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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte RONALD ALFRED LASKEY[1]

Appeal 2017-010120
Application 14/489,207
Technology Center 1600

Before DONALD E. ADAMS, RYAN H. FLAX, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

FLAX, *Administrative Patent Judge*.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134(a) involving claims directed to a diagnostic or prognostic assay for the detection of prostate cancer cells in a urine sample. Claims 1–5, 7–10, 13, 14, and 17–21 are on appeal as rejected under 35 U.S.C. § 101. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

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[1] Appellant identifies the Real Party in Interest as "Cytosystems Limited." Br. 1.

STATEMENT OF THE CASE

Claims 1 is representative and is reproduced below:

> 1. A diagnostic or prognostic assay for the detection of prostate cancer cells in a urine sample, the assay comprising the steps of:
>
> i) obtaining an isolated cell sample from said urine sample and contacting the isolated cell sample with a binding agent that specifically binds a minichromosome maintenance (MCM) polypeptide;
>
> ii) contacting the isolated cell sample with a further binding agent that specifically binds an androgen receptor polypeptide [AR];
>
> iii) contacting the isolated cell sample with a still further binding agent that specifically binds prostate specific antigen [PSA];
>
> iv) detecting the binding of two or more of the binding agents having different specificities; and
>
> v) determining the number of cells in said isolated cell sample that positively bind the two or more binding agents, wherein the number of positive cells is an indicator of the presence of prostate cancer cells in the urine sample;
>
> wherein the binding agents are antibodies.

Supp. Br. 3 (Claims Appendix). Claim 14, the other independent claim, is similar, but differs in requiring detecting PSA in serum. *Id.* at 4–5.

The following rejections are appealed:

Claims 1–5, 7–10, 13, 14, and 17–21 stand rejected under 35 U.S.C. § 101 as directed to patent-ineligible subject matter. Final Action 2.

DISCUSSION

"[T]he examiner bears the initial burden, on review of the prior art ***or on any other ground***, of presenting a *prima facie* case of unpatentability. If

that burden is met, the burden of coming forward with evidence or argument shifts to the applicant." *In re Oetiker*, 977 F.2d 1443, 1445 (Fed. Cir. 1992) (emphasis added).

"Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Mayo Collaborative Servs. v. Prometheus Labs, Inc.*, 566 U.S. 66, 71 (2012) (quoting *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972)). Claims directed to *nothing more* than abstract ideas (such as mathematical algorithms), natural phenomena, and laws of nature are not eligible for patent protection. *Diamond v. Diehr*, 450 U.S. 175, 185 (1981); *accord* MPEP § 2106 (II) (discussing *Diehr*); *see also Parker v. Flook*, 437 U.S. 584, 592–94 (1978) (if, once the mathematical algorithm is removed from consideration, nothing patentable remains, the claims are not patent-eligible).

In analyzing patent-eligibility questions under 35 U.S.C. § 101, the Supreme Court instructs us to "first determine whether the claims at issue are directed to a patent-ineligible concept." *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014). If the claims are so-directed, we then move to a second step and "consider the elements of each claim both individually and 'as an ordered combination' to determine whether the additional elements 'transform the nature of the claim' into a patent-eligible application." *Id.* (quoting *Mayo*, 566 U.S. at 78–79).

Here, under *Alice's* step one, the Examiner determined, "[c]laim(s) 1-5, 7-10, 13, 14 and 17-21 is/are directed to the natural phenomena of expression of MCM, AR, and PSA expression [sic] in prostate cancer cells

in urine or serum." Final Action 2. Under *Alice's* step two, the Examiner determined that "[t]he claim(s) does/do not include additional elements that are sufficient to amount to significantly more than the judicial exceptions because beyond the judicial exception the claimed method steps recite routine steps of detecting MCM, AR, and/or PSA, e.g. antibody binding, which does not amount to significantly more than the judicial exception," noting specifically:

> Given that the claims 1-5, 7-10, 13, 14 and 17-21 simply describe and correlate natural processes, i.e. the MCM, AR, and PSA expression and cell number in urine or serum and their correlation with prostate cancer cells by routine methods known in the art. See teachings of Watkins et al. (Amer. Assoc. Cancer Res. 96th Annual Meeting April 16-20, 2005, Abstract# 3163, IDS) "Watkins[,"] US Pat No. 7,459,157 (Laskey et al. Dec. 2, 2009, IDS), "Laskey", US 2005/0079576 (French et al. Apr. 14, 2005, IDS), "French", Diallo et al. (Investigative Urology Feb. 2008, 101:1302-1309, IDS), "Diallo", and US Pat. No. 6,566,130 (Srivastava et al. May 20, 2003, IDS), "Srivastava" of record, the claimed invention is not directed to patent eligible subject matter.

Id. at 3; *see also* Answer 11–16.

Appellant argues that "the methods taken as a whole employ a non-routine (even taught away) series of narrowly focused steps." Br. 3, 6–7.

It is without question that "[t]he line between a patentable 'process' and an unpatentable 'principle' is not always clear." *Flook*, 437 U.S. at 589; *see also Synopsys, Inc. v. Mentor Graphics Corp.*, 839 F.3d 1138, 1150 (Fed. Cir. 2016) ("defining the precise abstract idea of patent claims in many cases is far from a 'straightforward' exercise") (quoting *DDR Holdings, LLC v. Hotels.com, L.P.*, 773 F.3d 1245, 1257 (Fed. Cir. 2014)). Here, a reasonable case could be made that the Examiner's determination under

Alice's step one is without error on the basis that the claims are directed to a natural correlation between the body's expression of certain proteins' and the existence of prostate cancer. *See, e.g.*, *Mayo*, 566 U.S. 66; *Genetic Technologies, Ltd. v. Merial L.L.C.*, 818 F.3d 1369 (Fed. Cir. 2016); *Ariosa Diagnostics, Inc. v. Seqenom, Inc.*, 788 F.3d 1371 (Fed. Cir. 2015); and *In re. BRCA1- and BRCA2-based Hereditary Cancer Test Patent Litigations*, 744 F.3d 755 (Fed. Cir. 2014). As noted by the Supreme Court, however, "all inventions at some level embody, use, reflect, rest upon, or apply laws of nature, natural phenomena, or abstract ideas" and "a process is not unpatentable simply because it contains a law of nature or a mathematical algorithm." *Mayo*, 566 U.S. at 71 (quoting *Diehr*, 450 U.S. at 187).

Even if the claims on appeal are "directed to" a natural phenomenon under the first step of the *Alice* framework as determined by the Examiner, we conclude that the Examiner has not established that the additional elements recited in the claims, considered individually and as an ordered combination, were well-understood, routine, and conventional as required under the second step of *Alice*. Regarding a determination that, e.g., non-natural-phenomenon, claim elements are merely routine and conventional, the Federal Circuit has explained that

> Whether something is well-understood, routine, and conventional to a skilled artisan at the time of the patent is a factual determination. Whether a particular technology is well-understood, routine, and conventional goes beyond what was simply known in the prior 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).

Here, after we strip away the Examiner-identified natural phenomenon (expression of MCM, AR, and PSA in prostate cancer cells in urine or serum), we are left with the claims' required coordinated steps of isolating cells from a urine (or serum) sample, performing a multi-marker immunoassay for MCM, AR, and PSA (or a 3-step assay therefor), and determining the number of cells binding at least two of the antibody agents for the MCM, AR, and PSA to then, thereby, determine the presence of prostate cancer. The Examiner concluded that the prior art references — Watkins, Laskey, French, Diallo, and Srivastava — evidenced that such additional steps beyond the natural correlation of such proteins to prostate cancer was no more than routine (and conventional). Final Action 3–11.

Although we agree with the Examiner that these cited prior art references may disclose using detected MCM, AR, and/or PSA to diagnose cancer, even based on urine samples in some instances, and sometimes using antibodies, we conclude that these references do not indicate that the claimed individual steps, much less the ordered combination thereof, were necessarily *routine* in the art. To the contrary, the references describe the relevant techniques individually as inventive or experimental.

For example, we note Watkins is directed to *an investigation of* "MCMs (Mini-chromosomal maintenance proteins), as alternative markers of prostate disease," because, Watkins notes, "[c]urrent diagnosis [using] Prostate Specific Antigen (PSA) and digital rectal examination," i.e., the conventional and routine ways of diagnosing prostate cancer, was questionable with respect to sensitivity and specificity because "PSA is not

prostate specific." Watkins 1. Thus, Watkins is not evidence that the claimed ordered combination of steps was routine or conventional.

Laskey is directed to *an invention* where target polypeptides, including MCM, are detected in cells spun from urine to detect cancer using immunoassay. Laskey Abstract, 5:27–50. Regarding immunoassay cancer screening prior to its invention, Laskey indicates that such techniques had been attempted, but only with limited success. *Id.* at 4:53–56. As with Watkins, this does not indicate that the claimed ordered combination of steps was routine or conventional.

French discloses that prior to *its invention*, which was directed to a DNA sequence coding for a protein similar to AR, studies *suggested* a positive correlation *may* exist between AR in cancer cells and the cancer's growth. French ¶ 5. French indicated that assays for AR were based on tritium-labeled androgen, which binds to AR (not immunoassays). *Id.* Again, this does not indicate the claimed ordered combination of steps was routine or conventional.

Diallo is directed to the question of whether or not (nuclear) AR expression might be a precursor to prostate cancer. Diallo 1302. Thus, Diallo suggests it was not established that AR was known to have been a good marker to indicate prostate cancer. Thus, Diallo does not evidence that AR detection using an immunoassay, individually or with MCM and PSA, followed by a cell count, was routine or conventional.

Srivastava is directed to using androgen-regulated nucleic acids for cancer diagnosis. Srivastava Abstract. Srivastava indicates that, prior to its *invention*, PSA tests were the customary way of detecting prostate cancer,

but that these tests had a very high false positive rate. *Id.* at 1:30–35. Srivastava indicated that AR had been reported in advanced prostate cancer, but that its role was poorly understood. *Id.* at 1:57–64. However, Srivastava does not indicate that an immunoassay for AR, alone or with MCM and PSA, followed by a cell count, was routine and customary.

Thus, while the prior art might teach or suggest the individual steps recited by the appealed claims, or components thereof, the evidence on appeal does not support the conclusion that the claimed steps, as an ordered combination, constitute mere routine and customary techniques that do not provide the "something more" than the natural phenomenon upon which they rely so as to provide an inventive concept.

For these reasons, we find the rejection insufficient.

SUMMARY

The rejection of the claims as directed to patent-ineligible subject matter is reversed.

REVERSED