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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 14/233,113 | 04/28/2014 | Zsuzsanna Nagy | 1194-P05918US00 | 2905 |

110 7590 07/30/2018

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| EXAMINER | |
|---|---|
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| ART UNIT | PAPER NUMBER |
|---|---|
| 1634 | |

| MAIL DATE | DELIVERY MODE |
|---|---|
| 07/30/2018 | PAPER |

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UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* ZSUZSANNA NAGY

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Appeal 2017-008793
Application 14/233,113[1]
Technology Center 1600

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Before DONALD E. ADAMS, ULRIKE W. JENKS, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

Opinion Dissenting by *Administrative Patent Judge* Paulraj.

DECISION ON APPEAL

This Appeal under 35 U.S.C. § 134(a) involves claims 2, 4, 16–18, 20, 27, 29, and 31 (Final Act.[2] 1). Examiner entered a rejection under 35 U.S.C. § 101. We have jurisdiction under 35 U.S.C. § 6(b).

We AFFIRM.

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[1] Appellant identifies "University of Birmingham, Edgbaston, Birmingham, United Kingdom" as the real party in interest (Br. 1).
[2] Office Action mailed May 25, 2016.

## STATEMENT OF THE CASE

Appellant's disclosure

> relates to diagnosis and monitoring of Alzheimer's disease in the live subject. Particularly, although not exclusively, the invention relates to methods involving the measurement of differential gene expression in non-neuronal cells taken from human subjects suspected of having Alzheimer's disease. The invention also relates to a method by which to monitor mTOR [signaling] in a human cell.

(Spec. 1: 5–9.) Claims 2 and 27 are representative and reproduced below:

> 2. A method of assessing the risk of Alzheimer's disease progression in a human subject suspected of having Alzheimer's disease, which method comprises
>
> (i) obtaining lymphocytes from said human subject suspected of having Alzheimer's disease and from an age-matched healthy subject with normal cognitive ability;
>
> (ii) inducing cell division in the lymphocytes taken from the human subject suspected of having Alzheimer's disease;
>
> (iii) separating the dividing lymphocytes of (ii) into two pools and treating one pool of lymphocytes with rapamycin;
>
> (iv) assaying the level of protein of at least one interleukin selected from interleukin 1 beta (IL1B), interleukin 2 (IL-2), interleukin 6 (IL-6), or interleukin 10 (IL-10) in the pool of lymphocytes treated with rapamycin and in the untreated pool;
>
> (v) comparing the level of protein of the at 1east one interleukin obtained in (iv) for the pool of rapamycin-treated lymphocytes and the untreated lymphocyte pool to quantify the change in protein levels in response to rapamycin;
>
> (vi) repeating steps (ii) - (v) using control lymphocytes taken from the age-matched healthy subject with normal cognitive ability; and
>
> (vii) determining that said human subject suspected of having Alzheimer's disease is at increased risk of Alzheimer's disease progression when (a) the reduction of IL1B or IL10

protein levels in response to rapamycin is higher in control lymphocytes as compared to lymphocytes taken from the human subject suspected of having Alzheimer's disease; or (b) the reduction of IL-2 or IL-6 protein levels in response to rapamycin is lower in control lymphocytes as compared to lymphocytes taken from the human subject suspected of having Alzheimer's disease; or (c) the reduction of IL1B or IL10 protein levels in response to rapamycin is higher in control lymphocytes as compared to lymphocytes taken from the human subject suspected of having Alzheimer's disease and the reduction of IL-2 or IL-6 protein levels in response to rapamycin is lower in control lymphocytes as compared to lymphocytes taken from the human subject suspected of having Alzheimer's disease.

(Br. 10.)

27. A method by which to monitor mTOR signaling in a human lymphocyte, which method comprises:

(i) isolating lymphocytes from a human subject;

(ii) inducing cell division in said lymphocytes;

(iii) separating the dividing lymphocytes of (ii) into two pools and treating one pool of lymphocytes with rapamycin;

(iv) assaying the level of protein of at least one interleukin selected from interleukin I beta (IL1B), interleukin 2 (IL-2), interleukin 6 (IL-6), or interleukin 10 (IL-10) in the pool of lymphocytes treated with rapamycin and in the untreated pool;

(v) comparing the level of protein of the at least one interleukin obtained in (iv) for the pool of rapamycin-treated lymphocytes and the untreated lymphocyte pool to detect a reduction in protein levels in response to rapamycin;

(vi) determining that mTOR signaling is decreased if there is a decrease in the protein level of at least one interleukin 1 beta (IL1B), interleukin 2 (IL-2), interleukin 6 (IL-6), or interleukin 10 (IL-10).

(*Id.* at 11–12.)

The claims stand rejected as follows:

Claims 2, 4, 16–18, 20, 27, 29, and 31 stand rejected under 35 U.S.C. § 101.

ISSUE

Does the evidence of record support Examiner's finding that Appellants' claimed invention is directed to patent ineligible subject matter?

ANALYSIS

Examiner finds that Appellant's claimed invention is directed to patent ineligible subject matter (*see* Final Act. 3–8). We agree.

The Supreme Court articulated a two-step test for patent eligibility under § 101 that "distinguish[es] patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (*citing Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S. Ct. at 1296–97). "First," *Alice* instructs a court to "determine whether the claims at issue are directed to one of those patent-ineligible concepts. *Id.* (citation and quotations omitted). If the claims are directed to a patent-ineligible concept then the court must proceed to the second step of the test — the "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." *Id.* (quotations and alterations omitted).

The methods set forth in Appellant's independent claims 2 and 27 correlate changes in lymphocyte IL1B, IL-2, IL-6 or IL-10 protein levels resulting from rapamycin exposure to either (a) an increased risk of Alzheimer's disease progression in a human subject suspected of having

Alzheimer's disease (claim 2) or (b) decrease in mTOR signaling (claim 27) (*see* Br. 10 and 11–12; *id.* at 7 ("claim [27] is focused on the process of determining whether mTOR signaling is decreased in a lymphocyte sample after rapamycin treatment"); *see also* Final Act. 3 and 4). As Appellant explains, "it is ultimately the differential response to rapamycin observed in certain human subjects that is informative for the purposes of the presently-claimed methods, and not the rapamycin response or changes in interleukin gene expression *per se*" (Br. 6). Thus, here as in *Mayo*, the claims are not directed to a method of treating a disease. To the contrary, Appellant's claims are similar to those in *Mayo*, which "were directed to a diagnostic method based on the 'relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.'" *Vanda Pharms., Inc. v. West-Ward Pharms. Int'l Ltd.*, 887 F.3d 1117, 1134 (Fed. Cir. 2018), quoting *Mayo*, 132 S. Ct. at 1289. "This 'relation is a consequence of the ways in which thiopurine compounds are metabolized by the body—entirely natural processes. And so a patent that simply describes that relation sets forth a natural law.'" *Id.*, quoting *Mayo*, 132 S. Ct. at 1289. Thus, here, as in *Mayo*, the relationship between certain interleukin protein levels and either the risk of Alzheimer's disease progression or the decrease in mTOR signaling, are entirely natural processes and Appellant's claims do no more than simply describe that relationship, thereby, setting forth a natural law. *See* Final Act. 3–8; *Mayo*, 132 S. Ct. 1289.

Therefore, with respect to the first step of the *Alice* test, we agree with Examiner's finding that Appellant's claim a natural law (*see* Final Act. 3).[3] For the foregoing reasons, we are not persuaded by Appellant's contentions to the contrary (*see* Br. 3–7).

Turning to the second step of the *Alice* test, the search for an "inventive concept," we agree with Examiner's finding that Appellant's "claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception" (Final Act. 2). In this regard, Examiner finds the additional steps set forth in Appellant's claims "of

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[3] We also agree with Examiner's finding that neither Appellant's Specification nor claims define the terms "comparing" and "determining," as set forth in Appellant's claims (Final Act. 3; *see also id.* at 4; *see, e.g.*, Br. 10 and 11–12). We, therefore, find no error in Examiner's interpretation of the comparing and determining steps of Appellant's claimed invention as encompassing the mental step of thinking about expression levels and risk, respectively (*id.* at 3–4; *see also id.* at 5 ("The recited steps may [] be performed mentally or verbally or in writing and do not require the transformation of a specific article" and "thereby encompass abstract processes")). *Cf. In re BRCA1- and BRCA2-Based Hereditary Cancer Test Patent Litigation*, 774 F.3d 755, 763 (Fed. Cir. 2014) (citation omitted) ("'comparing' and 'analyzing' two gene sequences" is "an abstract mental process"). In this regard, Examiner finds that "[m]ental activities, data analysis, and mathematical analysis are all considered to be abstract ideas" (Final Act. 4). *See Fair Warning Ip, LLC v. Iatric Systems, Inc.*, 839 F.3d 1089, 1093 (Fed. Cir. 2016) ("analyzing information by steps people go through in their minds, or by mathematical algorithms, without more," are "essentially mental processes within the abstract-idea category"); *Synopsys, Inc. v. Mentor Graphics Corp.*, 839 F.3d 1138, 1146 (Fed. Cir. 2016) ("Methods which can be performed entirely in the human mind are unpatentable . . . because [they] embody the 'basic tools of scientific and technological work' that are free to all men and reserved exclusively to none").

'obtaining' a lymphocyte sample, 'inducing' cell division, 'separating' the dividing lymphocytes into two pools, 'treating' one of the pools of lymphocytes with rapamycin, and 'assaying' the level of protein expression in the treated pool and the untreated pool," "when considered alone or in combination are conventional, well understood, and routinely practiced in the art for just about any protein one cares to detect" . . . and "do NOT add anything significant to the judicial exceptions" (Final Act. 6; *see id.* ("Nagy[4] . . . teaches obtaining a sample of lymphocytes from a[n] AD subject and from age matched healthy controls, treating the samples with rapamycin, and measuring protein expression (*see* [Nagy ¶¶] . . . 0011, 0018, 0019, 0025, and 0029)")). We agree.

Nagy qualifies as prior art on this record. Therefore, we are not persuaded by Appellant's intimation that Nagy, which is Appellant's own work, is not available as prior art on this record (*see* Br. 8). We are also not persuaded by Appellant's contention that because Nagy fails to teach determining increased risk of Alzheimer's disease progression or a method of mTOR signal monitoring, Examiner cannot rely upon Nagy to establish that elements of Appellant's claimed invention are conventional, well understood, and routine in this art (*see id.*; *cf.* Final Act. 6 (citing Nagy ¶¶ 0011, 0018, 0019, 0025, and 0029)). In addition, in response to Appellant's contentions regarding Nagy, Examiner provided additional evidence to support Examiner's finding of what was well known, conventional and routine in this art at the time of Appellant's claimed invention (*see* Ans. 9; *cf.* Br. 8 ("it cannot reasonably be maintained that a single prior art document, regardless of its date of publication, establishes, as

[4] Nagy, US 2004/0132113, published July 8, 2004.

a matter of fact, that the methodology described therein is conventional, well understood and routinely practiced in the art")). *See Berkheimer v. HP Inc.*, 881 F.3d 1360, 1369 (Fed. Cir. 2018) ("[w]hether something is well-understood, routine, and conventional to a skilled artisan at the time of the patent is a factual determination"). Appellant does not contest Examiner's supplemental evidence and findings. Arguments not made are waived.

For the foregoing reasons, we are not persuaded by Appellant's contention that Appellant's "claims [] include additional elements that are neither routine nor conventional but rather amount to significantly more than the alleged judicial exception" (Br. 7). Therefore, we agree with Examiner's finding that "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 patent-eligible" (Final Act. 6; *see also* Ans. 6 and 9).

In sum, when Appellant's claims are considered as a whole, we find no error in Examiner's finding that Appellant's claimed invention is directed to patent ineligible subject matter (*see, e.g.*, Final Act. 8).

## CONCLUSION

The evidence of record supports Examiner's finding that Appellant's claimed invention is directed to patent ineligible subject matter. The rejection of claims 2 and 27 under 35 U.S.C. § 101 is affirmed. Claims 4, 16–18, 20, 29, and 31 are not separately argued and fall with claims 2 and 27 respectively.

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

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE PATENT TRIAL AND APPEAL BOARD

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*Ex parte* ZSUZSANNA NAGY

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Appeal 2017-008793
Application 14/233,113
Technology Center 1600

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Before DONALD E. ADAMS, ULRIKE W. JENKS, and CHRISTOPHER G. PAULRAJ, *Administrative Patent Judges*.

PAULRAJ, *Administrative Patent Judge*, dissenting.

I respectfully dissent. I agree with the majority that, under *Alice* "step one," the claims on appeal are directed to a judicial exception (law of nature) insofar as they recite steps of "comparing" levels of certain interleukin proteins in different pools of lymphocytes and "determining," based on the comparative protein levels, whether there is either an increased risk of Alzheimer's disease progression (claim 2) or decreased mTOR signaling (claim 27). However, I disagree with the majority's conclusion that the Examiner has shown, under *Alice* "step two," that all the additional steps set forth in Appellant's claims were well-understood, routine, and conventional.

In particular, step (iii) of the claims includes the requirement of treating one pool of lymphocytes with the drug rapamycin. The Examiner acknowledges that this step does not recite or describe any recognized judicial exception (Ans. 6–7), and thus it must be shown to "involve well-understood, routine, conventional activity previously engaged in by

researchers in the field." *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 566 U.S. 66, 73 (2012). In *Mayo*, the Supreme Court noted that the claim step of "administering a [thiopurine] drug" to a patient did not transform the nature of the claims because it "simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs," where "doctors used thiopurine drugs to treat patients suffering from autoimmune disorders long before anyone asserted these claims." *Id.* at 78. The Examiner has not made a similar showing with respect to treating lymphocytes with rapamycin.

The Examiner relies upon prior art references Nagy (the only reference identified in the Final Rejection) and Zhou[1] (identified for the first time in the Examiner's Answer) to assert that treatment of lymphocytes with rapamycin was previously known in the art. Fin. Rej. 6; Ans. 9. Nagy is a publication of Applicant's own prior work, and describes the use of rapamycin as a cell division inhibitor in a diagnostic screen for Alzheimer's disease. *See, e.g.*, Nagy ¶¶ 94–96. Zhou likewise describes the use of rapamycin as a "$G_1$/S transition blocker" to treat lymphocytes derived from Alzheimer's disease patients. *See* Zhou, 321–22. But, other than in the context of the specific experiments and studies described therein, neither reference suggests that treatment of lymphocytes with rapamycin was a well-recognized technique used for the diagnosis of Alzheimer's disease or any other purpose. "Whether a particular technology is well-understood, routine, and conventional goes beyond what was simply known in the prior

[1] Zhou et al., P53-mediated G1/S checkpoint dysfunction in lymphocytes from Alzheimer's disease patients, Neuroscience Letters 468 (2010) 320–325.

art. The mere fact that something is disclosed in a piece of prior art, for example, does not mean it was well-understood, routine, and conventional." *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1369 (Fed. Cir. 2018). Accordingly, in my view, the Examiner's citations to Nagy and Zhou are insufficient to establish either that "the prior art demonstrated *numerous* references where scientists were treating lymphocytes with rapamycin and studying its effects on gene expression in the context of cancer, lupus, Alzheimer's disease, etc.," or that "the use of rapamycin in gene expression studies was *widely prevalent*." Ans. 9 (emphasis added).

I, therefore, conclude that the Examiner has not made a prima facie case of patent ineligibility.