. Br. 17 "the active step of administering AD therapy to [a sub-]class of [AD] patients is not a well understood, routine, and conventional activity engaged by the medical community").

Therefore, we find that, here, as in *Mayo*, Appellant's

> 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, 132 S. Ct. 1298.

Appellant's dependent claims which limit the scope of Appellant's independent claims 26 and 42 to a female or male (*see* Appellant's claims 27–28 and 44–45, respectively; *cf.* FF 3 and 5) or to a treatment that

comprises administering medication, changing the diet or lifestyle of the patient (*see* Appellant's claims 30–32 and 47–49, respectively; *cf.* FF 3 and 7) simply append routine, conventional steps to a natural phenomenon, which, when the claims are read as a whole, are specified at a high level of generality and do not supply an inventive concept to Appellant's claims (*see* Ans. 20 (Appellant's "claims are set forth with a high degree of generality and therefore do not recite elements/steps in addition to the judicial exception that would narrow the scope of the claims . . . . The steps are highly generalized")). Therefore, we are not persuaded by Appellant's contention that "the rejection be . . . withdrawn, at least in regard to [Appellant's] claims 30-32 and 47-49" (App. Br. 18).

CONCLUSION OF LAW

The evidence of record supports Examiner's finding that Appellant's claimed invention is not directed to patent-eligible subject matter.

The rejection of claims 26–28, 30–32, 42, 44, 45, and 47–49 under 35 U.S.C. § 101 is affirmed.

TIME PERIOD FOR RESPONSE

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