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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte PASCALE PAUL, SOPHIE CAILLAT ZUCMAN, and GERALDINE PORCU[1]

Appeal 2014-003571
Application 12/521,793
Technology Center 1600

Before DONALD E. ADAMS, TAWEN CHANG, 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 methods of determining IVF outcome, which have been rejected as directed to non-statutory subject matter. We have jurisdiction under 35 U.S.C. § 6(b).

We affirm.

STATEMENT OF THE CASE

"Diagnosis and management of infertility is a prevalent health concern in young adults." (Spec. 1.) One option for infertile couples is *in vitro* fertilization, but it is associated with clinical complications. (*Id.*) "Prediction of the chances for infertile women to give birth to a viable baby

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[1] Appellants identify the Real Party in Interest as Reprosource Inc. (Br. 1.)

after IVF treatment is . . . a major issue in the optimisation of the medical response to increasing demands of infertile couples." (*Id.*) According to the Specification, the "search for biomarkers that may predict pregnancy issues after IVF, before initiation of treatment, remains a major challenge." (*Id.*) Further according to the Specification, Appellants' invention "provides for the first time a biomarker allowing the non-invasive evaluation and prediction of IVF outcome." (Spec. 2.)

Claims 36, 39–41, 43, 46–48, 50–53, 57, and 64–67 are on appeal. Claims 36, 43, 57, 64, and 66 are representative and read as follows:

> 36. A method for determining *in vitro* fertilization (IVF) outcome comprising:
>
> *in vitro* assaying for the level of soluble MHC class I chain-related protein A (MICA) in a serum, plasma, or blood sample from a subject;
>
> comparing said level to a control;
>
> predicting IVF outcome from said step of comparing, the increased level of MICA relative to said matched control being indicative of poor IVF outcome, increased implantation failure rates, increased likelihood of IVF failure, and/or increased likelihood of miscarriage; and
>
> administering hormonal conditioning treatment to said subject based on said step of predicting.
>
> 43. A method for selecting a subject for IVF comprising:
>
> *in vitro* assaying for soluble MICA protein in a serum, plasma, or blood sample;
>
> selecting the subject for IVF having a level of MICA indicative of a successful IVF probability, said level corresponding to a level of soluble MICA protein in a matched sample from a fertile control subject; and
>
> transferring an embryo to said subject.
>
> 57. A method for determining the probability of pregnancy complications in a subject comprising:

in vitro assaying for soluble MICA protein in a serum, plasma, or blood sample from a subject;

comparing said level to a control;

predicting a pregnancy complication from said step of comparing, wherein an increased level of MICA relative to a matched control is indicative of an increased probability of pregnancy complications in the subject, wherein the pregnancy complications are miscarriage, vascular pregnancy diseases (VPD), preeclampsia (PE), severe preeclampsia, vascular intrauterine growth retardation (IUGR), associated or not with preeclampsia, HELLP syndrome, gravidic steatosis, gravidic nephropathy or intra-uterine foetal death (IUFD), pregnancy diseases, or infertility associated with auto immune pathologies; and

administering treatment of one or more pregnancy complications to said subject based on said step of predicting.

64. A method for preparing to administer *in vitro* fertilization (IVF) comprising:

in vitro assaying for the level of soluble MHC class I chain-related protein A (MICA) in a serum, plasma, or blood sample from a subject;

comparing said level to a matched control;

predicting a reduced likelihood of successful IVF outcome from said step of comparing due to an increased level of MICA relative to said matched control suggesting an increased likelihood of poor IVF outcome, increased implantation failure rates, increased likelihood of IVF failure, and/or increased likelihood of miscarriage; and

administering hormonal conditioning treatment to said subject based on said step of predicting.

66. A method for *in vitro* fertilization comprising:

in vitro assaying for the level of soluble MHC class I chain-related protein A (MICA) in a serum, plasma, or blood sample from a subject;

comparing said level to a matched control;

predicting a reduced likelihood of success of *in vitro* fertilization from said step of comparing due to an increased level of MICA relative to said matched control suggesting

> greater risk of poor IVF outcome, implantation failure rates, IVF failure, and/or miscarriage; and
>
> administering *in vitro* fertilization to said subject based on said step of predicting.

(Br. 12–16.)[2, 3] The single ground of rejection by the Examiner that is before us on review is:

Claims 36, 39–41, 43, 46–48, 50–53, 57, and 64–67 are rejected under 35 U.S.C. § 101 as directed to non-statutory subject matter.

DISCUSSION

The Examiner finds that "it is not in dispute that Appellant[s] ha[ve] discovered a correlation between increased levels of sMICA [i.e., soluble MHC class I chain-related protein A,] and a reduced likelihood of a woman delivering a viable baby." (Ans. 6.) The Examiner notes that "the specification teaches that soluble MICA levels in the serum greater than 2.45 ng/ml is indicative of higher implantation failure rates and greater than 3.2 ng/ml prior to IVF cycles predicted a higher chance of miscarriage." (Ans. 3.) The Examiner explains that, despite Appellants discovery, "the claims recite a naturally existing relationship between the increased level of soluble MICA in the serum, plasma or blood and the increased likelihood of

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[2] In their Response to the Restriction/Election Requirement filed October 10, 2011, Appellants elected miscarriage as the pregnancy complication. (Ans. 22.) Pending claims 54–56 and 60–63 stand withdrawn from consideration as drawn to a non-elected invention. (Ans. 2.)

[3] We recognize Appellants' January 29, 2014 Reply Brief, which addresses an obviousness rejection of subject matter relating to "a silicon based electrode in an electrochemical device." (*See* Reply Br. 1–3.) Neither an obviousness rejection nor subject matter relating to a silicon based electrode in an electrochemical device is before this panel. Therefore, we will not further discuss Appellants' Reply Brief.

IVF failure" and only add "well-understood, routine, conventional activity already engaged in by the scientific community [in the art of assisted reproduction technology]." (Ans. 3–4.) The Examiner concludes, therefore, that the claims do not include steps that are applications of a natural law that represent patentable subject matter. (Ans. 6.) In particular, citing prior art, the Examiner finds that "in vitro assay methods for measuring soluble MICA [such as by Enzyme-Linked Immunosorbent Assay] are well known in the art," in addition to being a step that "merely informs a relevant audience about a certain relationship that exists in nature." (Ans. 4.) As to the additional steps of "administering hormonal conditioning treatment" (claims 36 and 64), "transferring an embryo" (claim 43), or "administering treatment of one or more pregnancy complications" (claim 57), the Examiner notes that the art of record provides evidence that these are routine in the art of *in vitro* fertilization (Ans. 4, 9 (noting the generalized "hormonal conditioning treatment" includes that which has been accomplished in the prior art routine ovarian stimulation protocol), 18–20 (noting that embryo transfer was routine in the field of assisted reproduction), 23 (noting that the generalized "treatment" step includes that which has been accomplished in the prior art as "treatment or care provided to patients who have undergone or who are about to undergo a miscarriage"). As to claim 66, which requires administering *in vitro* fertilization based on data gathering and a thought process (making a prediction based on the comparison to measured levels of sMICA and a matched control), the Examiner finds that the claim is simply "the use of [the] correlation [between sMICA and IVF outcome] to [determine whether to] undertake IVF treatment . . . , [and the] steps involved in IVF consist of well understood, routine, conventional activity

already engaged in by the scientific community." (Ans. 27–31.) The Examiner concludes that the pending claims all "recite[] a law of nature or natural correlation, with additional steps that involve well-understood, routine and conventional activity previously engaged in by researchers in the field [and are] not patent-eligible." (Ans. 5, 14, 28, 33–34.)

We agree with the Examiner's conclusion that representative claims 36, 43, 57, 64, and 66 are directed to non-statutory subject matter consistent with controlling caselaw. We "note that the Supreme Court instructs that '[g]roundbreaking, innovative, or even brilliant discovery does not by itself satisfy the § 101 inquiry.'" *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, 788 F.3d 1371, 1379 (Fed. Cir. 2015) (quoting *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 133 S. Ct. 2107, 2117 (2013)). Thus, whether or not "[t]he specification represents the first disclosure of a relationship between the levels of sMICA in the blood, plasma, or serum and the outcome or establishment of pregnancy" (Br. 4), is not determinative of whether the representative claims are patent eligible.

The framework for distinguishing patents that claim laws of nature or natural phenomena from those that claim patent eligible applications of those concepts involves the following two steps:

1. determine whether the claims at issue are directed to a patent ineligible concept
2. if they are, 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, i.e., search for 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 1375–76 (Fed. Cir. 2015) (quoting *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289, 1294, 1298 (2012)).

Appellants do not dispute that the representative claims depend upon a natural law or phenomena. (Br. 4 ("increased levels of sMICA correlate to a reduced likelihood of a woman delivering a viable baby"). And we agree with the Examiner's assessment that "[i]n the instant case, the claims recite a naturally existing relationship between the increased level of soluble MICA in the serum, plasma or blood and the increased likelihood of IVF failure." (Ans. 3.) Thus, we move to the second step.

Appellants contend that "[t]he present claims recite specific, narrow, and unconventional applications that involve steps such as administering hormonal conditioning treatment, transferring an embryo, administering *in vitro* fertilization, or treating a pregnancy complication . . . [which] represent concrete applications of any natural law falling under the claims and make all claims patent eligible under 35 U.S.C. § 101." (Br. 4.) We disagree that the recited steps transform the claims into patent eligible subject matter.

The representative patent claims 36, 43, 57, 64, and 66 focus on a newly discovered fact about human biology (sMICA levels and the relationship to *in vitro* fertilization outcome), involve no creation or alteration of natural products, and do not purport to identify novel detection techniques. And, as explained by the Examiner, these claims do not involve novel treatment steps or *in vitro* fertilization steps. (Ans. 4, 9 (noting the generalized "hormonal conditioning treatment" includes that which has been accomplished in the prior art routine ovarian stimulation protocol), 18–20

(noting that embryo transfer was routine in the field of assisted reproduction), 23 (noting that the generalized "treatment" step includes that which has been accomplished in the prior art as "treatment or care provided to patients who have undergone or who are about to undergo a miscarriage"), 30–31 (noting that *in vitro* assaying and administering IVF was known in the art and citing prior art to show same). Indeed, Appellants do not dispute that the additional steps of "administering hormonal conditioning treatment" (claims 36 and 64), "transferring an embryo" (claim 43), "administering treatment of one or more pregnancy complications" (claim 57), or administering IVF (claim 66) were conventional and routine in assisted reproductive technology and IVF at the time the claimed inventions were made.

Appellants' argument that the field of invention is sMICA and the specific treatments administered by the claims are unconventional in that field is unpersuasive. (Br. 3–4, 6, 8, 9.) As the Examiner correctly found, "[t]he field of the invention is not limited to the 'sMICA art' (studies involving MHC class I chain-related protein A) . . . [but rather fall] more broadly within the field of assisted reproduction technology and *in vitro* fertilization." (Ans. 13.) In particular, as the Examiner noted, "instant claims 36 and 64 are drawn to methods for determining IVF outcome and preparing to administer IVF respectively" (Ans. 14); claim 43 involves the routine act of embryo transfer that was routinely carried out "in the art of assisted reproduction at the time of the invention" (Ans. 18–19); under the "broadest reasonable interpretation of [claim 57] when read in light of the specification and from the view of one of ordinary skill in the art, [that claim] would encompass any routine treatment or care provided to patients

[undergoing IVF] who have undergone or who are about to undergo a miscarriage" (Ans. 24–25); and claim 66 recites "administering IVF to a subject based on the prediction [of the likelihood of establishing pregnancy based on the step of comparing sMICA levels to a matched control]" (Ans. 26).

As was the case in *Mayo* and *Ariosa*, the method claims at issue here amount to "nothing significantly more than an instruction to doctors to apply the applicable laws when treating their patients" using "conventional steps, specified at a high level of generality." *Mayo*, 132 S. Ct. at 1298, 1300; *Ariosa*, 788 F.3d at 1377–78. Such claims are patent ineligible. *Mayo*, 132 S. Ct. at 1300; *Ariosa*, 788 F.3d at 1378.

Appellants argue that the varied methods recited indicate that none individually preempts all uses of the natural phenomena, thus avoiding the "primary concern of the Supreme Court in *Mayo*." (Br. 10.) This argument also does not persuade us that the representative claims are patent eligible. "While preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." *Ariosa*, 788 F.3d at 1379. "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." *Id.*

For the reasons discussed, Appellants do not persuade us that the Examiner erred in rejecting claims 36, 43, 57, 64, and 66 as directed to non-statutory subject matter. Claims 39–41, 46–48, 50–53, 65, and 67 have not been argued separately and therefore fall with claims 36, 43, 57, 64, and 66. 37 C.F.R. § 41.37(c)(1)(iv).

SUMMARY

We affirm the rejection of claims 36, 39–41, 43, 46–48, 50–53, 57, and 64–67 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