

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte SHYAM RAMAKRISHNAN

Appeal No. 2006-3253
Application No. 10/276,547

ON BRIEF

Before SCHEINER, GRIMES, and LINCK, Administrative Patent Judges.

GRIMES, Administrative Patent Judge.

DECISION ON APPEAL

This appeal involves claims to a screening method for identifying candidate therapeutic agents, which the examiner has rejected for lack of patentable utility. We have jurisdiction under 35 U.S.C. § 134. We affirm.

Background

“The family of G-protein coupled receptors (GPCR) includes receptors for hormones, neurotransmitters, growth factors, and viruses.” Page 1, lines 16-18. “The GPCR protein superfamily now contains over 250 types of paralogues, receptors that represent variants generated by gene duplications . . . , as opposed to orthologues, the same receptor from different species.” Page 1, lines 26-28.

The specification discloses a “human dopamine-like G protein-coupled receptor.” Page 8, line 18. “Human DA-like GPCR is 30% identical over 350 amino acids to the D. melanogaster protein . . . annotated as a dopamine 1 receptor precursor.” Page 10, lines 7-9. The disclosed GPCR has the amino acid sequence shown in SEQ ID NO:2. See page 11, lines 7-9.

The specification discloses “assays for screening test compounds which bind to or modulate the activity of a DA-like GPCR polypeptide. . . . A test compound preferably binds to a DA-like GPCR polypeptide.” Page 36, lines 28-31. The specification states that “compounds which activate a GPCR may be employed for therapeutic purposes, such as the treatment of asthma, Parkinson’s disease, acute heart failure, urinary retention, and osteoporosis. In particular, compounds which activate GPCRs are useful in treating various cardiovascular ailments. . . . In addition, these compounds may also be used in treating various physiological disorders relating to abnormal control of fluid and electrolyte homeostasis.” Page 49, lines 1-8.

The specification also states that

regulation of DA-like GPCR can be used to treat anxiety, depression, hypertension, migraine, compulsive disorders, schizophrenia, autism, neurodegenerative disorders, such as Alzheimer’s disease, Parkinsonism, and Huntington’s chorea, and cancer chemotherapy-induced vomiting, as well as sleep and eating disorders, pain control, disorders involving regulation of body temperature and blood pressure.

. . . [A]gents which modulate this gene . . . or its products are useful for treating obesity, overweight, anorexia, cachexia, wasting disorders, appetite suppression, appetite enhancement, increases or decreases in satiety, modulation of body weight, and/or other eating disorders such as bulimia.

Page 49, lines 20-29.

The specification also states that

[A]gents which modulate this gene . . . or its products are useful for treating obesity/overweight-associated comorbidities including hypertension, type 2 diabetes, coronary artery disease, hyperlipidemia, stroke, gallbladder disease, gout, osteoarthritis, sleep apnea and respiratory problems, some types of cancer . . . , thrombotic disease, polycystic ovarian syndrome; reduced fertility, complications of pregnancy, menstrual irregularities, hirsutism, stress incontinence, and depression.

Page 50, lines 13-20.

The specification also states that “[h]uman DA-like GPCRs provide a potential target for treating cancer.” Page 50, line 22. Finally, the specification states that

[d]iabetes also can be potentially treated by regulating the activity of human DA-like GPCR. . . .

Type 1 diabetes is initiated by an autoimmune reaction that attacks the insulin secreting cells (beta cells) in the pancreatic islets. Agents that prevent this reaction . . . are potential therapies for this disease. Other agents that induce beta cell proliferation and regeneration are also potential therapies.

Type II diabetes is the most common of the two diabetic conditions. . . . Therapies that increase the response by the beta cell to glucose would offer an important new treatment for this disease.

The defect in insulin action in Type II diabetic subjects is another target for therapeutic intervention. Agents that increase the activity of the insulin receptor in muscle, liver and fat will cause a decrease in blood glucose. . . . Other therapies can directly activate the cellular end product . . . to generate an insulin-like effect and therefore [] produce [a] beneficial outcome. Because overweight subjects have a greater susceptibility to Type II diabetes, any agent that reduces body weight is a possible therapy.

Both Type I and Type [II] diabetes can be treated with agents that mimic insulin action or that treat diabetic complications by reducing blood glucose levels.

Page 51, line 28, to page 52, line 29.

The specification includes several prophetic examples and one example (Example 15) that appears to have been actually carried out.¹ That example reports the “[t]issue-specific expression of Dopamine-like GPCR.” Page 75, line 3. See Table 1 (page 77). The specification reports: “Relative[ly] high expression is detected in Alzheimer’s brain compared to normal brain and in cancer tissue compared to the corresponding normal tissue.” Page 77, lines 5-7.

Discussion

1. Claims

Claims 102 and 104 are pending and on appeal, and read as follows:

102. A method of screening for candidate therapeutic agents, comprising the steps of:

contacting a protein comprising the amino acid sequence shown in SEQ ID NO:2 with a test compound, wherein either the test compound or the protein comprises a detectable label;

assaying for binding between the protein and the test compound; and

identifying a test compound that binds to the protein as a candidate therapeutic agent that may be useful for regulating activity of the protein.

104. The method of claim 102 wherein either the test compound or the protein is bound to a solid support.

The claims are directed to a method of assaying test compounds to determine whether they bind to the human DA-like GPCR of SEQ ID NO:2, where binding of the compound to the protein is said to “identify[] a test compound . . . as a candidate therapeutic agent that may be useful for regulating activity of the protein.”

¹ Example 15 switches between present tense and past tense, so it is not completely clear that it represents a working, rather than prophetic, example. Since the example includes what appear to be actual data, however, we will presume that the experiment described was actually carried out.

2. Utility

The examiner rejected claims 102 and 104 under 35 U.S.C. §§ 101 and 112, first paragraph, as lacking patentable utility. The examiner reasoned that

[t]he instant application does not disclose a specific biological role for this protein or its significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect. Therefore, the instant claimed method of screening for compounds that bind to the protein of unknown physiological significance as potential candidate therapeutic agents does not meet the requirements of 35 U.S.C. § 101 as being useful.

Examiner's Answer, page 3.

With respect to the similarity of SEQ ID NO:2 to a protein from Drosophila melanogaster, the examiner noted that "since the specific biological role of the Drosophila dopamine 1 receptor precursor protein is currently unknown, there appears to be no scientific reason to assign any particular function to the instant protein of SEQ ID NO:2 based solely on their limited structural similarity." Id., page 5. Finally, the examiner concluded that "[w]ithout knowledge of the natural ligand of the claimed DA-like GPCR, one would not know the specific pathway that is regulated by this instant GPCR, and, consequently, [would] not be able to use the claimed polypeptide [sic, agonist or antagonist of the polypeptide] to regulate any physiological function." Id., page 6.

We agree with the examiner that the specification does not disclose a patentable utility for the "candidate therapeutic agents" identified via the claimed screening method, and that, therefore, the claimed method lacks patentable utility. The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement. See In re Fisher, 421 F.3d 1365, 76 USPQ2d 1225 (Fed. Cir. 2005). The Fisher court held that

§ 101 requires a utility that is both substantial and specific. Id. at 1371, 76 USPQ2d at 1229.

The court held that disclosing a substantial utility means “show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the ‘substantial’ utility requirement, an asserted use must show that that claimed invention has a significant and presently available benefit to the public.” Id., 76 USPQ2d at 1230. A specific utility is “a use which is not so vague as to be meaningless.” Id. In other words, “in addition to providing a ‘substantial’ utility, an asserted use must show that th[e] claimed invention can be used to provide a well-defined and particular benefit to the public.” Id.

In this case, the specification lays out a laundry list of conditions that might involve the polypeptide of SEQ ID NO:2. The specification provides no guidance, however, that would lead the skilled artisan to conclude that SEQ ID NO:2 is likely to be involved with any particular one of the disclosed conditions. The specification provides little evidence linking the activity of the protein of SEQ ID NO:2 with any of the listed conditions. Thus, the specification provides inadequate evidence to show that a compound that binds the protein of SEQ ID NO:2 would be useful in treating any of the listed conditions.

Those skilled in the art would conclude that the specification does not disclose a substantial utility for the claimed method; i.e., an invention that is useful to the public in its current form, rather than potentially useful in the future after further research. See Fisher, 421 F.3d at 1371, 76 USPQ2d at 1230. We agree with the examiner that the specification does not disclose a substantial, credible utility for the claimed method.

Appellant argues the Geerts declaration² and the Soga reference³ provide “data [that] confirms the specification’s teaching of the protein’s utility: ‘Diabetes also can be potentially treated by regulating the activity of human DA-like GPCR.’” Appeal Brief, page 5 (quoting the specification at page 51, lines 28-29). Specifically, Appellant points to the declaration and the reference as evidence that compounds that bind the protein of SEQ ID NO:2 would potentially be useful in treating diabetes.

We do not agree with Appellant’s position. The Geerts declaration provides tissue-specific expression data similar to that of the specification’s Table 1. ¶ 9 and Exhibit 1. The data in the Geerts declaration show relative expression levels in different tissue samples. The relative level of expression in pancreas is 138. Exhibit 1, page 3. Equal or higher expression levels are shown for 47 of the 136 tissue samples tested. Id., pages 1-6. Ten of the tissue samples showed relative expression levels of over 1000. Id. The declarant concludes that “[t]he data show high expression levels in pancreas. This differential expression in pancreas makes the target protein useful for screening compounds for the treatment of diabetes.” ¶ 9.

While declaratory evidence as to issues of fact is entitled to substantial weight, In re Alton, 76 F.3d 1168, 37 USPQ2d 1578 (Fed. Cir. 1996), “[a]n expert opinion is no better than the soundness of the reasons supporting it.” Perreira v. Secretary of the Dept. of HHS, 33 F.3d 1375, 1377 (Fed. Cir. 1994). In this case, the declarant provided no scientific basis for his conclusion that a relative expression level of 138, lower than 46 of the 136 tested samples, means that the protein of SEQ ID NO:2 is “useful for

² Declaration of Andreas Geerts submitted under 37 CFR § 1.132, filed April 21, 2005.

³ Soga et al., “Lysophosphatidylcholine enhances glucose-dependent insulin secretion via an orphan G-protein-coupled receptor,” Biochem. Biophys. Res. Comm., Vol. 326, pp. 744-751 (2005).

screening compounds for the treatment of diabetes.” No such reason is apparent to us: the expression level in pancreas does not seem unusually high compared to many of the other tested samples, and even if the protein had been overexpressed in pancreas, pancreas-specific expression does not necessarily mean the protein is involved in diabetes. The conclusion of the Geerts declaration is not supported by the evidence or by sound scientific reasoning; therefore, we do not find it credible.

Appellant also cites the Soga reference as evidence that the protein of SEQ ID NO:2 is involved in diabetes. Appellant notes that Soga teaches that a protein called GPR119 is expressed in pancreas and involved in glucose-dependent insulin secretion. See the Appeal Brief, page 6. According to Appellant, human GPR119 and the protein of SEQ ID NO:2 have identical amino acid sequences. See id., paragraph bridging pages 5 and 6. Thus, Appellant asserts, “Soga is strong evidence that one skilled in the art would find credible the specification’s asserted utility for the recited protein.” Id., page 7.

Soga was published in 2005. The instant application claims an effective filing date of May 18, 2000. “Enablement, or utility, is determined as of the application filing date.” In re Brana, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995). Appellant has provided no evidence to show that the evidence disclosed by Soga in 2005 was available to those skilled in the art as of May 18, 2000. Therefore, Soga’s statement that GPR119 “is a potential target for anti-diabetic drug development” cannot be relied on to show the utility of the protein of SEQ ID NO:2.

Appellant argues, however, that Soga is being relied on merely as evidence supporting the utility asserted in the specification as filed. See the Appeal Brief, page 7

(footnote 5). Appellant cites In re Langer, 503 F.2d 1380, 1391, 183 USPQ 288, 297 (CCPA 1974), and In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 370 n.4 (CCPA 1971), as supporting the use of post-filing evidence to “show that the specification’s assertion of utility – a fact – is credible.” Id.

It is true that post-filing evidence can be relied on for certain purposes. See Gould v. Quigg, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1305 (Fed. Cir. 1987):

[A] later dated publication cannot supplement an insufficient disclosure in a prior dated application to render it enabling. . . . [However, a later publication can be used] as evidence of the level of ordinary skill in the art at the time of the application and as evidence that the disclosed device would have been operative. Compare In re Hogan, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977) (‘This court has approved use of later publications as evidence of the state of the art existing on the filing date of an application.’ (footnotes omitted) (emphasis in original)) with In re Glass, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974) (later publications which add to the knowledge of the art cannot be used to supplement an insufficient disclosure).

As the Glass court put it: “It is an applicant’s obligation to supply enabling disclosure without reliance on what others may publish after he has filed an application on what is supposed to be a completed invention. If he cannot supply enabling information, he is not yet in a position to file.” Glass, 492 F.2d at 1232, 181 USPQ at 34. The Glass court addressed the enablement requirement of § 112, but the same rule applies to the utility requirement of § 101. Brana, 51 F.3d at 1567 n.19, 34 USPQ2d at 1441 n.19 (both enablement and utility determined as of application’s filing date).

It is true that the present specification states that “[d]iabetes also can be potentially treated by regulating the activity of human DA-like GPCR.” Page 51, lines 28-29. However, those skilled in the art would not have found the asserted utility to be credible based on the evidence of record at the time of filing. The specification

states that compounds having certain properties might be useful for treating Type I or Type II diabetes but provides no evidence that either the protein of SEQ ID NO:2 or compounds that bind to it have those properties or reasonably would have been expected to have them.

The specification states that Type I diabetes can potentially be treated with agents that prevent the underlying autoimmune reaction or that “induce beta cell proliferation and regeneration.” Page 52, lines 5-9. The specification states that Type II diabetes can potentially be treated with agents “that increase the response by the beta cell to glucose,” that “increase the activity of the insulin receptor in muscle, liver and fat,” or that “directly activate the cellular end product . . . to generate an insulin-like effect,” as well as by “any agent that reduces body weight.” Page 52, lines 11-26. The specification also states that “[b]oth Type I and Type [II] diabetes can be treated with agents that mimic insulin action or that treat diabetic complications by reducing blood glucose levels.” Page 52, lines 28-29.

The evidence of record, however, does not show that the protein of SEQ ID NO:2 or compounds that bind to it were recognized as having any of these properties, or reasonably would have been expected to have any of these properties, as of the effective filing date. The only evidence apparent in the specification that would be relevant to diabetes is in Table 1 (page 77). Table 1 shows that the protein of SEQ ID NO: 2 has a relative expression level of 240.57 in pancreas (compared to 1.00 in “spleen liver cirrhosis” and 2499.15 in “uterus”). The examiner has not disputed the accuracy of the expression data, but even assuming that Table 1 represents actual,

accurate data, the expression data do not credibly support the asserted utility for the reasons discussed above.

Appellant cites In re Langer, 503 F.2d 1380, 183 USPQ 288 (CCPA 1974), as supporting the use of post-filing evidence to support “the specification’s assertion of utility – a fact.” Appeal Brief, page 7, n.5. The facts of this case, however, distinguish it from Langer.

The claims in Langer were directed to products and methods for inhibiting dental cavities with stannous chelates such as Sn₂EDTA (distannous ethylenediaminetetraacetic acid). See 503 F.2d at 1386, 183 USPQ at 293. The specification stated that the claimed products prevented dental cavities and provided working examples showing, among other things, that rats having the claimed toothpaste composition applied to their teeth experienced a 40% reduction in cavities compared to control rats. See id. at 1385-1386, 183 USPQ at 292-293.

The examiner rejected the claims for lack of utility, citing several references that taught that stannous chelates were not effective in preventing cavities, and the applicant filed an affidavit providing toxicity data and confirming several of the working examples in the specification. See id. at 1387, 183 USPQ at 294. The court considered the evidence and concluded that

the in vivo dental paste experiment (employing standard experimental animals) described in [the applicant’s] affidavit, which verifie[d] Example 16 of appellant’s specification, is sufficient to rebut the prima facie case and prove utility to one skilled in the art for Sn₂EDTA.

Id. at 1393, 183 USPQ at 298.

Most relevant here is the Langer court's treatment of the references cited by the examiner. The court noted that the examiner's references were not cited as "prior art" and, in fact, many had been published after the effective filing date of the application. The court nonetheless held that the "references [we]re properly cited for the purpose of showing a fact under the principle of In re Wilson, . . . 311 F.2d 266, 135 USPQ 442 ([CCPA] 1962)." Id. at 1391, 183 USPQ at 296-97.

The claims in Wilson defined a method of making polyurethane foam: the applicants claimed that a foam with an open cell structure could be formed by combining all the required components except water and allowing them to react for at least thirty seconds before adding the water. Wilson, 311 F.2d at 267, 135 USPQ at 443. The examiner cited a reference ("the DuPont publication") as evidence that an open cell structure was a normal characteristic of polyurethane foams. See id. at 268, 135 USPQ at 444. The court concluded that "the publication was properly cited to show a state of fact. . . . As evidence of the characteristics of prior art foam products, . . . we know of no reason in law why it is not acceptable." Id. at 268, 135 USPQ at 444.

Here, by comparison, the specification discloses the following characteristics of the human DA-like GPCR used in the claimed method: (1) it has the amino acid sequence shown in SEQ ID NO:2; (2) it is "30% identical over 350 amino acids to the D. melanogaster protein . . . annotated as a dopamine 1 receptor precursor" (specification, page 10); and (3) it has the tissue-specific expression pattern shown in Table 1.

The examiner has not disputed any of these factual assertions, and Appellant does not rely on the post-filing evidence to prove any of these facts. Rather, Appellant relies on the post-filing evidence to further characterize the protein of SEQ ID NO:2:

- “Soga . . . teaches a murine GPCR, ‘GPR119.’ . . . [T]he amino acid sequence of human GPR119 . . . is 100% identical to the amino acid sequence of SEQ ID NO:2” (Appeal Brief, pages 5-6);
- “Soga teaches that mouse GPR119 polynucleotide, like the polynucleotide that encodes SEQ ID NO:2, is expressed in the pancreas” (Appeal Brief, page 6);
- “Soga teaches that GPR119 is involved in glucose-dependent insulin secretion. . . . Soga suggests that, because GPR119 is involved in glucose-dependent insulin secretion . . . it is a likely target for diabetes therapy” (Appeal Brief, page 6).

The instant specification does not disclose that the protein of SEQ ID NO:2 is similar to a murine protein (GPR119) that is involved in glucose-dependent insulin secretion. Nor does the specification disclose the tissue-specific expression pattern shown in Soga’s Figure 4: Soga shows that GPR119 is expressed in pancreas at a level at least five times higher than in any tissue tested, and not expressed at all in uterus (Fig. 4A). The instant specification’s Table 1, by contrast, shows that the protein of SEQ ID NO:2 is expressed abundantly in spleen, stomach, small intestine, and skeletal muscle, as well as pancreas, and is expressed in uterus at a level over ten times as high as in pancreas.

Appellant is not citing Soga “as evidence of the state of the art existing on the filing date of an application,” In re Hogan, 559 F.2d at 605, 194 USPQ at 537, but for its disclosure of knowledge that became available to those skilled in the art only after the filing date of the instant application. Appellant seeks to rely on the later-published reference in order to bolster the evidence that SEQ ID NO:2 is likely to be useful in identifying diabetes treatments. A later-published reference cannot be relied on for such a purpose:

It is an applicant’s obligation to supply enabling disclosure without reliance on what others may publish after he has filed an application on what is

supposed to be a completed invention. If he cannot supply enabling information, he is not yet in a position to file.

Glass, 492 F.2d at 1232, 181 USPQ at 34. An “enabling disclosure” must include a utility that satisfies § 101. See In re Fisher, 421 F.3d 1365, 1378, 76 USPQ2d 1225, 1235 (Fed. Cir. 2005) (“It is well established that the enablement requirement of § 112 incorporates the utility requirement of § 101.”); In re Kirk, 376 F.2d 936, 942, 153 USPQ 48, 53 (CCPA 1967) (“[S]urely Congress intended § 112 to pre-suppose full satisfaction of the requirements of § 101. Necessarily, compliance with § 112 requires a description of how to use presently useful inventions, otherwise an applicant would anomalously be required to teach how to use a useless invention.”).

Appellant has argued that Langer applies because the specification’s assertion of utility is an issue of fact. Appeal Brief, page 7, n.5. Whether a claimed invention is supported by a patentable utility is indeed a question of fact, not law. Newman v. Quigg, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed. Cir. 1989) (“Utility under 35 U.S.C. § 101 is a question of fact.”). No case that we are aware of, however, has held that post-filing evidence can be relied on with respect to any issue that is considered a question of fact rather than one of law. Such a rule would do nothing to encourage the full, enabling disclosure that is “[t]he sine qua non of a valid patent.” White Consolidated Inds., Inc. v. Vega Servo-Control, Inc., 713 F.2d 788, 791, 218 USPQ 961, 963 (Fed. Cir. 1983).

Rather, it would encourage applications based on speculation. In the biotech context, inventors would be rewarded for filing applications that disclose a protein and assert that it is useful for treating diseases, and listing every disease the inventor can

think of. The inventor could then hope that evidence could be developed later to show that one of the guesses was right, and submit the later-arising data as evidence “confirming” the statement of utility in at least one respect.

The purpose of the patent system is to encourage innovation, not speculation. If an inventor cannot disclose at least one specific, substantial, and credible utility for a claimed invention, he is not ready to file a patent application. Cf. Glass, 492 F.2d at 1232, 181 USPQ at 34 (“It is an applicant’s obligation to supply enabling disclosure without reliance on what others may publish after he has filed an application on what is supposed to be a completed invention. If he cannot supply enabling information, he is not yet in a position to file.”).

In the words of the Supreme Court, “what now seems without ‘use’ may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” Brenner v. Manson, 383 U.S. 519, 536, 148 USPQ 689, 696 (1966).

Summary

The specification does not disclose a substantial, credible utility for the compounds identified in the claimed method, and Appellant cannot rely on post-filing evidence to bolster the specification's disclosure. The rejections under 35 U.S.C. §§ 101 and 112, first paragraph are affirmed.

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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