

The opinion in support of the decision being entered today  
is *not* binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

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BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES

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*Ex parte* YE FANG,  
YULONG HONG, JOYDEEP LAHIRI, FANG LAI,  
JINLIN PENG, BRIAN L. WEBB, and ANN M. FERRIE

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Appeal 2007-1824  
Application 10/639,718  
Technology Center 1600

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Decided: August 23, 2007

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Before TONI R. SCHEINER, DONALD E. ADAMS, and NANCY J.  
LINCK, *Administrative Patent Judges*.

ADAMS, *Administrative Patent Judge*.

**DECISION ON APPEAL**

This appeal under 35 U.S.C. § 134 involves claims 1-18 and 43-51, the only claims pending in this application. We have jurisdiction under 35 U.S.C. § 6(b).

## INTRODUCTION

The claims are directed to a method for identifying or evaluating target compounds (claims 1-17, 43, 44), a method to determine binding affinity of labeled ligands using microarrays (claim 18), a method for determining binding affinities between ligands and membrane proteins (claims 45 and 46), and a method for conducting protein array assays (claims 47-51). Claims 1 and 16 are illustrative:

1. A method for identifying or evaluating target compounds capable of modulating ligand-receptor interactions, the method comprising: a) providing a plurality of receptor microspots on a substrate to form an array; b) preparing a cocktail solution of labeled ligands, each labeled ligand having an affinity of from about 0.1 nM to about 20 nM and a specificity of at least 50% to bind with at least one corresponding paired receptor in said array and a cross activity of no more than 10% with receptors on said array other than said at least one corresponding paired receptor; c) contacting said cocktail solution with said array in the presence of a target compound; and d) detecting a level of binding between each said labeled ligand and its respective paired receptor, wherein a change in the level of binding between one of said labeled ligands and its respective paired receptor in the presence of said target compound, as compared to a control level of binding, is indicative that said target compound is capable of modulating the interaction between said one labeled ligand and its respective paired receptor.

16. The method according to claim 1, wherein said method comprises providing at least two receptors co-immobilized within a single microspot, in combination with a two-color detection technique, to at least double the capacity of probe elements.

The Examiner relies on the following prior art references to show unpatentability:

Bryen A. Jordan, "Opioids and Their Complicated Receptor Complexes," *Neuropsychopharmacology*, 23(54), S5-S18 (2000).

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Barry Schweitzer, "Immunoassays with Rolling Circle DNA amplification: A versatile platform for ultrasensitive antigen detection," PNAS, 97(18), 10113-10119 (2000).

Lahiri	US 2002/0019015 A1	Feb. 14, 2002
Matray	US 6,649,351	Nov. 18, 2003

The rejections as presented by the Examiner are as follows:

1. Claims 1-15, 18, and 43-51 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, and Jordan.
2. Claims 16, 17, 50, and 51 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, Jordan, and Schweitzer.

We affirm.

## DISCUSSION

Claims 1-15, 18, and 43-51 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, and Jordan. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Therefore, we limit our discussion to representative claim 1. Claim 1 is directed to a method for identifying or evaluating target compounds capable of modulating ligand-receptor interactions. The method comprises four steps:

- a) providing a plurality of receptor microspots on a substrate to form an array;
- b) preparing a cocktail solution of labeled ligands;
- c) contacting the array with the cocktail solution in the presence of a target compound; and

d) detecting a level of binding between each labeled ligand in the cocktail solution and its respective paired receptor.

For clarity, we note that steps (a) – (d) of Appellants' claim 1 are directed to a competitive binding assay.

Step (b) of claim 1 also requires that each labeled ligand in the cocktail solution has (1) an affinity of from about 0.1 nM to about 20 nM and (2) a specificity of at least 50% to bind with at least one corresponding paired receptor in said array. In addition, claim 1 requires that each labeled ligand has a cross activity of no more than 10% with receptors on said array other than said at least one corresponding paired receptor.

According to claim 1, the detection of a change in the level of binding between one of the labeled ligands and its respective paired receptor in the presence of the target compound, as compared to a control level of binding, indicates that the target compound is capable of modulating the interaction between the labeled ligand and its respective paired receptor. Stated differently, the detection of a change in the level of binding is based on the comparison of a control, non-competitive assay, with the competitive binding assay recited in elements (a) – (d) of claim 1.

Lahiri teaches an array with a plurality of microspots stably associated with the surface of a substrate (Lahiri 3: ¶ 0047). Therefore, Lahiri teaches element (a) of Appellants' claimed invention. In addition, Lahiri teaches that it is preferred that the protein included in one microspot differs from the protein included on a second microspot of the same array (Lahiri 3-4: ¶ 0047). Lahiri teaches a competitive binding assay, in whichwherein the array is exposed to labeled cognate ligands for the proteins on each

microspot<sup>1</sup> of the array and unlabeled target which competes with the labeled cognate ligands for binding sites on the array (Lahiri 6: ¶ 0081). Therefore, Lahiri teaches the step of contacting a cocktail solution with an array in the presence of a target compound. According to Lahiri, the affinity of the target for the probe microspot relative to the labeled ligand is determined by the decrease in the amount of binding of the labeled ligand.

But for the specific affinity, specificity, and cross-reactivity of the cognate ligands, Lahiri teaches the method set forth in Appellants' claim 1. The Examiner relies on Matray and Jordan to make up for this deficiency in Lahiri. Specifically, the Examiner finds that Matray "teaches a plurality of specific binding pairs, each having a dissociation constant of 1 nM, in order to provide high affinity between the binding partner and analyte in assays to simultaneously detect a plurality of analytes in a sample. See column 3, lines 43-44 and column 13, lines 9-23" (Answer 6). In addition, the Examiner finds that Jordan "teaches highly selective ligands that eliminate any possibility of cross-reactivity between receptor types, in order to understand GPCR dimerization in a specific compound receptor field and to clarify the mechanism of the compounds towards the development of novel

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<sup>1</sup> Clearly, to perform a competitive assay on an array comprising microspots of different proteins, the labeled cognate ligands must be capable of binding to each protein microspotted to the substrate. To do otherwise would defeat the intended purpose of the competitive binding assay. *See KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741, 82 USPQ2d 1385, 1396 (2007) (It is proper to "take account of the inferences and creative steps that a person of ordinary skill in the art would employ."). *See also id.* at 1742, 82 USPQ2d at 1397 ("A person of ordinary skill is also a person of ordinary creativity, not an automaton.").

therapeutic drugs. See abstract" (*id.*). Based on this evidence, the Examiner finds that

[i]t would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Lahiri et al with a plurality of specific binding pairs, each having a dissociation constant of 1 nM, as taught by Matray et al in order to provide high affinity between the binding partner and analyte in assays to detect a plurality of analytes in a sample. The high affinity binding provides the advantage of a more accurate detection method when detecting a plurality of analytes, therefore providing the motivation to combine the teachings of Lahiri et al and Matray et al.

(Answer 6-7.) In addition, the Examiner finds that “[i]t would also have been obvious to modify the method of Lahiri et al with highly selective ligands that eliminate any possibility of cross-reactivity between receptor types, as taught by Jordan . . .” (Answer 7). On reflection, we find no error in the Examiner’s *prima facie* case of obviousness.

In response, Appellants assert that the combination of Lahiri, Matray, and Jordan fails to teach step (b) of the claimed invention (Br. 6). Regarding Lahiri, Appellants assert that the claimed invention “employs diverse multiplexed GPCR microarrays that have GPCR membrane microspots that do not have a common labeled ligand” (Br. 6). We disagree. GPCR microarrays are not required in Appellants’ claim 1. Further, GPCRs are only preferred proteins in Lahiri’s assays (Lahiri 2: ¶ 0021). Accordingly, we are not persuaded by Appellants’ arguments relating to GPCR assays.

Appellants recognize that Matray “teaches a dissociation constant of 1 nM between specific binding pairs to provide high affinity between the binding partner and analyte in assays for the detection of a plurality of analytes in a sample” (Br. 8). However, Appellants assert that “there is a

significant distinction between a homogenous assay, as taught by Matray, and a surface-mediated microarray assay, as taught by the present invention” (*id.*). Appellants assert that “binding affinity alone can not be used to predict the suitability of labeled ligand cocktail” (*id.*). While this may be true, the claim does not require that binding affinity alone be used to predict the suitability of a labeled ligand cocktail. In this regard, we find no error in the Examiner’s conclusion that high affinity binding provides the advantage of a more accurate detection method when detecting a plurality of analytes, therefore providing the motivation to combine the teachings of Lahiri and Matray (Answer 6-7). Accordingly, we are not persuaded by this assertion. Further, since claim 1 is not limited to Cy5-motilin or GPCR assays we are not persuaded by Appellants’ arguments relating to these two proteins.

Appellants also assert that Jordan’s teaching of the use of highly selective ligands does not guarantee that such ligands are suitable for multiplexed binding assays (Br. 8). Obviousness does not require guaranteed or absolute predictability of success. For obviousness under §103, all that is required is a reasonable expectation of success. *In re O’Farrell*, 853 F.2d 894, 904, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988). As discussed above, the Examiner has explained why a person of ordinary skill in the art would have had a reasonable expectation of success in performing the method. Specifically, as the Examiner explains, all three references teach the binding interactions between proteins and their receptors (Answer 19). In this regard, the Examiner finds that it would have been obvious to modify the method of Lahiri with highly selective ligands that eliminate any possibility of cross-reactivity between receptor types as taught by Jordan (Answer 7). In addition, the Examiner finds that high affinity binding

provides the advantage of a more accurate detection method when detecting a plurality of analytes, therefore providing the motivation to combine the teachings of Lahiri and Matray (Answer 6-7). In our opinion, a person of ordinary skill in the art performing a competitive assay on an array comprising microspots of different proteins, would have appreciated that ligands with high affinity for their respective receptor and low cross-reactivity between receptor types would be advantageous. “The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results.” *KSR Int’l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1739, 82 USPQ2d 1385, 1395 (2007). Accordingly, for the reasons set forth above, we are not persuaded by Appellants’ assertion that a person of ordinary skill in the art would not have had a reasonable expectation of success in combining the references as relied upon by the Examiner.

While Appellants focus their attention on assays utilizing GPCRs, claim 1 is not limited to GPCR assays. In addition, Appellants provide no evidence to suggest that their arguments relating to GPCR assays are representative of the entire genus of protein assays encompassed by claim 1. Stated differently, Appellants’ arguments are not commensurate in scope with their claimed invention. *In re Greenfield*, 571 F.2d 1185, 1189, 197 USPQ 227, 230 (CCPA 1978); *In re Lindner*, 457 F.2d 506, 508, 173 USPQ 356, 358 (CCPA 1972).

On reflection, we find no error in the Examiner’s *prima facie* case of obviousness. Accordingly, we affirm the rejection of claim 1 under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, and Jordan. Claims 2-15, 18, and 43-51 fall together with claim 1.

Claims 16, 17, 50, and 51 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, Jordan, and Schweitzer. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Therefore, we limit our discussion to representative claim 16. Claim 16 depends from and limits the method of claim 1 to further require providing at least two receptors co-immobilized within a single microspot, in combination with a two-color detection technique, to at least double the capacity of probe elements.

The Examiner relies on Lahiri, Matray, and Jordan as discussed above (Answer 10). In addition, the Examiner points out that Lahiri teaches the use of an array that comprises more than one protein in each microspot (*id.*; Lahiri 3-4: ¶ 0048). The Examiner recognizes, however, that the combination of Lahiri, Matray, and Jordan fails to teach a method utilizing a two-color detection technique (Answer 10). The Examiner relies on Schweitzer to make up for this deficiency in the combination of Lahiri, Matray, and Jordan.

The Examiner finds that Schweitzer teaches “that a two-color labeling system is used with a pure fluorescein or pure Cy3 spectra, in order for detecting two (or more) proteins simultaneously” (Answer 10-11). More specifically, Schweitzer teaches the use of a two-color labeling system for detecting two different proteins in an array (Schwitzer 10118: left column, 2nd paragraph).

Based on this evidence, the Examiner concludes that it would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method taught by the combination of Lahiri, Matray, and Jordan to include a two-color labeling system, as taught by Schweitzer, to detect at

least two proteins simultaneously (Answer 11). We find no error in the Examiner's prima facie case.

In response, Appellants assert that Schweitzer relates to immunoassays with rolling circle DNA amplification which is unrelated to the present invention (Br. 11). For the foregoing reasons, we are not persuaded by Appellants' assertion.

On reflection, we find no error in the Examiner's prima facie case of obviousness. Accordingly, we affirm the rejection of claim 16 under 35 U.S.C. § 103(a) as unpatentable over the combination of Lahiri, Matray, Jordan, and Schweitzer. Claims 17, 50, and 51 fall together with claim 16.<sup>2</sup>

## CONCLUSION

In summary, we affirm all rejections of record.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

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<sup>2</sup> To be complete, we recognize Appellants' assertion that "Schweitzer does not teach or suggest step (b) of claim 1 and the 'contacting' step and steps (a) – (c) of claim 47. . ." (Br. 11). For the reasons set forth herein, we are not persuaded by Appellants' assertion that the combination of references, as relied upon by the Examiner, fails to teach the claimed invention.