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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte S. ANANTH KARUMANCHI, VIKAS P. SUKHATME, MOURAD TOPORSIAN, and MICHELLE V. LETARTE[1]

Appeal 2015-000426
Application 12/227,658
Technology Center 1600

Before DEMETRA J. MILLS, JEFFREY N. FREDMAN, and RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of diagnosing pre-term pre-eclampsia or a predisposition to pre-term pre-eclampsia and treating the patient based on the diagnosis, which have been rejected as directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

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[1] Appellants identify the Real Party in Interest as Beth Israel Deaconess Medical Center, Inc. and The Hospital for Sick Children. (Br. 2.)

STATEMENT OF THE CASE

"Pre-eclampsia is a syndrome of hypertension, edema, and proteinuria." (Spec 1:10.) While there are no known cures for pre-eclampsia, there are treatments available, which vary depending on the severity of the syndrome, and include bed rest, and/or taking blood pressure medication or anticonvulsant medication. (Spec 1:19–24.)

"The symptoms of pre-eclampsia typically appear after the 20th week of pregnancy and are usually detected by routine measuring of the [pregnant] woman's blood pressure and urine." (Spec. 1:13–14.) "Several [growth] factors have been reported to have an association with. . . pre-eclampsia[, including] vascular endothelial growth factor (VEGF), soluble Flt-1[, fms-like tyrosine kinase,] receptor (sFlt-1), and placental growth factor (PIGF)." (Spec. 2:11–15.) Appellants' Specification notes that prior art monitoring methods for pre-eclampsia are ineffective for diagnosis of the syndrome at an early stage. (Spec. 1:15–16.) Appellants' claims are directed to a method for diagnosing pre-eclampsia or a propensity to develop the syndrome that relies on measuring sFlt-1 and soluble endoglin, a cell membrane glycoprotein, "shown to be a regulatory component of the TGF-β receptor complex, which modulates angiogenesis, proliferation, differentiation, and apoptosis." (Spec. 1:25–32, 9:5–11.)

Appellants "discovered that levels of soluble endoglin (sEng) are markedly elevated in placental tissue samples from pregnant women suffering from pregnancy complications associated with hypertension, including preeclampsia." (Spec. 3:10–13.) Flt-1 "is highly expressed by trophoblast cells which contribute to placental formation." (Spec. 2:20–21.)

Soluble Flt-1, ("sFlt-1"), lacking the transmembrane and cytoplasmic domains of the receptor, "was recently identified in a cultured medium of human umbilical vein endothelial cells and in vivo expression was subsequently demonstrated in placental tissue." (Spec. 2:27–29.)

Claims 58–66, 69–78, 80, 81, and 88–95 are on appeal. Claim 58 is representative and read as follows:

> 58. A method of diagnosing a subject as having, or having a predisposition to, preterm pre-eclampsia, said method comprising measuring the level of a soluble endoglin polypeptide and an sFlt-1 polypeptide from said subject and calculating the relationship between said levels of soluble endoglin and sFlt-1 using a [soluble endoglin x sFlt-1] metric, wherein an increase in the metric value in the subject sample relative to the metric value in a normal reference sample, is a diagnostic indicator of, or a propensity to develop, pre-term pre-eclampsia in said subject, and based on said diagnosis, treating said subject for said pre-eclampsia.

(Appeal Br. 9.)

The single ground of rejection by the Examiner that is before us on review is:

Claims 58–66, 69–78, 80, 81, and 88–95 under 35 U.S.C. § 101 as directed to non-statutory subject matter.

DISCUSSION

The Examiner finds that the method recited in claim 58 is "drawn to a mathematical relationship between polypeptide levels in a patient sample and the presence of a particular disorder[, which] . . . is a law of nature." (Final Action 6.) In particular, the Examiner finds that claim 58 is "directed to a method of diagnosing a pregnancy related hypertensive disorder in a

patient by measuring the concentration of markers present in a patient sample, calculating a value based upon a relationship between the measured values, and comparing the calculated patient's value with a value obtained using samples from a normal reference sample." (Final Action 6.) The markers "are soluble endoglin and soluble Flt-1." (*Id.*) The Examiner finds that these "markers . . . were known in the prior art and were even known to be important for the prediction of pregnancy induced hypertensive disorders, such as preeclampsia, as evidenced by US 2006/0067937 A1 (of record)." (Final Action 6.)

The Examiner further finds that the claimed measurement and treating steps are well-understood and/or conventional and routine. (Final Action 6–8.) Regarding the measurement step, the Examiner points to the statement on page 43 of the Specification that:

> Standard methods may be used to measure levels of soluble endoglin, free VEGF, free PIGF, sFlt-1, TGF-131, TGF-133, PGl2, or eNOS polypeptide in any bodily fluid, including, but not limited to, urine, serum, plasma, saliva, amniotic fluid, or cerebrospinal) fluid. Such methods include immunoassay, ELISA, western blotting using antibodies, [etc. . .].

(Final Action 6.) Regarding the "treating" step, the Examiner finds not only is the step "specified at a high level of generality as it encompasses any and all possible treatments" for pre-eclampsia, but that treating "after making a diagnosis. . . is obvious and routine in the medical arts." (Final Action 8.) In light of the foregoing, the Examiner concludes that "no matter how important, unexpected or useful" the discovery that "increased levels of sFlt-1 and soluble endoglin are correlated with increased risks for preeclampsia and other pregnancy-related hypertensive disorders" or the determination of

"the mathematical equation by which they can be combined to achieve a diagnosis of increased accuracy as compared to the prior art," the additional measurement and treating steps beyond the mathematical relationship recited in the claims do not transform the law of nature recited by the claim "into a patent-eligible *application* of such a law." (Final Action 7–8.)

We agree with the Examiner's conclusion that representative claim 58 is directed to non-statutory subject matter consistent with controlling caselaw. Appellants do not dispute that this claim is directed to a law of nature, but that the treatment step is "a specific, meaningful additional step that goes well beyond the correlation itself and is not simply an 'apply it' statement appended to the recitation of a law of nature as construed by the courts in *Mayo* [*Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294 (2012)]." (Br. 6.) We disagree; we conclude that, as in *Mayo*, there is "nothing significantly more [recited in claim 58] than an instruction to doctors to apply the applicable law[] when treating their patient[]." *Mayo*, 132 S. Ct. 1298.

As the Examiner noted, claim 58 does not "specify any particular type of treatment, such as use drug A rather than drug B." (Ans. 4.) Moreover, as the Examiner also noted, there is nothing in the general statement to treat after the diagnosis is made that could be deemed an unconventional step. (Final Action 8 ("treating a patient for a diseases after making a diagnosis of the same disease in the same patient is obvious and routine in the medical arts;" Ans. 6 (noting the claims do not recite the use of any novel product in the claimed "treatment" step).) As the Examiner

noted, claim 58 "preempt[s] all practical uses of the natural law/phenomenon/correlation." (Ans. 4.)

We disagree with Appellants that claim 58 "closely aligns to the facts of Example F" of the "2014 Guidance for Determining Subject Matter Eligibility of Claims Reciting or Involving Laws of Nature, Natural Phenomena, & Natural Products" such that the claimed treatment step should be deemed "a practical application of the natural principle" (Br. 7). We agree with the Examiner that, important to the analysis of patent eligibility in Example F, was the fact that the claim made use of a novel product. (Ans. 6.) No such limitation is provided in the treatment step of claim 58, or any other step for that matter.

Furthermore, we disagree with Appellants "that treatment based on the level of soluble endoglin and sFlt-1 together is a specific application of natural principles" that is not conventional (Br. 6). Appellants do not dispute that the prior art publication US2006/0067397 A1 "teaches methods for diagnosing pregnancy related hypertensive disorder or a predisposition to a pregnancy related hypertensive disorder, such as preeclampsia, by measuring soluble endoglin (sEng) in combination with other markers including soluble Flt-1 (sFlt-1), calculating a diagnostic index which adds sFlt-1 and sEng concentration values, and methods of treating women so diagnosed." (Ans. 3.) Thus, we agree with the Examiner that the only "unconventional" element of claim 58 is the recited mathematical equation correlating gathered data of soluble endoglin and sFlt-1 (Ans. 5), and not the ability to diagnose prior to "visible symptoms such as high blood pressure, high levels of protein in the urine, and bodily swelling[] in the late stages of

pregnancy" based on the level of soluble endoglin and sFlt-1 together, as asserted by Appellants (Br. 6).

Thus, we agree with the Examiner that neither the measuring steps, nor the treatment step are sufficient alone or in an ordered combination with the correlation to transform the unpatentable natural correlation claimed into patentable applications of it. (Final Action 6–7; Ans. 3–4.)

For the reasons discussed, Appellants do not persuade us that the Examiner erred in rejecting claims 58 as directed to non-statutory subject matter. Claims 59–66, 69–78, 80, 81, and 88–95 have not been argued separately and therefore fall with claim 58. 37 C.F.R. § 41.37(c)(1)(iv).

SUMMARY

We affirm the rejection of Claims 58–66, 69–78, 80, 81, and 88–95 under 35 U.S.C. § 101 as directed to non-statutory subject matter.

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