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BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte JUERGEN SCHMITZ, ANDRZEJ DZIONEK, and DAVID WILLIAM BUCK[1]

Appeal 2017-010045
Application 13/454,008
Technology Center 3700

Before RICHARD M. LEBOVITZ, JEFFREY N. FREDMAN, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims to methods of detecting BDCA-2 protein in a biological sample and of ligating an antibody or binding fragment to the BDCA-2 protein. The Examiner rejected the claims under 35 U.S.C. § 112 for lack of enablement and as indefinite, and under 35 U.S.C. § 101 as directed to patent ineligible subject matter. Appellants appeal the Examiner's determination that the claims are unpatentable. We have jurisdiction under 35 U.S.C. § 6(b). The rejections are reversed.

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[1] The Appeal Brief ("Appeal Br.") (Jan. 6, 2014), page 2, lists Miltenyi Biotec as the real-party-in-interest.

STATEMENT OF THE CASE

Claims 2–7 and 9–20 stand finally rejected by the Examiner as unpatentable for the following reasons:

Claims 2–7 and 10–20 under 35 U.S.C. § 101 because the claimed invention is directed to non-statutory subject matter. Ans. 7.

Claims 4, 19 and 20 under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Ans. 2.

Claims 5, 7, and 11–20 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Ans. 3.

Claim 2, which is representative of the rejected claims, is reproduced below:

> 2. A method of detecting BDCA-2 protein in a biological sample, comprising:
>
> a) combining the sample with a monoclonal, synthetic, or recombinant antibody or antigen binding fragment under conditions where the antibody or fragment will bind to BDCA-2 protein in the sample to form a complex, and
>
> b) detecting complex formed in step (a);
>
> wherein said antibody or antigen-binding fragment comprises a polypeptide domain that specifically binds a BDCA-2 protein encoded by SEQ ID NO: 1;
>
> wherein the BDCA-2 protein is encoded by exons 1-6; exons 1 and 3-6; exons 1-2 and 4-6; or exons 1-3 and 5-6 of SEQ ID NO: 1.

REJECTION UNDER § 101

The Examiner found that claims 2–7 and 10–20 are unpatentable under 35 U.S.C. § 101 as ineligible subject matter for a patent because the claims rely on a law of nature in which an anti-BDCA-2 antibody binds to a BDCA-2 protein "and cause[s] the 'modulations' of dependent Claims 4, 5, and 7." Ans. 7. For this reason, the Examiner concluded that the claims "simply recite the observation of the natural relationship between an antibody binding to its ligand and the physiological processes therein induced." *Id.* The Examiner also found that the method steps of the claims "i.e., the detecting of antibody binding, add nothing significant beyond the sum of their parts taken separately." *Id.*

We do not agree with the Examiner's analysis and reverse the rejection.

Claim 2 comprises a step (a) of combining antibody or antigen binding fragment with a sample containing BDCA-2 protein under conditions where the antibody or fragment binds to the protein. The second step (b) is detecting the complex formed in step (a). According to the Specification, the BDCA-2 protein is novel and the antibodies and binding fragments were newly produced against the BDCA-2 protein. Application Specification ("Spec.") ¶ 88.

While we agree with the Examiner that the claim involves a natural phenomenon because the binding of an antibody or antigen binding fragment to a protein is based on natural interactions between both molecules, the analysis does not end there. As held in in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.,* 566 U.S. 66 (2012), the fact that a claim

invokes a natural phenomenon does not necessarily exclude it from being patentable subject matter. The *Mayo* Court held:

> The Court has recognized, however, that too broad an interpretation of this exclusionary principle could eviscerate patent law. For all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas.

Mayo, 566 U.S. at 78.

To determine whether an unpatentable law of nature has been transformed "into a patent-eligible application of such law," the Court further held that the claim as a whole must be examined to determine whether it "also contain[s] other elements or a combination of elements, sometimes referred to as an 'inventive concept,' sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the natural law itself." *Id.* at 72–73. The Court further added that the additional recitation of "well-understood, routine, conventional activity previously engaged in by researchers in the field" is not sufficient to transform an ineligible law of nature into eligible subject matter. *Id.*

In this case, we are not convinced that the detection of BDCA-2 is a natural law or a natural phenomenon because it has not been established that the antibody and antigen binding fragments utilized to detect it are naturally-occurring. Thus, the binding between BDCA-2 and the antibody or binding fragment are only a natural phenomenon to the extent that the underlying molecular interaction reflects a natural process. The process, itself, has not been demonstrated to be merely a natural law or detection of natural process, but rather involves the production of, on the record before us, a new

antibody or binding fragment. Spec. ¶ 88. Consistently, the Examiner did not cite prior art against the claim.

In addition to this, even if the binding step of the claimed process is itself a natural law and ineligible for a patent, the additional element of the claim in which an antibody or binding fragment binds to the BRCA-2 protein enabling its detection is an "inventive concept" because the recited antibody and binding fragment are new and therefore do not constitute routine and conventional activity engaged in by researchers in the field. *Mayo*, 566 U.S. 72–73. Consequently, the claim is eligible for a patent under the guidance set forth in *Mayo*.

Our analysis is consistent the "Subject Matter Eligibility Examples: Life Sciences" issued by the USPTO on May 2016.[2] Example 29 in the Eligibility Examples is of a method claim of detecting a protein in a sample comprising a step in which the sample is contacted with an antibody and the binding between the protein and antibody is detected. Eligibility Examples 10. The eligibility guidance characterized the claim as eligible for a patent because the process is not directed to a judicial exception. *Id.* at 11.

With regard to claims 4 and 5, the Examiner stated that the claims are ineligible for a patent because they "simply recite the observation of the natural relationship between an antibody binding to its ligand and the physiological processes therein induced." Ans. 7.

In claims 4 and 5, the step of detecting comprises detecting a response of a cell to the antibody or fragment binding. While the observed response is a physiological and natural phenomenon, it is elicited by the new antibody

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[2] https://www.uspto.gov/sites/default/files/documents/ieg-may-2016-ex.pdf

and binding fragment and therefore the process as a whole is not routine and conventional. The claim as a whole must be examined for eligibility, not the individual steps which comprise it. *Mayo*, 566 U.S. at 79, 78.

Claim 6, and dependent claim 7, also involve binding of the new antibody and binding fragment to BDCA-2 and thus the same analysis for claim 2 applies.

For the foregoing reasons, the rejection of claims 2–7 and 10–20 as ineligible for a patent under 35 U.S.C. § 101 is reversed.

REJECTION UNDER § 112, FIRST PARAGRAPH

The Examiner rejected claims 5, 7, and 11–20 for lack of enablement. The Examiner stated that the claimed method "is clearly nonsensical as the same binding of an anti-BDCA-2 antibody to BDCA-2 is claimed to have several *opposite* effects, e.g., *both* the induction *and* down[-]regulation of *both* CD4+ *and* CD8+ responses, polarization towards *both* a Th1 *and* Th2 response, etc." Ans. 5. We do not agree with the Examiner's reasoning.

Claims 5 and 7 recite the following responses to antibody or fragment binding to BDCA-2 (numbering added in brackets for reference):

[1] down-regulation of type I interferon production,

[2] down-regulation of Th1 immune responses,

[3] induction of intracellular Ca^{++} mobilization, and/or

[4] polarization of an immune response to Th2.

The Specification explains that the binding of BDCA-2 with an anti-BDCA-2 antibody [3] induces intracellular Ca^{++} mobilization. Spec. ¶ 245. The mobilization of intracellular calcium, in turn, leads to physiological

responses, such as [1] the inhibition of secretion of a type I interferon (*id.* at ¶ 284).

The Specification also discloses:

> As type I interferon can induce Th1 type immune responses in humans (Parronchi et al. (1996) Eur. J. Immunol. 26:697–703), triggering of BDCA-2 polarizes CD4+ T cell responses towards Th2 cell development, whereas inhibition of BDCA-2 signaling polarizes CD4+ T cell responses towards Th1 cell development.

Id. at ¶ 246

Thus, triggering BDCA-2 with antibody binding [1] reduces interferon production ("down-regulation") and [2] down regulates the Th1 response, i.e., since interferon is reduced by the antibody binding, the Th1 response is reduced and down-regulated in comparison with the same conditions in the absence of the antibody. The immune response is therefore [4] polarized to Th2 (in a negative fashion). *Id.*

In sum, the functional consequences of antibody binding to BDCA-1 are not opposite or nonsensical, but rather emanate from the ability of the antibody to regulate the intracellular calcium pools and other responses of the cell triggered by the antibody or binding fragment's ability to activate BRCA-2.

To the extent that there are apparently "opposite" effects induced by bonding to BDCA-2, such effects would depend on whether the antibody or binding fragment is activating BDCA-2 or inhibiting its normal activation. Appeal Br. 6–7; Spec. ¶¶ 245, 246.

Because the Examiner did not establish that the claims were not enabled by the Specification, the enablement rejection of claims 5, 7, and 11–20 is reversed.

REJECTION UNDER § 112, 2ND PARAGRAPH

The Examiner found that recitation of "modulation of B cell responses and/or NK responses" in claims 4, 19, and 20 is indefinite because "the word has no real definition in the context in which it is being used in this line of the claim." Ans. 3. The Examiner further states that it is "unclear whether the word encompasses on/off, up/down, slower/faster, and/or induction/inhibition, etc. of said responses" and that "Clearly the claimed method could not accomplish all." *Id.*

The Examiner did not establish that the claim term is indefinite. First, claim 4 does not refer to modulating B or NK cell responses, but rather refers to modulating a dendritic cell. Second, it is clear from the Specification that "functional modulation" of a cell refers to changing, altering, enhancing, etc., a function of the cell by causing the antibody to bind to the BDCA-2 protein on the cell on the cell and elicit a response. *See* Spec. ¶¶ 40, 42, 46, 225. "[B]readth is not to be equated with indefiniteness." *In re Miller*, 441 F.2d 689, 693 (CCPA 1971). Thus, we do not agree with the Examiner that "modulation" has "no real definition in the context" of the claim. In addition to this, as indicated by Appellants, the term "modulation" is regularly used in the scientific literature. Appeal Br. 9.

With regard to the statement that claimed method could not accomplish an up and down, on and off, etc., modulation, as discussed in the rejection under § 112, first paragraph, the Specification discloses that antibody and binding fragment can cause different responses depending on whether BDCA2 signaling is activated (triggered) or inactivated (inhibited).

Spec. ¶¶ 245, 246. Thus, we are not persuaded, that the claims are indefinite. The rejection of claims 4, 19 and 20 is reversed.

REVERSED