NOTE: Pursuant to Fed. Cir. R. 47.6, this disposition is not citable as precedent. It is a public record.

United States Court of Appeals for the Federal Circuit

05-1072
(Reexamination Nos. 90/005,147 and 90/005,326)

IN RE SIBIA NEUROSCIENCES, INC.

DECIDED: November 29, 2005

Before NEWMAN, MAYER, and DYK, Circuit Judges.

Opinion for the court filed PER CURIAM. Dissenting opinion filed by Circuit Judge NEWMAN.

PER CURIAM.

Sibia Neurosciences, Inc. ("Sibia") appeals the decision of the United States Patent and Trademark Office, Board of Patent Appeals and Interferences ("board"), In re Sibia Neurosciences, Inc., Nos. 90/005147 and 90/005326 (Jul. 30, 2004), affirming

the examiner's rejection of claims 15-52 of U.S. Pat. No. 5,401,629 ("the '629 patent") as obvious under 35 U.S.C. § 103. We affirm.

Obviousness is a legal determination based on underlying questions of fact. In re Gartside, 203 F.3d 1305, 1316 (Fed. Cir. 2000). We review the board's conclusions of law de novo and affirm its findings of fact if they are supported by substantial evidence. Id. Findings of fact in an obviousness determination include, inter alia, the presence or absence of a motivation to combine references, id., and what a reference teaches, Para-Ordnance Mfg., Inc. v. SGS Imps. Int'l, Inc., 73 F.3d 1085, 1088 (Fed. Cir. 1995).

Sibia argues that the board erred in finding that U.S. Pat. No. 5,071,773 ("Evans"); U.S. Pat. No. 5,747,336 ("Bonner"); and Sassine-Corsi, et. al., "Induction of proto-oncogene fos transcription through the adenylate cyclase pathway: characterization of a c-AMP responsive element," Genes & Development, Vol. 2 (1988) ("Sassone-Corsi"), render claims 15-52 of the '629 patent obvious. Those claims are directed toward a method for using a reporter gene to identify compounds that modulate the activity of G protein-coupled receptors ("GCPRs"). An increase in cyclic AMP (cAMP) levels is an intermediate step between the GCPR and reporter gene activation. Sibia argues that there is no motivation to combine the three references, that there is no reasonable expectation of success, and that the references do not teach the elements of the claim.

The board determined that the Bonner reference teaches a method for measuring m1 muscarinic receptor activation by measuring changes in cAMP levels. The difference between the Bonner reference and the '629 patent is that Bonner

measured cAMP levels and not the reporter gene product. The reference states that "[t]he functional responses observed for one or more of the receptors include . . . increases or decreases in cyclic AMP levels [which] could form the basis of a functional assay for the screening." Bonner, Col. 5, lines 22-64. Thus, it cannot be said that the board's finding as to what Bonner teaches was not supported by substantial evidence.

The board also determined that the Sassone-Corsi reference teaches treating cells to increase levels of cAMP and then monitoring the effects of the cAMP levels on promoters and reporter genes. The reference covers the steps in the '629 patent between increases in cAMP levels and reporter gene activation. Therefore, the fact that the reference does not discuss GCPRs is irrelevant to its applicability to the step of the '629 patent described.

The board further found that Evans shows the use of reporter genes to monitor receptor activation in general, contrary to Sibia's contention that the reference only shows use of reporter genes to monitor activation of intracellular steroid hormone receptors. The board recognized the difference between GCPRs and steroid hormone receptors, but found that a person skilled in the art would not have considered the difference significant in this context. Thus, substantial evidence supports the finding that Evans provides a motivation to combine Bonner with Sassone-Corsi based on the idea that steroid receptor activation increases reporter gene activity.

Additionally, only a reasonable, not absolute, expectation of success is necessary to support an obviousness rejection. The board's determination that there was a reasonable expectation of success in light of Bonner, Sassone-Corsi, and Evans, as well as the high level of skill in the art, was supported by substantial evidence.

Lastly, secondary considerations of nonobviousness such as long-felt need and commercial success do not overcome the examiner's obviousness finding. Sibia failed to present evidence that its claimed method in the '629 patent met a long-felt need. Further, Sibia's declarations were directed toward the original claims 1-14, not the newly narrowed claims 15-52, and failed to provide the required nexus for nonobviousness based on commercial success. Therefore, substantial evidence supports the board's finding.

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IN RE SIBIA NEUROSCIENCES, INC.

NEWMAN, Circuit Judge, dissenting.

I respectfully dissent. There is no suggestion or motivation in the prior art to make the claimed combination, and no suggestion that, if made, the combination would be successful to achieve the highly useful result that was achieved, for the first time, by these inventors.

The invention is directed to the discovery of chemical/ biological compounds that modulate the activity of a G protein-coupled receptor ("GPCR") on the surface of a cell. The specification teaches that a compound binding to a cell surface GPCR induces a complex cascade of events, including the production of cyclic adenosine monophosphate ("cAMP") and ultimately produces a change in reporter gene expression. The complexity of

this mechanism was oversimplified by the Board, leading the Board to combine, in perfect hindsight, a reference showing that GPCR can cause changes in cAMP, and a reference showing that cAMP can cause changes in reporter gene levels. From these references, the Board adduced the claimed invention. The Board found no evidence of a motivation to combine these references, or any suggestion of an expectation of success in achieving a reliable screening method for compounds that affect GPCR activity.

No such motivation or suggestion can be found in the cited Bonner reference. Bonner describes a particular GPCR receptor that causes changes in cAMP levels, and speculates that such changes "could form the basis of a functional assay" for cAMP, by "standard procedure." The panel majority overstates that Bonner taught any procedure or "measured cAMP levels," for Bonner did neither. Sibia accurately points to the cAMP measuring procedures then known, as "cumbersome," and the statements that such procedures were expected to be replaced by methods that measured bioluminescence or fluorescence indicate that Bonner thus teaches away, not toward, the reporter gene approach of the Sibia invention.

The Sassone-Corsi reference, relied on by the Board as teaching that cAMP can affect reporter genes, contains no suggestion that GPCR receptors can be affected and activity screened with reference to receptor genes. Sassone-Corsi merely explores the relationship between cAMP and reporter gene expression, without any suggestion to apply this teaching to receptor signaling, or that such application would be successful. The majority reasons that because Sassone-Corsi "covers the steps" between Bonner and the Sibia invention, the fact that Sassone-Corsi does not discuss or mention GPCR is "irrelevant." I cannot agree. It is highly relevant that Sassone-Corsi makes no mention of

GPCR activity as related to reporter genes, and it is highly relevant that Bonner makes no mention of possible use of reporter genes to indicate GPCR activity. No reference contains any motivation or suggestion to combine these teachings; that comes only from PTO hindsight using the Sibia disclosure as the template.

Sibia points out that Sassone is a mechanistic study in which cAMP is shown to be responsive to extracellularly applied forskolin, and does not contain any suggestion that receptor-mediated cAMP operating as a secondary messenger could be produced at a sufficient level or be correctly localized so as to function as a signal and thereby be used in a screening method for a large number of candidate molecules. That discovery came from Sibia.

Finally, the Evans reference is clearly inapposite, for it relates to a completely different receptor technology, that of an intracellular receptor. The Board found that this difference is not "significant"; however, this conclusion is without support, as against Sibia's overwhelming showing. The structural and functional differences between intracellular and GPCR receptors are striking. The intracellular steroid receptors in Evans have a DNA binding domain but no trans-membrane domain, whereas GPCRs have a trans-membrane domain but no DNA binding domain. The intracellular steroid receptors localize and form a complex in the nucleus or cytoplasm of the cell, whereas the GPCRs localize and form a complex at the cell surface. The steroid receptors bind *directly* to the promoter of the reporter gene being monitored, whereas the GPCRs induce a complex sequence of events that ultimately results in a change in reporter gene expression -- any missing link in this sequence may result in nonresponsiveness of the reporter gene. Sibia well demonstrated that persons experienced in this field would recognize the large differences between the

receptor studies in Evans and the cell surface receptor mechanisms of the claimed invention, and the absence of predictable interchangeability of methodologies.

In this complex case of biological advance, the Board's decision is not supported by substantial evidence, and should be reversed. From the panel majority's contrary holding, I must respectfully dissent.