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for publication and is not binding precedent of the Board.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 SE-JIN LEE

Appeal No. 2004-1346[1]
Application No. 08/971,338

ON BRIEF

Before WINTERS, ADAMS and MILLS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 4-10 and 22-33, which are all the claims pending in the application.

Claim 9 is illustrative of the subject matter on appeal and is reproduced below:

9. A recombinantly produced GDF-1 protein having the GDF-1 amino acid sequence given in Figure 2, 11A or 11B.

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[1] Appellant identifies (Brief, page 1), Application No. 08/966,233, Appeal No. 2004-1369 as a related divisional application of the instant application. In addition, we note that the Brief and Answer are essentially the same in both applications on appeal. Accordingly, we have considered these two appeals together.

The references relied upon by the examiner are:

Akhurst, et al. (Akhurst), "Transforming Growth Factor Betas in Mammalian Embryogenesis," Progress in Growth Factor Research, Volume 2, pages 153-168 (1990)

Ernfors, et al. (Ernfors), "Molecular cloning and neurotrophic activities of a protein with structural similarities to nerve growth factor: Developmental and topographical expression in the brain," Proceedings of the National Academy of Sciences, Volume 87, pages 5454-5458 (1990)

Massague, "The Transforming Growth Factor-β Family," Annual Review of Cell Biology, Volume 6, pages 597-641 (1990)

Hoban, et al. (Hoban), "Activation of Second Messenger Pathways by GDF-1," Society for Neuroscience Abstracts, Volume 19, page 653, Abst. No. 275.9, (1993)

Ebendal, et al. (Ebendal '95), "Glial Cell Line-Derived Neurotrophic Factor Stimulates Fiber Formation and Survival in Cultured Neurons From Peripheral Autonomic Ganglia," Journal of Neuroscience Research, Volume 40, pages 276-284 (1995)

Krieglstein, et al. (Krieglstein), "Distinct Modulatory Actions of TGF-β and LIF on Neurotrophin-Mediated Survival of Developing Sensory Neurons," Neurochemical Research, Volume 21, Number 7, pages 843-850 (1996)

Bengtsson, et al. (Bengtsson), "Potentiating Interactions Between Morphogenetic Protein and Neurotrophic Factors in Developing Neurons," Journal of Neuroscience Research, Volume 53, pages 559-568 (1998)

Ebendal, et al. (Ebendal '98), "Bone Morphogenetic Proteins and Their Receptors: Potential Functions in the Brain," Journal of Neuroscience Research, Volume 51, pages 139-146 (1998)

Rankin, et al. (Rankin), "Regulation of left-right patterning in mice by growth/differentiation factor-1," Nature Genetics, Volume 24, pages 262-265 (2000)

GROUNDS OF REJECTION

Claims 4-10 and 22-33 stand rejected under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph, for lack of enablement based on the finding of lack of utility.

Claims 4-7, 22, 24, 25 and 28-30 stand rejected under 35 U.S.C. § 112, first paragraph, as based on a specification which fails to adequately describe the claimed invention.

We affirm the utility rejection under 35 U.S.C. § 101 as lacking utility and § 112, first paragraph. Having disposed of all claims on appeal, we do not reach the merits of the rejection under the written description provision of 35 U.S.C. § 112, first paragraph[2].

BACKGROUND

"The present invention relates, in general, to DNA segments encoding proteins of the transforming growth factor superfamily. In particular, the present invention relates to a DNA segment encoding GDF-1…." Specification, page 1. "The GDF-1 gene was isolated by virtue of its homology to the transforming growth factor beta (TGF- β) superfamily." Brief, page 2. Accordingly, appellant asserts (id.), "[p]otential uses for GDF-1 as a therapeutic and diagnostic tool are suggested based on the known biological activities of other members of this superfamily…."[3]

In this regard, we note that appellant discloses (specification, page 20), "GDF-1 is most homologous to VG-1 (52% and least homologous to inhibin-α

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[2] For clarity, we note that appellant characterizes this issue as comprising two parts, (1) a written description rejection of claims 4-7, 22, 24, 25, 30, 34 and 35; and (2) a new matter rejection of claims of claims 34 and 35. See Brief, pages 5-6. According to the examiner (Answer, page 3), however,

> [c]laims 4-7, 22, 24, 25 and 28-30 are rejected under 35 U[.]S[.]C[. §] 112[, first paragraph] with respect to written description. Claims 34 and 35 were particularly addressed with respect to new matter ….

However, contrary to appellant's characterization, claims 34 and 35 were not separated from the rejection of claims 4-7, 22, 24, 25 and 28-30 in this ground of rejection.

[3] In this regard, we note that according to the examiner (Answer, page 6), "the specification discloses that the activities of the members of the TFG-β [sic] superfamily vary quite widely. (See specification at pages 1-2 and 12-15.)[.]"

(22%) and the TGF-β's (26-30%)." However, as the examiner points out (Answer, page 21), despite appellant's emphasis on the structural similarity of GDF-1 to members of the TGF-β superfamily, the similarity accounts for less than half of the GDF-1 protein. In other words, only about 107 of GDF-1's 357 amino acids share similarity with TGF-β. While GDF-1 is disclosed by appellant to be least homologous to the TGF-β superfamily appellant discloses (specification, page 12),

> The TGF-β superfamily encompasses a group of proteins affecting a wide range of differentiation processes. The structural homology between GDF-1 and the known members of the TGF-β superfamily and the pattern of expression [of] GDF-1 during embryogenesis indicate that GDF-1 is a new member of this family of growth and differentiation factors. Based on the known properties of the other members of the [sic] this superfamily, GDF-1 can be expected to possess biological properties of diagnostic and/or therapeutic benefit in a clinical setting.

However, as set forth in the specification (page 14), "[a] determination of the specific clinical settings in which GDF-1 will be used as a diagnostic or as a therapeutic tool await further characterization of the expression patterns and

biological properties of GDF-1 both under normal physiological conditions and during disease states."

DISCUSSION

Utility:

According to appellant (Brief, page 6), "[c]laims 4-10 and 22-33 may be considered together with regard to the utility and enablement (how to use) arguments." We understand this statement to mean that claims 4-10 and 22-33 stand or fall together. Since all claims stand or fall together, we limit our discussion to representative independent claim 9. Claims 4-8, 10 and 22-33 will stand or fall together with claim 9. In re Young, 927 F.2d 588, 590, 18 USPQ2d 1089, 1091 (Fed. Cir. 1991).

The examiner bears the initial burden of showing that a claimed invention lacks patentable utility. See In re Brana, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995) ("Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince such a person of the invention's asserted utility."). In our opinion, the examiner has met her burden of showing that the claimed invention lacks patentable utility, and we adopt the examiner's reasoning as our own. The remainder of our discussion serves to emphasize the evidentiary basis supporting our decision to affirm the examiner.

The seminal decision interpreting the utility requirement of § 101 is Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (1966). At issue in Brenner

was a claim to "a chemical process which yields an already known product whose utility—other than as a possible object of scientific inquiry—ha[d] not yet been evidenced." Id. at 529, 148 USPQ at 693. The Patent Office had rejected the claimed process for lack of utility, on the basis that the product produced by the claimed process had not been shown to be useful. See id. at 521-22, 148 USPQ at 690. On appeal, the Court of Customs and Patent Appeals reversed, on the basis that "where a claimed process produces a known product it is not necessary to show utility for the product." Id. at 522, 148 USPQ at 691.

The Brenner Court noted that although § 101 requires that an invention be "useful," that "simple, everyday word can be pregnant with ambiguity when applied to the facts of life." Id. at 529, 148 USPQ at 693. Thus,

> [it] is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry, where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility"—if that word is given its broadest reach.

Id. at 530, 148 USPQ at 694.[4]

The Court, finding "no specific assistance in the legislative materials underlying § 101," based its analysis on "the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other." Id. at 532, 148 USPQ at 695. The Court concluded that "[t]he basic quid pro quo contemplated by the Constitution and the Congress for granting a patent

[4] The invention at issue in Brenner was a process, but the Court expressly noted that its holding "would apply equally to the patenting of the product produced by the process." Id. at 535, 148 USPQ at 695-96.

monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point—where specific benefit exists in currently available form—there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." Id. at 534-35, 148 USPQ at 695.

The Court considered and rejected the applicant's argument that attenuating the requirement of utility "would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge." The Court noted that, while there is value to encouraging disclosure, "a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development." Id. at 534, 148 USPQ at 695.

The Court took pains to note that it did not "mean to disparage the importance of contributions to the fund of scientific information short of the invention of something 'useful,'" and that it was not "blind to the prospect that what now seems without 'use' may tomorrow command the grateful attention of the public." Id. at 535-36, 148 USPQ at 696. Those considerations did not

sway the Court, however, because "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion." Id.

Subsequent decisions of the CCPA and the Court of Appeals for the Federal Circuit have added further layers of judicial gloss to the meaning of § 101's utility requirement. The first opinion of the CCPA applying Brenner was In re Kirk, 376 F.2d 936, 153 USPQ 48 (CCPA 1967). The invention claimed in Kirk was a set of steroid derivatives said to have valuable biological properties and to be of value "in the furtherance of steroidal research and in the application of steroidal materials to veterinary or medical practice." Id. at 938, 153 USPQ at 50. The claims had been rejected for lack of utility. In response, the applicants submitted an affidavit which purportedly "show[ed] that one skilled in the art would be able to determine the biological uses of the claimed compounds by routine tests." Id. at 939, 153 USPQ at 51.

The court held that "nebulous expressions [like] 'biological activity' or 'biological properties'" did not adequately convey how to use the claimed compounds. Id. at 941, 153 USPQ at 52. Nor did the applicants' affidavit help their case: "the sum and substance of the affidavit appear[ed] to be that one of ordinary skill in the art would know 'how to use' the compounds to find out in the first instance whether the compounds are—or are not—in fact useful or possess useful properties, and to ascertain what those properties are." Id. at 942, 153 USPQ at 53.

The Kirk court held that an earlier CCPA decision, holding that a chemical compound meets the requirements of § 101 if it is useful to chemists doing

research on steroids, had effectively been overruled by Brenner. "There can be no doubt that the insubstantial, superficial nature of vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher' was recognized, and clearly rejected, by the Supreme Court" in Brenner. See Kirk, 376 F.2d at 945, 153 USPQ at 55.

More recently, in In re Ziegler, 992 F.2d 1197, 26 USPQ2d 1600 (Fed. Cir. 1993), the Federal Circuit considered the degree of specificity required to show utility for a claim to polypropylene. The U.S. application on appeal in Ziegler claimed priority to a German application filed in 1954. "In the German application, Ziegler disclosed only that solid granules of polypropylene could be pressed into a flexible film with a characteristic infrared spectrum and that the polypropylene was 'plastic-like.'" Id. at 1203, 26 USPQ2d at 1605. "Ziegler did not assert any practical use for the polypropylene or its film, and Ziegler did not disclose any characteristics of the polypropylene or its film that demonstrated its utility." Id. The court held that the German application did not satisfy the requirements of § 101 and therefore could not be relied on to overcome a rejection based on an intervening reference. See id., 26 USPQ2d at 1606. "[At] best, Ziegler was on the way to discovering a practical utility for polypropylene at the time of the filing of the German application; but in that application Ziegler had not yet gotten there." Id., 26 USPQ2d at 1605.

On the other hand, the CCPA reversed a rejection for lack of utility in In re Jolles, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). The applicant in Jolles claimed pharmaceutical compositions that were disclosed to be useful in treating

acute myeloblastic leukemia. See id. at 1323, 206 USPQ at 886. The active ingredients in the compositions were closely related to daunorubicin and doxorubicin, both of which were "well recognized in the art as valuable for use in cancer chemotherapy." Id., 206 USPQ at 887. The applicant also submitted declaratory evidence showing that eight of the claimed compositions were effective in treating tumors in a mouse model, and one was effective in treating humans. See id. at 1323-24, 206 USPQ at 887-88. The court noted that the data derived from the mouse model were "relevant to the treatment of humans and [were] not to be disregarded," id. at 1327, 206 USPQ at 890, and held that the evidence was sufficient to support the asserted therapeutic utility. See id. at 1327-28, 206 USPQ at 891.

The Federal Circuit held in Cross v. Iizuka, 753 F.2d 1040, 224 USPQ 739 (Fed. Cir. 1985), that in vivo testing (as in Jolles) was not necessarily required to show utility in the pharmaceutical context. The Cross court stated that "[it] is axiomatic that an invention cannot be considered 'useful,' in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious." Id. at 1044, 224 USPQ at 742 (citing Brenner v. Manson). The court "perceive[d] no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, in vitro testing, may establish a practical utility for the compound in question." Id. at 1051, 224 USPQ at 748. Successful in vitro testing could provide an immediate benefit to the public, by "marshal[ling] resources and direct[ing] the expenditure of effort to further in vivo testing of the

most potent compounds . . ., analogous to the benefit provided by the showing of an in vivo utility." Id. On the facts of that case – successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds – the court held that in vitro activity was sufficient to meet the requirements of § 101. See id.

The Federal Circuit confirmed in In re Brana, 51 F.3d 1560, 34 USPQ2d 1436 (Fed. Cir. 1995), that human testing is not necessary to establish utility for a method of treatment. The invention claimed in Brana was a group of compounds disclosed to have antitumor activity. See id. at 1562, 34 USPQ2d at 1437-38. The claimed compounds were disclosed to have higher antitumor activity than related compounds known to have antitumor activity, and the applicants provided declaratory evidence of in vivo activity against tumors in a mouse model. See id., 34 USPQ2d at 1438. The court held that these data were sufficient to satisfy § 101; usefulness in patent law does not require that the invention be ready to be administered to humans. See id. at 1567, 34 USPQ2d at 1442.

Several lessons can be drawn from Brenner and its progeny. First, § 101's requirement that an invention be "useful" is not to be given its broadest reach, such that little or nothing of a chemical nature would be found to lack utility. See Brenner, 383 U.S. at 530, 148 USPQ at 694. Thus, not every "use" that can be asserted will be sufficient to satisfy § 101. For example, the steroid compound at issue in Brenner was useful as a possible object of scientific inquiry, and the polypropylene claimed in Ziegler was useful for pressing into a

flexible film, yet both lacked sufficient utility to satisfy § 101. See Brenner, 383 U.S. at 529, 148 USPQ at 696; Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

Rather than setting a de minimis standard, § 101 requires a utility that is "substantial", i.e., one that provides a specific benefit in currently available form. Brenner, 383 U.S. at 534-35, 148 USPQ at 695. This standard has been found to be met by pharmaceutical compositions shown to be useful in mouse models and in humans for treating acute myeloblastic leukemia (Jolles, 628 F.2d at 1327-28, 206 USPQ at 891); by evidence showing successful in vitro testing supplemented by similar in vitro and in vivo activities of structurally similar compounds (Cross, 753 F.2d at 1051, 224 USPQ at 748); and by evidence showing in vivo antitumor activity in mice, combined with a disclosure that the claimed compounds had higher antitumor activity than a related compound known to have antitumor activity (Brana, 51 F.3d at 1567, 34 USPQ2d at 1442).

By contrast, Brenner's standard has been interpreted to mean that "vague, general disclosures or arguments of 'useful in research' or 'useful as building blocks of value to the researcher'" would not satisfy § 101. See Kirk, 376 F.2d at 945, 153 USPQ at 55 (interpreting Brenner). Likewise, a disclosure of a "plastic-like" polypropylene capable of being pressed into a flexible film was held to show that the applicant was "at best . . . on the way to discovering a practical utility for polypropylene at the time of the filing," but not yet there. Ziegler, 992 F.2d at 1203, 26 USPQ2d at 1605.

On this record, the examiner finds (Answer, page 5),

> [t]he protein products lack patentable utility for the reasons set forth below. Without knowing how to use the end product, the process

> for purification of GDF-1 proteins (claims 24-30) also lacks patentable utility.

According to the examiner (Answer, page 8),

> [t]he specification speculates on possible activities of GDF-1. None of the particular activities disclosed for other TGF-β superfamily members have been demonstrated for this protein in the specification and none were known at the time of the invention. None of the uses set forth in the specification could be practiced at the time of the invention without undue experimentation. Providing a laundry list of potential uses [as set forth in appellant's specification], some of which are diametrically opposed to each other, is not deemed to be enabling.

To emphasize the "laundry list" of potential uses set forth in appellant's specification the examiner reproduces portions of appellant's disclosure found at pages 1, 2, 12-15, and 20 into the answer. See Answer, pages 8-13. For example, the portions of appellant's specification reproduced by the examiner identify several potential uses for GDF-1 including, inter alia, "as a specific marker for the presence of tumors arising from cell types that normally express GDF-1" (specification, page 12; Answer, page 10); "as an indicator for the presence of developmental anomalies in prenatal screens for potential birth defects" (id.); and "in prenatal screens for genetic diseases that either directly correlate with the expression or function of GDF-1 or are closely linked to the GDF-1 gene" (specification, page 13; Answer, page 11). Nevertheless, despite the assertion of "potential uses for GDF-1" appellant admits (specification, page 14; Answer, page 12), "[a] determination of the specific clinical settings in which GDF-1 will be used as a diagnostic or as a therapeutic tool await further characterization of the expression patterns and biological properties of GDF-1 both under normal physiological conditions and during disease states."

After what appears to be a comprehensive review of appellant's disclosure, the examiner finds (Answer, page 14),

> the specification does not enable using GDF-1 in any capacity without undue experimentation. Again, the specification is an invitation to experiment without clear direction or guidance as to the particular biological activity to investigate. Embryogenesis and mediation of cell differentiation are broad areas of basic research. No tumors nor developmental defects are identified as being associated for any screening or diagnostic methods. No normal or abnormal levels for GDF-1 are disclosed in the specification for any cell type or tissue. No direction or guidance as to particular known tumors or known developmental defects to be investigated are provided.

In response, appellant presents several different arguments. We take each argument in turn.

I. <u>TGF-β activity varies quite widely</u>:

Appellant asserts (Brief, bridging paragraph, pages 7-8) that the examiner provides no documentary evidence to support the assertion that the activities of the members of the TGF-β superfamily "vary quite widely" and that some members of the superfamily have diverse activities in embryonic development while others have no role in development.

In response, the examiner finds (Answer, page 16), "[a]ppellant relies upon Akhurst et al." With reference to page 164-165 of Akhurst, the examiner finds (Answer, page 17), Akhurst teach "the evidence would suggest that each isoform of TGF-β (i.e. TGF-β1, TGF-β2, and TGF-β3) has a distinct function <u>in vivo</u>." Further, the examiner notes (Answer, page 6) that appellant's own specification (at pages 1, 2 and 12-15) supports her assertion regarding the activities of members of the TGF-β superfamily. In this regard, we note that

pages 1-2 of appellant's specification identify a variety of different biological activities that are attributed to what appellant characterizes as a "growing number of polypeptide factors … found to be structurally homologous to transforming growth factor β (TGF-β)."

Thus, contrary to appellant's assertion, it is our opinion that the examiner provided the documentary evidence necessary to support her assertion.

II. TGF-β superfamily members play "a pivotal role" in embryonic processes:

Appellant asserts (Brief, page 8), "the Akhurst reference was published in 1990, which is the year that the earliest priority application to the present application was filed.[5] Therefore, the Akhurst reference is an appropriate measure of what was known in the art relating to transforming growth factors at the time the application was filed." As set forth in In re Hogan, 559 F.2d 595, 605, 194 USPQ 527, 537 (CCPA 1977), emphasis original, "use of later publications as evidence of the state of art existing on the filing date of an

[5] This application claims priority through a series of continuing applications to Application No. 07/538,372, filed June 15, 1990. See Answer, page 23, "[a]ppellant is relying upon the filing date of the ultimate parent application, 07/538,372, filed 6/15/90."

application" is acceptable. Accordingly, we have considered Akhurst as representative of the state of the art relating to transforming growth factors at the time the application was filed.

In this regard, we note that appellant emphasizes that Akhurst characterize the TGF-β superfamily "as 'a large superfamily of related proteins, each of which plays a pivotal role in embryonic processes'…." See e.g., Brief, page 8. We note that the concept of a "pivotal role" appears to be a major theme in appellant's Brief. See e.g., Brief, pages 8-10, wherein "pivotal role" is mentioned no less than five times. There is no doubt that the abstract (page 153) of Akhurst uses the term "pivotal role." However, what appellant fails to point out or discuss is Akhurst's statement (page 155), "[a]s yet there is no definitive evidence that any of the TGFβs are endogenous regulators of mammalian embryonic processes." Accordingly, as we understand the Akhurst article, while members of the TGF-β superfamily may potentially play a role in embryonic processes there is, at the time this invention was filed, no definitive evidence to support this assertion.

Thus, when Akhurst is considered as representative of the state of the art at the time of appellant's filing date, it appears that Akhurst would agree with appellant's disclosure (specification, page 14) that "[a] determination of the specific clinical settings in which GDF-1 will be used as a diagnostic or as a therapeutic tool await further characterization of the expression patterns and

biological properties of GDF-1 both under normal physiological conditions and during disease states." See also, Answer, page 17, wherein the examiner points out that Akhurst teach that "it is essential that more functional studies are carried out" to manipulate TGF-β isoform expression or isoform function. See Akhurst page 165. Accordingly, we agree with the examiner that, at best, Akhurst "supports the examiner's position that further research would be required to reasonably determine or confirm any activity or involvement of GDF-1 in embryogenesis." Answer, page 17.

In addition, we note that Akhurst identify several activities in which TGF-β may be involved in mammalian embryogenesis. By way of example we note the following activities taught by Akhurst, and the respective transforming growth factor isoforms associated with each activity:

1. Haematopoiesis: Akhurst, page 157, endnotes omitted, wherein Akhurst point out that "[s]ince TGFβ1 is known to be a potent inhibitor of haematopoiesis…, it is likely that this growth factor acts as an autocrine negative regulator of cell growth. … Neither TGFβ2 or β3 RNAs have been detected in haematopoietic tissue of mouse or man…."

   Appellant has not identified on this record whether GDF-1 exhibits TGFβ1, TGFβ2 or TGFβ3 activity.

2. Vascularization and Angiogenesis: Akhurst, page 157, endnote omitted, wherein Akhurst point out that "[t]he endothelial cell response to TGFβ is clearly isoform-specific in vitro. Though TGFβ1 is a potent growth inhibitor of this cell type, at physiological concentrations, TGFβ2 shows no such activity.

   Appellant has not identified on this record whether GDF-1 exhibits TGFβ1 or TGFβ2 activity.

3. Skeletal Development: Akhurst, page 159-161, wherein Akhurst point out (page 161, endnotes omitted):

> TGFβ1 expression is associated with more overtly differentiated cell types in areas of ossification, namely osteoblasts, osteocytes and osteoclasts…. It has been reported that TGFβ2 is also expressed in these cell types…, though this has been questioned by others…. Unlike TGFβ2 and β3, TGFβ1 is, thus, more likely to be involved in control of osteoblast/ osteoclast function, including bone remodeling which continues in the adult, and is influenced by osteotropic hormones.

Again, appellant has not identified on this record whether GDF-1 exhibits TGFβ1, TGFβ2 or TGFβ3 activity.

Accordingly, we agree with the examiner's finding (Answer, page 17) that Akhurst amply illustrates that embryogenesis is a highly diverse and complex process including skeletal development, hematopoiesis, vascularization, and so forth. (See pages 157-164.)[.] This is also acknowledged by the specification as filed on page 2, lines 15-20. As such, a disclosure that GDF-1 may be involved in embryogenesis cannot be considered to convey to those of ordinary skill in the art any specific or clear biological activity. It provides no direction or guidance as to which aspect or to a particular activity.

Thus, we disagree with appellant's intimation (Brief, page 8) that by assigning GDF-1 to the TGF-β superfamily, GDF-1 can be imputed with the same specific, substantial, and credible utility to the TGF-β family. As set forth above, different isoforms of the TGF-β family exhibit different activities. On this record, appellant failed to identify any evidence, and we find none, to support the assertion that GDF-1 will share the activity of all isoforms of TGF-β. Nor do we find any evidence on this record that appellant's specification identifies with any

degree of specificity that GDF-1 will share the activity of a particular TGF-β isoform, or any other particular member of the TGF-β superfamily to which GDF-1 is least homologous with.

Accordingly, we also disagree with appellant's assertion (Brief, page 9) that "the [e]xaminer provides no evidence that those of skill in the art at the time the invention was made would have believed that members of the TGF-β super family exhibit such diverse activities as to preclude prediction of function based on this family assignment." In our opinion, as discussed above, the evidence relied upon by appellant – Akhurst – speaks for itself.

Thus, while appellant asserts (Brief, page 9), the specification "predicted that the GDF-1 protein was likely to play an important role in mediating developmental decisions related to cell differentiation…," appellant's specification fails to identify what precise role GDF-1 plays. In this regard, we agree with the examiner (Answer, page 14), "the specification is an invitation to experiment without clear direction or guidance as to the particular biological activity to investigate."

III. Post-filing date evidence:

Appellant asserts (Brief, page 10), "[t]he Rankin reference was submitted to demonstrate that the GDF-1 protein has the utilities that were predicted in the specification, and is suitable evidence for that purpose even though it was published after the filing date of the present application." In this regard, appellant asserts (id.), Rankin's "results with the GDF-1 knockout mouse prove

that GDF-[]1 is required for the proper development and positioning of organs during embryogenesis … it has now been confirmed that aberrant expression of GDF-1 has significant and substantial effects on embryonic development." In support of this assertion appellant attempts to draw a nexus between the results in Rankin, and appellant's specification (page 2, lines 25-29), wherein appellant discloses, GDF-1 "like other members of this [TGF-β] superfamily, are [sic] likely [to] play an important role in mediating developmental decisions related to cell differentiation."

We disagree with appellant's assertions. As the examiner points out (Answer, page 21), "[a]ppellant is relying upon the filing date of the ultimate parent application, 07/538,372, filed 6/15/90. The Rankin et al. (March 2000) [reference] was published well [(10 years)] after the effective filing date of the instant invention and the abstract itself admits that the function of GDF-1 was not known when discovered by [the] inventor Lee. [6]" According to Rankin (Abstract), "[o]ur findings suggest that Gdf1 acts early in the pathway of gene activation that leads to the establishment of left-right asymmetry." Appellant admits (Brief, page 11), "the appellant has not asserted that the specification teaches that GDF-1 regulates left-right patterning or axis formation in mice." Rather it is appellant's position that Rankin merely provides proof that appellant's prediction that GDF-1 plays a role in embryonic development is correct. Id. Specifically, appellant asserts (id.), "the specification discloses at the paragraph bridging pages 12-13

[6] Specifically, the Rankin abstract (published a decade after the effective filing date of the instant application) expressly states, endnotes omitted, emphasis added, GDF-1 "is a TGF-β family member of unknown function that was originally isolated from an early mouse embryo cDNA library…."

that abnormal levels of GDF-1 could be associated with developmental anomalies or structural defects in the developing fetus." We fail to see the nexus between this vague, general disclosure in appellant's specification and the specific teaching in Rankin provided a decade after appellants earliest effective filing date that GDF-1 regulates left-right patterning or axis formation in mice.

For clarity, we reproduce the asserted speculated uses of the claimed invention as they appear on pages 12-14 of the specification, emphasis added:

> [O]ne potential use for GDF-1 as a diagnostic tool is as a specific marker for the presence of tumors arising from cell types that normally express GDF-1 … one member of this superfamily, namely, inhibin, has been shown to be useful as a marker for certain ovarian tumors…
>
> A second potential diagnostic use for GDF-1 is as an indicator for the presence of <u>developmental</u> <u>anomalies</u> in prenatal screens for potential birth defects. For example, abnormally high serum or amniotic fluids [sic] levels of GDF-1 may indicate the presence of <u>structural</u> <u>defects</u> in the developing fetus … another embryonic marker namely, alpha fetoprotein, is currently used routinely in prenatal screens for neural tube defects. Conversely, abnormally low levels of GDF-1 may indicate the presence of developmental anomalies directly related to the tissues normally expressing GDF-1.
>
> A third potential diagnostic use for GDF-1 is in prenatal scrrns for genetic diseases that either directly correlate with the expression or function of GDF-1 or are closely linked to the GDF-1 gene. <u>Other potential diagnostic uses will become evident upon further characterization of the expression and function of GDF-1.</u>
>
> … [O]ne potential therapeutic use for GDF-1 is as an anti-cancer drug to inhibit the growth of tumors derived from cell types that are normally responsive to GDF-1. … one member of this superfamily, namely Mullerian inhibiting substance, has been shown to be cytotoxic for human ovarian and endometiral tumor cells either grown in culture … or when transplanted into nude mice….
>
> <u>Conversely</u>, <u>if</u> GDF-1 functions as a growth-stimulatory factor for specific cell types, other potential therapeutic uses will be apparent. For example, one member of this superfamily, namely, activin, has been shown to function as a nerve cell survival molecule. … <u>Alternatively</u>, <u>if</u> the target cells for GDF-1 in the

> nervous system are the support cells, GDF-1 will likely prove to be of therapeutic benefit in the treatment of disease processes leading to demyelination.
>
> Many of the members of this superfamily, including GDF-1, are also likely to be clinically useful for tissue repair and remodeling. For example, the remarkable capacity of the bone morphogenetic proteins to induce new bone growth … has suggested their utility for the treatment of bone defects caused by trauma, surgery, or degenerative diseases like osteoporosis….
>
> A determination of the specific clinical settings in which GDF-1 will be used as a diagnostic or as a therapeutic tool await further characterization of the expression patterns and biological properties of GDF-1 both under normal physiological conditions and during disease states.

Consistent with the cited sections of appellant's disclosure, the examiner points out (Answer, page 8), "[t]he specification speculates on possible activities of GDF-1[,] [n]one of the particular activities disclosed for other TGF-β superfamily members have been demonstrated for this protein in the specification and none were known at the time of the invention." Now, with evidence from a reference published a decade after appellant's effective filing date, appellant asserts that their prediction was correct. Specifically, the "prediction" that a "second potential diagnostic use for GDF-1 is as an indicator for the presence of developmental anomalies in prenatal screens for potential birth defects … [and] may indicate the presence of structural defects in the developing fetus." Specification, bridging paragraph, pages 12-13. In our opinion, appellant's specification cannot be stretched this far. As the examiner explains (Answer, page 21), Rankin uses "information, materials, assays, and/or techniques that were not known at the time of the invention and thus make clear that one of ordinary skill in the art trying to determine what activity GDF-1 had at the time of the invention would have been required to go beyond routine

experimentation." Specifically, the examiner points out (id.), "[t]he specification does not disclose nor contemplate knockout mouse experimental models" as used in Rankin.

We remind appellants that the utility requirement must be met as of the filing date of the application. See In re Brana, 51 F.3d 1560, 1567 n.19, 34 USPQ2d 1436, 1441 n.19 (Fed. Cir. 1995) ("Enablement, or utility, is determined as of the application filing date."). An applicant cannot rely on post-filing advances in the art to supplement a disclosure that was inadequate at the time it was filed. See In re Glass, 492 F.2d 1228, 1232, 181 USPQ 31, 34 (CCPA 1974):

> [A]pplication sufficiency under § 112, first paragraph, must be judged as of its filing date. 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.

The Rankin reference was published a decade after the filing date of the application, and appellants have cited no evidence to show that those skilled in the art would have been aware of the relevant disclosures as of the application's filing date. Therefore, the post-filing date Rankin reference cannot be relied upon to establish the utility of the claimed nucleic acid.

For the same reasons we are not persuaded by appellant's assertion that the Ebendal declaration, and the post-filing date references relied upon therein, are sufficient "to demonstrate that the utilities predicted in the specification were correct." This disclosure, however, was not provided in the instant specification, nor does the evidence show that it was known to those skilled in the art at the

time this application was filed. According to the examiner (Answer, page 19), the references relied upon in support of the assertions made in the Ebendal declaration were derived from post-filing date references. Accordingly, we are not persuaded by the Ebendal declaration.

IV. The locus of GDF-1 expression:

According to appellant (Brief, page 12), "Figure 7 of the specification shows that GDF-1 is expressed almost exclusively in the brain. Thus, a GDF-1 nucleic acid may be used to determine for instance whether a brain tumor is a primary tumor or a metastasis from a tissue that does not express GDF-1." As the examiner points out, however, appellant's specification discloses (page 23 and Figure 7), "[n]orthern analysis demonstrated that the GDF-1 probe detected an mRNA species in adult brain, adrenal gland, ovary, and oviduct." Answer, page 22. In addition, the examiner finds (id.), "[t]he specification does not identify any tumor (brain or otherwise) associated with GDF-1 nor enable any such diagnostic or therapeutic uses." To the contrary, we find that the specification discloses (page 14), "[a] determination of the specific clinical settings in which GDF-1 will be used as a diagnostic or as a therapeutic tool await further characterization of the expression patterns and biological properties of GDF-1 both under normal physiological conditions and during disease states." Accordingly, we are not persuaded by appellant's assertion.

SUMMARY

On reflection, we agree with the examiner (Answer, page 18) that the facts of record here are analogous to those in Kirk. In our opinion, the disclosure of the originally filed specification does not provide a specific, substantial, and credible asserted utility nor a well established utility for the claimed invention. See also, Answer, page 21. As set forth in Kirk, 376 F.2d at 945, 153 USPQ at 55, "[t]here can be no doubt that the insubstantial, superficial nature of vague, general disclosures … was recognized, and clearly rejected, by the Supreme Court" in Brenner.

For the foregoing reasons, we affirm the rejection of claim 9 under 35 U.S.C. § 101 as lacking utility and § 112[7], first paragraph, for lack of enablement based on the finding of lack of utility. As set forth above, claims 4-8, 10 and 22-33 fall together with claim 9.

Written Description:

Having disposed of all claims on appeal, see supra, we do not reach the merits of the written description rejection under 35 U.S.C. § 112, first paragraph.

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

[7] The nonenablement rejection was presented simply as a corollary of the finding of lack of utility. See e.g., Answer, page 5. Therefore, although we discuss only the § 101 rejection, our conclusion also applies to the § 112 rejection.

AFFIRMED

	)
Sherman D. Winters	)
Administrative Patent Judge	)
	)
	)
	) BOARD OF PATENT
Donald E. Adams	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Demetra J. Mills	)
Administrative Patent Judge	)

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