United States Court of Appeals for the Federal Circuit

DAVID V. GOEDDEL AND ROBERTO CREA,
Appellants,

v.

HARUO SUGANO, MASAMI MURAMATSU, AND TADATSUGU TANIGUCHI,
Appellees.

2009-1156,-1157
(Interferences No. 105,334 and 105,337)

Appeal from the United States Patent and Trademark Office, Board of Patent Appeals and Interferences.

Decided: September 7, 2010

THOMAS E. FRIEBEL, Jones Day, of New York, New York, argued for appellants. With him on the brief was GREGORY A. CASTANIAS, of Washington, DC. Of counsel on the brief were GEORGE M. GOULD, WILLIAM H. EPSTEIN, and DAVID E. DE LORENZI, Gibbons P.C., of Newark, New Jersey.

NOAH A. LEVINE, Wilmer Cutler Pickering Hale and Dorr LLP, of New York, New York, argued for appellees. With him on the brief were NELS T. LIPPERT and JANE M.

LOVE, of New York, New York; GREGORY H. LANTIER and ARTHUR W. COVIELLO, of Washington, DC; and WILLIAM W. KIM, of Palo Alto, California.

Before NEWMAN, LOURIE, AND BRYSON, *Circuit Judges*.

NEWMAN, *Circuit Judge*.

This consolidated appeal is from two decisions of the Board of Patent Appeals and Interferences of the United States Patent and Trademark Office ("the Board") in two related patent interference priority contests between the party Haruo Sugano, Masami Muramatsu, and Tadatsugu Taniguchi (together "Sugano") and the party David V. Goeddel and Roberto Crea (together "Goeddel"). The Board held that Sugano is entitled to the benefit of the filing date of its initial Japanese application, and awarded Sugano priority as to the counts of both interferences.[1] On appellate review, we conclude that the Japanese application does not establish constructive reduction to practice of the subject matter of the counts. The priority decisions of the Board are reversed.

BACKGROUND

The focus of both interferences is human fibroblast interferon ("hFIF"), also called interferon beta or ß-IF. This interferon is produced naturally in the human body, in very small amounts. Its effectiveness in combating pathogens

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[1] *Goeddel v. Sugano*, Interf. No. 105,334, Paper No. 109 (B.P.A.I. Sept. 29, 2008) ("*Board Opinion*"); *Goeddel v. Sugano*, Interf. No. 105,337, Paper No. 112 (B.P.A.I. Sept. 29, 2008). The content of the Board's opinions in both interferences is the same. For simplicity we only provide citations to the Board's opinion in Interference No. 105, 334.

and tumors was recognized, and scientists have sought to produce hFIF in sufficient quantities for therapeutic use.

The scientific premises underlying the interference issues are set forth in the Board decisions, and are briefly summarized as follows: hFIF is a protein (or polypeptide) that is produced in the human body by a complex process. Within the human genome, which exists in almost all cells of the body, is a naturally occurring gene (that is, a segment of DNA) that codes for hFIF. The expression of this naturally occurring gene produces a precursor form of hFIF, consisting of 187 amino acids in a specific sequence. This precursor protein is not the active form of hFIF. The active form, called "mature" hFIF, is a protein consisting of 166 amino acids, which is produced inside the human cell upon cleavage of the first 21 amino acids from the precursor sequence of 187 amino acids. The cleaved sequence of 21 amino acids is called a "presequence" or "signal peptide." The cleavage of the presequence occurs in the endoplasmic reticulum of the cell, before the protein is secreted from the cell as mature hFIF.

In the patents and patent applications involved in this interference, the parties describe and claim a recombinant DNA process for directly producing mature hFIF. By this process the naturally occurring gene is modified, and the modified gene is inserted into a bacterium under conditions whereby the bacterium produces the desired mature hFIF without the presequence of the precursor hFIF. The question of priority turns on whether Sugano's initial Japanese Patent Application No. 33931/80 constitutes a constructive reduction to practice of the invention set forth in the Interference Counts, for only Sugano's initial Japanese Application predates Goeddel's priority date.

The interference counts

The interferences are referred to as the "DNA Interference" and the "Protein Interference." The DNA Interference, No. 105,334, is directed to the modified DNA that codes the 166 amino acid sequence of mature hFIF. The Protein Interference, No. 105,337, relates to the non-glycosylated mature hFIF that is thereby obtained.

The DNA Interference was declared between Goeddel's U.S. Patent Application No. 07/374,311, and two Sugano patents, U.S. Patent No. 5,326,859 and its continuation-in-part No. 5,514,567. Goeddel's '311 patent application claims priority from U.S. Application No. 06/190,799, filed on September 25, 1980. The Board awarded Sugano priority of invention based on the Japanese Application, which was filed on March 19, 1980. Goeddel argues that only a later Sugano application supports the subject matter of the interference counts, and that Sugano is not entitled to the Japanese Application priority date.

The sole count of the DNA Interference is:

> A DNA encoding a mature human fibroblast interferon having a total of 166 amino acids of the sequence
>
> > Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln
> > Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu
> > Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
> > Cys Leu Lys Asp Arg Met Asn Phe Asp Ile
> > Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe
> > Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr
> > Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
> > Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
> > Glu Thr Ile Val Glu Asn Leu Leu Ala Asn
> > Val Tyr His Gln Ile Asn His Leu Lys Thr
> > Val Leu Glu Glu Lys Leu Glu Lys Glu Asp

> Phe Thr Arg Gly Lys Leu Met Ser Ser Leu
> His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu
> His Tyr Leu Lys Ala Lys Glu Tyr Ser His
> Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu
> Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
> Gly Tyr Leu Arg Asn
>
> and unaccompanied by a human fibroblast interferon presequence.

Goeddel stresses that the count is directed to DNA encoding for direct expression of the 166 amino acid mature hFIF without the presequence, as opposed to the naturally occurring DNA that expresses only the 187 amino acid precursor hFIF including the presequence. It is not disputed that known recombinant techniques were not effective to produce mature hFIF directly from the naturally occurring gene because the bacterial cells used in recombinant procedures could not reliably cleave the 21 amino acid presequence from the precursor hFIF.

The Protein Interference was declared between Sugano's U.S. Application No. 08/463,757, filed June 5, 1995, and Goeddel's U.S. Patent No. 5,460,811, which claims priority from U.S. Application No. 06/190,799 filed on September 25, 1980. The Board awarded Sugano's '757 application the benefit of the Japanese Application's March 19, 1980 filing date. The sole count of the Protein Interference is:

> A composition comprising water and a nonglycosylated mature human fibroblast interferon polypeptide having a total of 166 amino acids and the following amino acid sequence

> Met Ser Tyr Asn Leu Leu Gly Phe Leu Gln
> Arg Ser Ser Asn Phe Gln Cys Gln Lys Leu
> Leu Trp Gln Leu Asn Gly Arg Leu Glu Tyr
> Cys Leu Lys Asp Arg Met Asn Phe Asp Ile
> Pro Glu Glu Ile Lys Gln Leu Gln Gln Phe
> Gln Lys Glu Asp Ala Ala Leu Thr Ile Tyr
> Glu Met Leu Gln Asn Ile Phe Ala Ile Phe
> Arg Gln Asp Ser Ser Ser Thr Gly Trp Asn
> Glu Thr Ile Val Glu Asn Leu Leu Ala Asn
> Val Tyr His Gln Ile Asn His Leu Lys Thr
> Val Leu Glu Glu Lys Leu Glu Lys Glu Asp
> Phe Thr Arg Gly Lys Leu Met Ser Ser Leu
> His Leu Lys Arg Tyr Tyr Gly Arg Ile Leu
> His Tyr Leu Lys Ala Lys Glu Tyr Ser His
> Cys Ala Trp Thr Ile Val Arg Val Glu Ile Leu
> Arg Asn Phe Tyr Phe Ile Asn Arg Leu Thr
> Gly Tyr Leu Arg Asn
>
> said composition being free of any glycosylated human fibroblast interferon.

The Board held that Sugano's Japanese Application constituted constructive reduction to practice of the subject matter of the counts of both interferences, and awarded priority to Sugano. Goeddel argues that the Japanese Application does not meet the written description and enablement requirements of 35 U.S.C. §112 with respect to the interference counts, and therefore is not a constructive reduction to practice of the counts. Goeddel points out that the Japanese Application "is devoid of any disclosure of a method of making the claimed subject matter," *Board Opinion* at 40, and that the plasmids described in the Japanese Application "would not function to express mature hFIF," as Sugano conceded. *Board Opinion* at 38. Sugano responds that persons experienced in this field would have known how to modify the precursor hFIF gene so that it

would express mature hFIF, using the teachings in the Japanese Application, and that judicial deference is owed to the Board's findings and priority decisions.

DISCUSSION

In accordance with the criteria of the Administrative Procedure Act, 5 U.S.C. §706, the Board's legal conclusions receive plenary review, and factual findings are reviewed to determine whether they are supported by substantial evidence. These standards apply to an appeal of patent interference rulings. *See Capon v. Eshhar*, 418 F.3d 1349, 1351 (Fed. Cir. 2005).

Interference priority is awarded to the first applicant to conceive the invention, provided that the invention is duly reduced to practice, actually or constructively. *See Hyatt v. Boone*, 146 F.3d 1348, 1351 (Fed. Cir. 1998); *see generally* Charles L. Gholz, *Interference Practice*, in 6 *Patent Practice*, 24-1, 24-6 (Irving Kayton and Karyl S. Kayton eds., 4th ed. 1989). Reduction to practice of the subject of the interference count may be established by evidence of its actual performance, *see Cooper v. Goldfarb*, 154 F.3d 1321, 1327 (Fed. Cir. 1998), or constructively by filing a patent application that describes and enables its practice in accordance with 35 U.S.C. §112, *see Hyatt*, 146 F.3d at 1352. An invention for which the priority of a foreign patent application is available in accordance with treaty and statute may rely on the content of the foreign application for constructive reduction to practice, provided that the requirements of §112 are met. *See* Gholz, *supra*, at 24-8.

The Sugano Japanese Application describes the invention therein as: "a novel recombinant plasmid, having a gene which encompasses at least the entire coding region of the human fibroblast interferon messenger RNA . . . ." J.A.

306436 (English Translation of Japanese Translation) [hereinafter "JP 931 Transl."]. The application states: "The 'entire coding region' means the part specifying the whole amino acid sequence of the protein of the human fibroblast interferon in the human fibroblast interferon messenger RNA sequence. JP 931 Transl. Table 5 of the Japanese Application lists the entire 187 amino acid sequence, without indication of either the presequence or the mature hFIF sequence JP 931 Transl. The Board found that the gene described in the Japanese Application encodes the 187 amino acid precursor hFIF. *Board Opinion* at 38. The Board also found that "[t]he sequences of mature hFIF DNA or polypeptide are not explicitly disclosed." *Board Opinion* at 44.

However, in awarding priority to Sugano the Board found that mature hFIF would be "readily apparent" to a person skilled in this field, in view of the Japanese Application's description of the precursor hFIF and a scientific article by Knight that is referenced in the Japanese Application as follows:

> It is important that in the sequence there exist without any errors the base sequence [three base pairs] corresponding to the amino acid sequence from the amino-terminal to 13th amino acid of the human fibroblast interferon reported by Knight, et al. [*Science* vol. 207, p. 525-526, (1980)]. The fact proves that # 319-13 plasmid has the human fibroblast interferon mRNA sequence. Further, it is apparent from the data of the primary sequence that the plasmid encompasses the entire coding region of the protein of the above mRNA and probably the coding region of the signal peptide.

JP 931 Transl. The Knight article is entitled "Human Fibroblast Interferon: Amino Acid Sequence Analysis and Amino Terminal Amino Acid Sequence," and identifies the first 13 amino acids of secreted (mature) hFIF. Sugano argues that the partial Knight sequence "demarcated the line between the DNA encoding the hFIF signal peptide and the DNA encoding mature hFIF." Sugano Br. at 30. Goeddel argues that the reference to the Knight article was for the purpose of verifying that Sugano had obtained "the entire coding region," but not to identify the separation between the presequence and the mature hFIF sequence. Goeddel stresses that the Japanese Application, including the Knight sequence, does not describe a modified gene that encodes only mature hFIF, does not describe mature hFIF as directly expressed, and does not suggest such products or the production of such products. Thus Goeddel argues that the Japanese Application does not meet either the written description or the enablement requirements.

The Board held that the Japanese Application satisfies the requirements of constructive reduction to practice because Knight's partial sequence of the first 13 amino acids of mature hFIF would allow a person skilled in the field of the invention to determine where in the 187 amino acid precursor the presequence ends and the mature sequence begins. The Board stated that Goeddel's expert, Dr. Rik Derynck, admitted that a person skilled in this field would have known how to trim the nucleotide sequence of the precursor to create a recombinant plasmid for use in bacteria to directly express mature hFIF, citing a declaration submitted by Dr. Derynck in a European Patent Office proceeding (concerning erythropoietin) in which he had stated that once the complete DNA sequence encoding a protein is known, it requires "no new technology" to express the protein using bacterial expression cells. The Board held that one skilled in this field "should have been able to

envision" the DNA molecule that would encode mature hFIF unaccompanied by its presequence, on the following reasoning:

> (1) Table 5 [of the Japanese Application] disclosed the precursor sequence,
>
> (2) Knight is discussed in the '931 JP application as disclosing the first 13 amino acids of mature hFIF, and
>
> (3) Table 5 discloses the end point of hFIF.

Board Opinion at 44-45. Referring to the high level of skill in this field, the Board held that although not explicitly described in the Japanese Application, "the amino acid of, and DNA sequence encoding, mature hFIF would be readily apparent." *Board Opinion* at 44-45. Accordingly, the Board held that a person of skill in the field of the invention, reading the Japanese Application, would conclude that Sugano was in possession of the invention of the interference counts.

Goeddel argues that the Board erred in finding constructive reduction to practice, for the Japanese Application describes only the expression of precursor hFIF. Sugano conceded before the Board that the Japanese Application does not describe plasmids that express mature hFIF directly. *Board Opinion* at 38. Sugano's expert, Dr. Thomas Roberts, testified that the Japanese Application does not state where the presequence ends and where the mature hFIF sequence begins:

> Page 15 of the Japanese application lists the nucleotide sequence of the human fibroblast interferon cDNA and encoded amino acids. The amino acid sequence contains the leader or presequence of inter-

> feron as well as the mature protein sequence, but does not explicitly demarcate where the presequence ends and where the mature protein sequence begins.

J.A. 306518-19 at ¶44 n.1 (Roberts Declaration). Although Dr. Roberts's opinion was that "in view of the Knight disclosures, one of ordinary skill would have immediately understood that the presequence consists of the first 21 amino acids because the Knight disclosures teach that the mature sequence begins with the amino acid sequence Met-Ser-Tyr-Asn-Leu-Leu-Gly-Phe-Leu-GIn-Arg-Ser-Ser," *id.*, constructive reduction to practice "is 'not a question of whether one skilled in the art might be able to construct the patentee's device from the teachings of the disclosure. . . . Rather, it is a question whether the application necessarily discloses that particular device.'" *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320, 1326-27 (Fed. Cir. 2000) (quoting *Jepson v. Coleman*, 314 F.2d 533, 536 (CCPA 1963)).

Dr. Derynck agreed that the Japanese Application identified the DNA coding for precursor hFIF, and recognized the Japanese Application's statement that the sequence disclosed therein "probably [includes] the coding region of the signal peptide," but testified that the Japanese Application "does not identify the reported 187-amino acid sequence as a precursor protein, nor does this application identify either the 166-amino acid mature form of human fibroblast [interferon] nor the 21-amino acid signal peptide." J.A.301544 at ¶157 (Derynck Declaration).

Sugano does not dispute that the Japanese Application does not explicitly show a DNA encoding mature hFIF or suggest using such DNA to encode mature hFIF without the presequence. Instead, Sugano argues that it is unnecessary for the Japanese Application to describe explicitly the amino

acid sequence of mature hFIF or suggest obtaining mature hFIF. Sugano argues that patent applications are "written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before," and thus "it is unnecessary to spell out every detail of the invention in the specification." *Lizard Tech, Inc. v. Earth Res. Mapping, Inc.,* 424 F.3d 1336, 1345 (Fed. Cir. 2005). Thus Sugano argues that it sufficed that the Japanese Application referred to the Knight article, for with that article the Japanese Application "conveyed" mature hFIF with "reasonable clarity" to a person of skill in the art, citing *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64 (Fed. Cir. 1991) for its "reasonable clarity" standard. Sugano states that Goeddel conceded, as the Board found, that "[a]s of March 19, 1980, one of ordinary skill recognized that a DNA encoding the hFIF precursor would not be itself useful for expressing mature hFIF in E. coli," *Board Opinion* at 19, thereby indicating that one of ordinary skill would read the Japanese Application with particular attention to any information related to identifying DNA coding for mature hFIF.

Goeddel responds that the problem of obtaining mature hFIF was indeed recognized, but that Sugano did not solve it. Although the experts for both sides agreed that a skilled person "could" identify the boundary between the presequence and the mature hFIF based on the Knight article, the Japanese Application does not describe the subject matter of the interference counts. The Japanese Application does not describe mature hFIF and does not describe the DNA coding for mature hFIF unaccompanied by the presequence. Sugano described its invention, in the initial Japanese Application, as the recombinant production of the 187 amino acid precursor, using a gene that encompasses "at least the entire coding region." Section 112, in the context of interference priority, requires that the subject matter of

the counts be described sufficiently to show that the applicant was in possession of the invention. That a modified gene encoding the 166 amino acid protein could have been "envisioned" does not establish constructive reduction to practice of the modified gene. The question is not whether one skilled in this field of science might have been able to produce mature hFIF by building upon the teachings of the Japanese Application, but rather whether that application "convey[ed] to those skilled in the art that the inventor had possession of the claimed subject matter as of the filing date." *Ariad Pharm., Inc. v. Eli Lilly & Co.*, 598 F.3d 1336, 1351 (Fed. Cir. 2010) (en banc); *see also Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997) (in claiming priority under §120, "[a] description which renders obvious the invention for which an earlier filing date is sought is not sufficient"); *Bradford Co. v. Conteyor North Am., Inc.*, 603 F.3d 1262, 1269 (Fed. Cir. 2010) (same). The Japanese application does not describe a bacterial expression vector that directly produces the mature hFIF, nor does it suggest producing a modified gene to directly encode the 166 amino acid mature hFIF.

The Board erred in ruling that priority is established if a person of skill in the art could "envision" the invention of the counts. Sugano argues that this ruling is supported by *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 323 F.3d 956, 968 (Fed. Cir. 2002) and *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 923 (Fed. Cir. 2004), but these cases do not hold that envisioning an invention not yet made is a constructive reduction to practice of that invention. In *Enzo Biochem* the court confirmed that depositing an actual sample may meet the written description requirement when science is not capable of a complete written description. *Enzo Biochem*, 323 F.3d at 970. In *University of Rochester* the court held that the description of the COX-2 enzyme did not also serve to describe all unknown compounds capable of

inhibiting the enzyme. *University of Rochester*, 358 F.3d at 926-27. Precedent in evolving science is attuned to the state of the science, but remains bound by the requirement of showing "that the inventor actually invented the invention claimed." *Bradford*, 603 F.3d at 1269; *see Fiers v. Revel*, 984 F.2d 1164, 1170 (Fed. Cir. 1993).

The Board's decision that the Japanese Application constitutes constructive reduction to practice of the subject matter of these interferences is not in accordance with law, for the Japanese Application does not meet the criteria of §112, first paragraph, as to this subject matter. The award of priority to Sugano is reversed. The cases are remanded for appropriate further proceedings.

REVERSED AND REMANDED