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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DAVID BRIAN GALLOWAY[1]

Appeal 2017-005972
Application 13/000,942
Technology Center 1600

Before ERIC B. GRIMES, RICHARD M. LEBOVITZ, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of detecting prostate cancer cells, which have been rejected as obvious and as directed to patent ineligible subject matter. 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, Ltd. Appeal Br. 1.

STATEMENT OF THE CASE

"MCMs [minichromosome maintenance proteins] were identified as useful biomarkers of 'cell cycle state', i.e. whether a cell is capable of proliferating rather than being quiescent or senescent." Spec. 1.

> Although MCMs can be used as targets in the detection of malignant cells in a body fluid such as urine, they are not tissue specific. There is, therefore, a need for a means of specifically detecting prostate cancer cells in urine. The present invention is based on the determination that prostate epithelial cells can be detected in urine which can in turn be analysed for malignancy.

Id. at 2. The Specification states that prostate epithelial cells can be detected based on their expression of "Prostate Specific Antigen (PSA)," among other antigens. *Id.*

Claims 29–35, 39–42, and 49 are on appeal. Claim 40 is the only independent claim and reads as follows:

40. A method of detecting or determining the presence of prostate cancer cells in a sample of body fluid from a subject,

(i) isolating cells from said sample to provide a cell sample;

(ii) contacting said cell sample first with a monoclonal antibody or fragment thereof, having an antigen binding domain specific fora [sic, for a] prostate antigen;

(iii) washing said cell sample;

(iv) contacting said cell sample from step (iii) with a monoclonal antibody or fragment thereof, having an antigen binding domain specific for a minichromosome maintenance MCM-2 polypeptide; and

(iv) determining the binding of both of said monoclonal antibodies or fragments thereof, to the cell sample to detect prostate cancer cells in said subject.

The claims stand rejected as follows:[2]

Claims 29–35, 39–42, and 49 under 35 U.S.C. § 103(a) as obvious based on Meng,[3] Bolduc,[4] Oesterling,[5] and Reeves[6] (Ans. 4) and

Claims 29–35, 39–42, and 49 under 35 U.S.C. § 101 as directed to patent ineligible subject matter (Ans. 2).

I

The Examiner has rejected all of the claims on appeal as obvious based on Meng, Bolduc, Oesterling, and Reeves. The Examiner finds that "Meng teaches detecting prostate cancer cells in tissue samples of prostate cancer patients using monoclonal anti-MCM2 antibody" and suggests that "'biochemical analysis of prostate epithelial cells shed into the seminal fluid

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[2] The Final Action also included a rejection under 35 U.S.C. § 112, second paragraph, and two rejections under 35 U.S.C. § 103(a) based on Laskey (US 6,303,323 B1, issued Oct. 16, 2001), among other references. Office Action mailed Sept. 17, 2015, pages 4–8. However, after Appellant amended the claims, the Examiner stated that "[t]he amendment and response does NOT place the application in condition for allowance because" of the § 101 rejection and § 103 rejection based on Meng, Bolduc, Oesterling, and Reeves. Adv. Action mailed Dec. 30, 2015. We therefore understand the rejections under 35 U.S.C. § 112, second paragraph, and the rejections under 35 U.S.C. § 103(a) based on Laskey to be withdrawn.

[3] Maxwell V. Meng et al., *Minichromosome Maintenance Protein 2 Expression in Prostate: Characterization and Association with Outcome after Therapy for Cancer*, 7 Clinical Cancer Research 2712–2718 (2001).

[4] Stéphane Bolduc et al., *Urinary PSA: A Potential Useful Marker When Serum PSA is Between 2.5ng/ml and 10/ng/ml*, 1 CUAJ 377–381 (2007).

[5] Joseph E. Oesterling, *Prostate Specific Antigen: A Critical Assessment of the Most Useful Tumor Marker For Adenocarcinoma of the Prostate*, 145 Journal of Urology 907–923 (1991).

[6] Reeves et al., WO 2006/133560 A1, Dec. 21, 2006.

could provide an early, noninvasive assay for prostate cancer detection.'" Ans. 4.

The Examiner finds that Bolduc teaches "urinary (body fluid) PSA as a useful marker in diagnosis of prostate cancer" and teaches "determining urinary PSA with ELISA using a monoclonal anti-PSA antibody." *Id.* at 5. The Examiner finds that Oesterling and Reeves disclose the limitations of dependent claims 32–34. *Id.*

The Examiner concludes that it would have been obvious "[t]o detect[] prostate cancer cells in body fluid (e.g. urine) of prostate cancer patients using PSA and MCM2 as biomarkers" because Meng suggests that detection of MCM2 in prostate cells in seminal fluid could provide an early, noninvasive assay for prostate cancer and Bolduc teaches that urinary PSA is a useful marker for diagnosing prostate cancer. *Id.* The Examiner reasons that it would have been obvious to assay for both proteins because "using a panel of biomarkers will increase accuracy for diagnosis." *Id.* at 6.

Appellant argues that Meng teaches detection in tissue samples, not a body fluid sample, and Bolduc teaches that "reduced urine PSA is correlated to prostate cancer." Appeal Br. 3. Appellant also argues that, "[e]ven if Meng did refer to cells in seminal fluid, this would conflict with the teachings of the secondary Bolduc reference which expressly avoids semen in his urine PSA assays. That is, Bolduc prohibits urine samples within 24 hours post ejaculation." *Id.* at 4. Appellant argues that "[j]ust because the markers were correlated in two different samples does not motivate one to use the markers together in a third type of sample, particularly since one marker is taught as correlating negatively to the disease state." Reply Br. 5.

We agree with Appellant that the Examiner has not established that the method of claim 40 would have been obvious to a person of ordinary skill in the art based on the cited references. Meng states that "[t]umors from 92 patients who underwent radical prostatectomy for prostate cancer . . . were examined for Mcm 2 expression by immunohistochemistry using a monoclonal antibody." Meng 2712, Abstract. "Patients with high Mcm 2 expression exhibited shorter disease-free survival." *Id.* Meng states that "Mcm 2 expression is an independent predictor of disease-free survival after definitive local therapy and has potential as a molecular marker for clinical outcome in prostate cancer." *Id.* Meng suggests that "biochemical analysis of prostate epithelial cells shed into the seminal fluid could provide an early, noninvasive assay for prostate cancer." *Id.* at 2718, left col.

Bolduc discloses a study "to evaluate the usefulness of urinary prostate specific antigen (PSA) in the differential diagnosis of benign prostatic hyperplasia (BPH) and prostate cancer." Bolduc 377, Abstract. Bolduc states that the "study supports urinary PSA as a useful marker in the differential diagnosis of prostate cancer and BPH. . . . Low urinary PSA and PSA ratios [urinary PSA:serum PSA] point toward prostate cancer." *Id.* In Bolduc's study, patients "provided blood samples to measure serum PSA. . . . [P]atients also provided a 50-ml sample of first-voided urine, any time during the day, but after at least 1 hour of continence, no sexual intercourse within 24 hours." *Id.* at 378, left col. Urinary PSA was measured "using a polyclonal antibody, 'Poly PSA,' and a monoclonal antibody, '4D1.'" *Id.* at 378, right col.

Thus, Meng suggests that detection of MCM2 in or on prostate cells shed into seminal fluid might provide a useful assay for prostate cancer, and

Bolduc discloses that the level of PSA in urine is useful in distinguishing prostate cancer from BPH. The claims specifically require binding of the antibody to prostate cancer cells in the sample. However, Bolduc does not describe the PSA in urine as being found in or on prostate cells, as opposed to being secreted into the urine by such cells. Nor does Bolduc state that detecting PSA in or on prostate cells in the urine provides a useful result in distinguishing prostate cancer from BPH.

The Examiner has not pointed to evidence showing that those skilled in the art would have expected to find prostate cells in urine or would have expected that the level of PSA in seminal fluid would be useful in either diagnosing prostate cancer or distinguishing between prostate cancer and BPH. In summary, the evidence does not support the conclusion that a person of ordinary skill in the art would have considered it obvious to test the *same* sample of body fluid for both a prostate antigen (e.g., PSA) and MCM2. We therefore reverse the rejection under 35 U.S.C. § 103(a).

II

The Examiner has rejected all of the claims on appeal under 35 U.S.C. § 101 on the basis that they "are directed to detecting the judicial exception of naturally occurring levels of a prostate antigen and MCM-2 in a bodily fluid sample from prostate cancer patient." Ans. 2. The Examiner finds that "[t]he steps of measuring levels of a prostate antigen and MCM-2 including using antibodies, are considered known, routine steps and are typically taken by those in the field." *Id.* at 2–3 (citing Meng and Bolduc). The Examiner concludes that

> the additional steps in the claims are considered as routine data gathering steps in order to test for the correlation between the

> two marker levels and prostate disease state. These routine laboratory steps do not add a meaningful limitation to the method as they would be routinely used by those of ordinary skill in the art in order to apply the correlation.

Id. at 3.

Appellant argues that "[t]he claims recite elements and non-routine steps in addition to the natural product." Appeal Br. 6. That is, "[t]he steps focus the [claimed] method to address a single problem in a specific way requiring an unusual combination of components and specific steps." *Id.* at 7. Appellant argues that

> the rejection is wrong in suggesting, e.g., that it was routine to detect the well known PSA protein in urine cell sample much less in combination with MCM2 detection in urine cells. The invention is not stealing the detection of well known antigens, but inventively contributing an odd combination of two antigens with specific cells and sequential method steps to solve an old problem.

Id. at 8.

We agree with Appellant that the claimed method is eligible for patenting. The Supreme Court has set out a two-step test for

> distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts. First, we determine whether the claims at issue are directed to one of those patent-ineligible concepts. If so, we then ask, "[w]hat else is there in the claims before us?" To answer that question, we 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. We have described step two of this analysis as a 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."

Alice Corp. Pty. Ltd. v. CLS Bank Int'l, 134 S. Ct 2347, 2355 (2014) (citations omitted, alterations in original).

With regard to the second step of the test, the Court has held that "well-understood, routine, conventional activity previously engaged in by scientists who work in the field . . . is normally not sufficient to transform an unpatentable law of nature into a patent-eligible application of such a law." *Mayo Collaborative Services v. Prometheus Labs., Inc.*, 566 U.S. 66, 79 (2012).

Here, we agree with the Examiner that the claims are directed to a patent-ineligible concept; specifically, the correlation between MCM2 and a prostate-specific antigen, in or on prostate cells, and the presence of prostate cancer. However, when the steps of the claimed method are considered "as an ordered combination," *id.*, we conclude that they amount to a patent-eligible application of the natural phenomenon rather than an attempt to claim the natural phenomenon itself.

Specifically, the claims require testing a body fluid sample for the presence of prostate cells, using a monoclonal antibody (or fragment of one) specific for a prostate antigen, and then testing the same sample for the presence of MCM2 using a second monoclonal antibody. Assuming for the sake of discussion that it was routine and conventional to test urine for the presence of PSA (Bolduc) and to test seminal fluid for the presence of MCM2 (Meng), the evidence does not show that it was routine and conventional to sequentially test the *same* sample of body fluid for the presence of both antigens, as required by the claims.

We therefore conclude that the claimed method "has additional features that provide practical assurance that the process is more than a

drafting effort designed to monopolize the law of nature itself." *Mayo*, 566 U.S. at 77. Because the claimed method includes more than routine and conventional activity in addition to the natural phenomenon on which it is based, it is eligible for patenting under 35 U.S.C. § 101.

SUMMARY

We reverse both of the rejections on appeal.

REVERSED