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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte VINEET GUPTA and M. AMIN ARNAOUT[1]

Appeal 2017-010886
Application 14/311,069
Technology Center 1600

Before ULRIKE W. JENKS, JOHN E. SCHNEIDER, and TIMOTHY G. MAJORS, *Administrative Patent Judges*.

SCHNEIDER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal[2] under 35 U.S.C. § 134 from the Examiner's rejection of claims to a cell based assay which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We REVERSE.

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[1] Appellants identify the Real Party in Interest as The General Hospital Corporation. Br. 3.

[2] We have considered and herein refer to the Specification of June 20, 2014 ("Spec."); Final Office Action of Apr. 25, 2016 ("Final Act."); Appeal Brief of Mar. 23, 2017 ("Br."); and Examiner's Answer of May 24, 2017 ("Ans.").

STATEMENT OF THE CASE

"Integrins are non-covalently linked α/ß heterodimeric receptors that mediate cell adhesion, migration and signaling. Together with their ligands, integrins play central roles in many processes including development, hemostasis, inflammation and immunity, and in pathologic conditions such as cancer invasion and cardiovascular disease." Spec. ¶ 2. "The ß2 integrins, which have a common ß-subunit (ß2, CD18) but distinct α-subunits (CD11a, CD11b, CD11c and CD11d), are critical leukocyte receptors that are important not only for the function of leukocytes but also the development of the inflammatory response in vivo." *Id.*

> Current assays for the identification of regulators of CD11b/CD18 rely on purified proteins adsorbed to microtiter plates. Even though these assays are compatible with high-throughput screening (HTS), purification of the requisite amount of CD11b/CD18 from mammalian cells for a HTS campaign can be exceedingly difficult and the natural conformation of integrin may not be retained upon adsorption to the plastic surfaces.

Id. ¶ 4. The Specification describes an assay for the rapid identification of small molecule modulators of integrin CD11b/CD18. *Id.* ¶ 13.

Claims 1–5, 7–9, 11, and 13–18 are on appeal. Claim 1 is representative reads as follows:

> 1. A no-wash, cell-based assay for the identification of small molecule modulators of integrin CD 11b/CD18, the assay consisting of:
>
> contacting cells with a solution comprising a test compound on a substrate treated with a compound that affects cell adhesion;
>
> inverting the substrate such that non-adherent cells move away from the substrate by the action of gravity;

removing the solution from the substrate after inverting the substrate without contacting the substrate with an additional liquid to wash or rinse the substrate; and

detecting adherent cells on the substrate.

Claims 1–5, 7–9, 11, and 13–18 have been rejected under 35 U.S.C. § 103(a) as unpatentable over Xiong[3] in view of Arnaout[4] and in further view of Gallatin,[5] Ason,[6] and Young.[7]

DISCUSSION

Issue

The issue with respect to this rejection is whether a preponderance of the evidence supports the Examiner's conclusion that the subject matter of the claims would have been obvious over Xiong combined with Arnaout, Gallatin, Ason, and Young.

The Examiner finds that Xiong teaches an assay for identification of CD11b/CD18 modulation where the adhesion to a substrate is performed in the presence of calcium and magnesium ions. Final Act. 4. The Examiner finds that Arnaout teaches contacting cells with a solution comprising a test

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[3] Xiong et al., *Modulation of CD11b/CD18 Adhesive Activity by Its Extracellular, Membrane-Proximal Regions*, 171 J. Immunol. 1042 (2003) ("Xiong").
[4] Arnaout, US 2005/0227296 A1, published Oct. 13, 2005 ("Arnaout").
[5] Gallatin et al., US 6,251,395 B1, issued June 26, 2001 ("Gallatin").
[6] Ason and Reznikoff, *A high-throughput assay for Tn5Tnp-induced DNA cleavage*, 32 Nucleic Acids Res. E83 (2004) ("Ason"). Citations are to the pages numbers in the reprint.
[7] Young et al., *High-Throughput with HyperCyt® Flow Cytometry to Detect Small Molecule Formylpeptide Receptor Ligands*, 10 J. Biomolecular Screening 374 (2005) ("Young").

compound on a substrate and physically repositioning the substrate such that non-adherent cells move away from the substrate. Final Act. 4. The Examiner finds that Arnaout teaches methods for identifying compounds capable of binding to selected integrins and selecting the compound that affects cell adhesion from the group comprising ICAM-1, icb3, fibrinogen, and NIF. *Id.* The Examiner goes on to find that Gallatin teaches assays which involve dislodging non-adherent cells from an inverted plate. *Id.* The Examiner finds that Ason teaches a no-wash step in a high throughput assay and that Young teaches a no-wash cell adhesion assay. *Id.*

The Examiner concludes:

> It would have been obvious to one of ordinary skill in the art to have been motivated to expand the teachings of Xiong to include small molecules as taught by Arnaout, modify the teaching of Xiong to include Ason's high throughput assay and substituting the minimal wash taught by Ason with a no-wash cell based assay of Young with a reasonable expectation of success because Ason teaches that the no wash steps are advantageous since it identifies effectors that are specific.

Id.

Appellants contend that the Examiner has failed to provide a reason why one skilled in the art would modify the teachings of Xiong, Arnaout or Gallatin to eliminate the steps of washing away the non-adherent cells or removing them by centrifugation. Br. 7–8. Appellants also contend that one skilled in the art would not be lead to combine the teachings of Young and Ason with the other references as Young and Ason relate to different types of assays. Br. 8. Finally, Appellants contend that there is evidence of unexpected results to overcome a prima facie case of obviousness. Br. 9–10.

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.
>
> After evidence or argument is submitted by the applicant in response, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of argument.

In re Oetiker, 977 F.2d 1443, 1445 (Fed. Cir. 1992).

"[R]ejections on obviousness grounds cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR Int'l Co. v. Teleflex Inc.*, 550 U.S. 398, 418 (2007) (quoting *In re Kahn*, 441 F.3d 977, 988 (Fed. Cir. 2006)).

"Obviousness requires more than a mere showing that the prior art includes separate references covering each separate limitation in a claim under examination." *Unigene Labs., Inc. v. Apotex, Inc.*, 655 F.3d 1352, 1360 (Fed. Cir. 2011). "Rather, obviousness requires the additional showing that a person of ordinary skill at the time of the invention would have selected and combined those prior art elements in the normal course of research and development to yield the claimed invention." *Id.*

Analysis

We have considered the arguments advanced by the Examiner and Appellants and find that Appellants have the better position. While Gallatin teaches inverting a plate containing adherent and non-adherent cells, it also teaches that the non-adherent cells are dislodged from the inverted plate

using centrifugation, not gravity as recited in the claims. Gallatin col. 101, ll. 16–19. The Examiner has not adequately explained why one skilled in the art would eliminate the centrifugation step Gallatin and use gravity for separating the non-adherent cells from the adherent cells.

The Examiner's only response to Appellants' argument relative to Gallatin is that Gallatin teaches dislodging the non-adherent cells from an inverted plate. Ans. 8. The Examiner does not address the issue of why one skilled in the art would use gravity to dislodge the cells as called for in the claims rather than using centrifugation as taught by Gallatin. *See id.*

Appellants argued that there is evidence in the record demonstrating unexpected results. Br. 9–10. In support of this contention, Appellants cite to the declaration[8] of one of the inventors, Dr. Gupta. While we do not rule on the sufficiency of Appellants' argument, we note that the Examiner failed to fully address this argument and the declaration in the Answer. *See* Ans. 9.

[8] Declaration Under 37 C.F.R. § 1.132, filed March 7, 2016 ("Decl.").

Conclusion of Law

We conclude that a preponderance of the evidence does not support the Examiner's conclusion that the subject matter of the claims would have been obvious over Xiong combined with Arnaout, Gallatin, Ason, and Young.

SUMMARY

We reverse the rejection under 35 U.S.C. § 103(a).

REVERSED