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EXAMINER	
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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte DAVID GALLOWAY and NICK COLEMAN

Appeal 2017-004696
Application 13/512,585
Technology Center 1600

Before DONALD E. ADAMS, DEMETRA J. MILLS, and ULRIKE W. JENKS, *Administrative Patent Judges*.

MILLS, *Administrative Patent Judge*.

DECISION ON APPEAL

STATEMENT OF CASE

This is an appeal under 35 U.S.C. § 134(a). The Examiner has rejected claims 35–48 for obviousness, and as directed to patent ineligible subject matter. Claims 1–34 have been cancelled. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

CLAIMED SUBJECT MATTER

The following claim is representative.

35. A method of diagnosing a subject with bladder cancer or at risk of developing bladder cancer comprising:

a) providing a urine sample isolated from said subject;

b) isolating cells from said sample and dispersing them on a slide, wherein said slide contains at least 5000 total cells;

c) contacting said cells with a labelled specific binding member capable of binding to a minichromosome maintenance 2 (MCM2) polypeptide to stain cells with that express MCM2; and

d) counting said stained cells to provide a cell count;

wherein if said cell count is at least 50 cells of said 5000 total cells said subject has bladder cancer or is at risk of developing bladder cancer.

Cited References

Laskey et al. ("Laskey")	US 7,056,690 B2	June 6, 2006

Laszlo Pajor et al., *Increased Efficiency of Detecting Genetically Aberrant Cells by UroVysion Test on Voided Urine Specimens Using Automated Immunophenotypical Preselection of Uroepithelial Cells*, International Society for Analytical, Cytometry Part A. (2008). ("Pajor")

Kai Stoeber et al., *Diagnosis of Genito-Urinary Tract Cancer by Detection of Minichromosome Maintenance 5 Protein in Urine Sediments*, J. Nat. Cancer Inst., Vol. 94, No. 14, 1071-1079 (2002). ("Stoeber")

Grounds of Rejection

1. Claims 35–48 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Laskey in view of Stoeber and Pajor.
2. Claims 35–48 are rejected under 35 U.S.C. § 101 because the claimed invention is directed to judicial exception(s) (i.e., a law of nature, a natural phenomenon, and/or an abstract idea) without significantly more.

FINDINGS OF FACT

The Examiner's findings of fact are set forth in the Final Action at pages 2–8, Answer pages 2–16.

PRINCIPLES OF LAW

In making our determination, we apply the preponderance of the evidence standard. *See, e.g.*, *Ethicon, Inc. v. Quigg*, 849 F.2d 1422, 1427 (Fed. Cir. 1988) (explaining the general evidentiary standard for proceedings before the Office).

"Obviousness requires a suggestion of all limitations in a claim." *CFMT, Inc. v. Yieldup Intern. Corp.*, 349 F.3d 1333, 1342 (Fed. Cir. 2003) (citing *In re Royka*, 490 F.2d 981, 985 (CCPA 1974)).

Obviousness Rejection

The Examiner finds that Laskey teaches each element claimed except Laskey does not specifically teach dispersing the cells on a slide containing

at least 5000 total cells, or " 'counting' dispersed cells which bind anti–MCM2 antibodies." Final Act. 3. The Examiner relies on Stoeber and Pajor for this teaching. Final Act. 4. The Examiner concludes that,

> One of ordinary skill in the art at the time the invention was made would have been motivated to non–invasively diagnose and treat bladder cancer comprising dispersing cells isolated by centrifugation from 30–120 ml of a urine sample from a subject on a slide and using an automated counter to count dispersed cells expressing MCM2 by performing the method of Pajor et al using the labeled anti–MCM2 antibodies of Laskey et al wherein the presence of (including 50 or more) MCM2–expressing cells is indicative of bladder cancer, wherein the subject is just any suspect suspected of having bladder cancer (including a subject with a previous occurrence of bladder cancer and those with hematuria) and administering a treatment regimen to a subject diagnosed with bladder cancer based on the presence of MCM2 expressing cells because subjects that have previously had bladder cancer are at high risk for recurrence, MCM2 is a biomarker for bladder cancer, and administering a treatment regimen specific for a cancer to a subject diagnosed with cancer would predictably result in a therapeutic benefit. As evidenced by the instant specification (see Example 2), 5000 cells would predictably be present in the 30–120 ml urine sample.

Final Act. 4–5.

Appellants contend, among other things, that

> The Examiner brings in the Pajor feature of using dispersed cells on a slide from a 30–120 ml urine sample and counting labeled cancer cells. However, this feature specifically incorporated does not provide the feature of a threshold of 50 positive cells per 5000 on a urine sediment slide. And, it is notable that Pajor does not actually count positive cells.

App. Br. 4.

The dispositive issue in the case is whether the Examiner has provided sufficient evidence on this record that the combination of cited references discloses a step of "d) counting said stained cells to provide a cell count, as in claim 35."

ANALYSIS

We do not find that the Examiner has provided evidence to support a prima facie case of obviousness.

The Examiner relies on Stoeber and Pajor for teaching counting of cells an element missing from Laskey. *See* Final Act. 3, Ans. 3. Specifically, the Examiner finds that

> Stoeber et al teaches a diagnostic method of detecting a subject suffering from bladder cancer comprising providing 50–80 ml of urine from a subject, isolating cells from said urine by centrifugation to provide a cell sample, contacting the sample with antibodies that specifically bind a biomarker on cancer cells, determining binding of said antibodies to the cell sample by measuring fluorescence, providing a cell count by comparing fluorescence of the sample to a threshold fluorescence obtained from 1500–6000 of Hela cells, and determining that the subject has bladder cancer when the fluorescence is elevated as compared to controls (Table 5, in particular).
>
> Pajor et al teaches methods of diagnosing bladder cancer by detecting the expression of a bladder cancer biomarker on cells isolated by centrifugation of 30–120ml of urine from subjects followed by dispersing the cells on a slide, contacting the dispersed cells with antibodies, and using an automated counter to count dispersed cells which bind the antibodies (see pages 260–261).

Ans. 3–4.

We are not persuaded that the Examiner has established that either Stoeber or Pajor teaches a step of counting cells, as claimed. Stoeber

teaches calculating the fluorescence values of clinical tumor, batch cell lysate samples labeled with Mcm5 antibody. Stoeber, p. 1073, col. 2, to 1074, col. 1. In Stoeber, fluorescence of the batch of cells was calculated by the Dissociation–Enhanced Lanthanide Fluorometric Immunoassay (DELFIA) method. *Id.* at p. 1073, col. 2. The Examiner points to no evidence or disclosure in Stoeber that individual cells were counted, and makes no supported finding that one of ordinary skill in the art would understand a correlation between a batch fluorescence value of cells and individual cell counts.

Similarly, Pajor placed a urine sediment on a slide (p. 260, col. 2), and positive cells of interest were identified by first identifying uroepithelial cells, followed by counting chromosomes in the intact cells to positively identify individual neoplastic cells using a scanning microscope (p. 262–263). Pajor discloses that the scanning of CK–7 and hematoxylin stained cell samples on slides from voided urine was done automatically on a predefined area of the slides using 20X objective at transmitted light mode. P. 260, col. 2. Pajor used immunostain microscopy with automated scanning to measure sample intensity. P. 260–261. The Examiner points to no evidence or disclosure in Pajor that individual cells were counted, and makes no supported finding that one of ordinary skill in the art would have understood there to be a correlation between a fluorescent intensity of cells obtaining by immunostain microscopy and individual cell counts.

Therefore, neither Stoeber nor Pajor make up for the deficiencies of Laskey. Because the Examiner has not provided evidence of each and every method step claimed, in particular the claimed cell counting step, we reverse the obviousness rejection of record.

101 Rejection – Patent Ineligible Law of Nature, Natural Phenomenon

The Examiner finds that

> **The "natural phenomenon" is: elevated numbers of MCM2 expressing cells in urine are indicative of bladder cancer or risk of developing bladder cancer.** A claim that focuses on judicial exception(s) can be shown to recite something "significantly more" than the judicial exception(s) by reciting a meaningful limitation. However, ***in the instant case, the claims only recite well–understood, routine and conventional limitations in addition to the judicial exception(s***). Such limitations are not meaningful limitations and are not enough to qualify the claimed method as reciting something "significantly more" than the judicial exception(s) (see Part l.B.1 of *the interim Guidance)*. Here, the claims do not contain any significant additional elements or steps beyond the observation of judicial exception(s) present when performing routine and conventional methods. Further, just as PCR was identified in *Ariosa v. Sequenom* as "well–known, routine, and conventional" (see first paragraph on page 13 of *Ariosa Diagnostics, Inc. v. Sequenom Inc*. (Fed. Cir. 2015)), detection methods encompassed by the instant claims are wellknown, routine, and conventional. The claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception because the additional elements (common methods of detecting expression and common therapeutic methods) are routinely performed in the art to obtain data regarding expression and treat subjects. The claims do not recite something "significantly more" than the judicial exception(s); rather, the claims "simply inform" the natural phenomenon to one performing routine active method steps and do not amount to significantly more than the judicial exception(s). See the *2014 Interim Guidance on Patent Subject Matter Eligibility* (79 FR 7 4618) *("the interim Guidance").*

Final Act. 6-7; bold italicized emphasis added.

Appellants contend that,

> The examiner maintains that the claims are not patent eligible because the claims are directed to a natural phenomenon and do not recite something "significantly more" than the natural phenomenon by reciting a meaningful limitation because the additional elements (when considered both individually and as an ordered combination) are limited to well understood, routine and conventional methods of detecting a known bladder cancer urine biomarker (MCM2 of Laskey) by modifying the generic method of Pajor et al of detecting bladder cancer biomarkers in urine.
>
> Emphasis added. The allegation is conclusory and fails to consider the claims as a whole. *The facts above, in the inventiveness analysis, show that the additional steps of the claimed methods were not routine in the art.* In fact the combination of Laskey and Pajor does not even provide all limitations of the claim and are conflicting technologies, not providing a routine path to practice the claims.

Reply Br. 4–5; italicized emphasis added.

PRINCIPLES OF LAW

"[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); *see e.g., Hyatt v. Dudas*, 492 F.3d 1365, 1369–71 (Fed. Cir. 2007) (once the examiner presents a prima facie case for unpatentability, e.g., under § 112, the burden is properly shifted to applicant).

ANALYSIS

We do not find that the Examiner has provided evidence to support a prima facie case of patent ineligible subject matter. "Whether something is well-understood, routine, and conventional to a skilled artisan at the time of the patent is a factual determination." *Berkheimer v. HP Inc.*, 881 F.3d 1360, 1369 (Fed. Cir. 2018).

The Examiner has not established with appropriate factual evidence that the claimed method uses conventional cell counting methods. In particular, as noted in the obviousness rejection discussed above, the Examiner did not establish with factual evidence, that the cell counting step, as claimed, is conventional or known in the art.

Therefore, we do not find that the Examiner has provided a prima facie case of patent ineligibility supported by factual evidence, and reverse the rejection of the claims as directed to an abstract idea or natural phenomenon.

CONCLUSION OF LAW

The cited references do not support the Examiner's obviousness rejection and lack of patentable subject matter rejection. These rejections are reversed.

REVERSED