UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte DANILO PORRO and MICHAEL SAUER

Appeal 2008-0184
Application 10/606,300
Technology Center 1600

Decided: March 11, 2008

Before TONI R. SCHEINER, DEMETRA J. MILLS, and ERIC GRIMES, *Administrative Patent Judges*.

GRIMES, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a method of making ascorbic acid, which the Examiner has rejected for lack of adequate written description. We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

BACKGROUND

The Specification states that, in one of the pathways for synthesis of ascorbic acid (vitamin C) in plants, the second-to-last step is catalyzed by the enzyme L-galactose dehydrogenase, or LGDH (Spec. 3: 19-25).

The Specification discloses a method for producing L-ascorbic acid in recombinant yeast (Spec. 11: 22-25). "In a preferred embodiment . . . , the coding region introduced into the recombinant yeast encodes an enzyme selected from L-galactose dehydrogenase," among others (*id.* at 12: 30 to 13: 1). In a "more preferred embodiment, the amino acid sequence of the LGDH enzyme has at least about . . . 90% identity with SEQ ID NO: 11" (*id.* at 13: 26-28). The amino acid sequence of SEQ ID NO: 11 is derived from *Arabidopsis thaliana* LGDH (Sequence Listing, SEQ ID NO: 11).

DISCUSSION

1. CLAIMS

Claims 12-14 are pending and on appeal. The claims have not been argued separately and therefore stand or fall together. 37 C.F.R. § 41.37(c)(1)(vii). Claim 13 is representative and reads as follows:

13. A method of generating ascorbic acid, comprising:

a) obtaining a recombinant yeast capable of converting an ascorbic acid precursor into ascorbic acid, wherein the yeast is functionally transformed with a coding region encoding L-galactose dehydrogenase (LGDH) enzyme having at least about 90% identity with SEQ ID NO: 11,

b) culturing the recombinant yeast in a medium comprising an ascorbic acid precursor, thereby forming ascorbic acid, and

c) isolating the ascorbic acid.

2. WRITTEN DESCRIPTION

Claims 12-14 stand rejected under 35 U.S.C. § 112, first paragraph, as lacking adequate written description in the Specification (Ans. 4). The Examiner reasons that the claims are directed to a method of using yeast "transformed with any one of . . . a set of nucleic acids encoding LGDH enzymes having at least about 90% *identity* to SEQ ID NO:11. . . . Thus the claims comprise a set of coding regions/amino acids defined by the function of the encoded protein" (*id.*).

The Examiner finds that the Specification discloses a single LGDH sequence, derived from *Arabidopsis thaliana* (*id.* at 5). The Examiner also finds that the prior art does not make up for the deficiencies of the Specification by showing that LGDH enzymes with 90% identity to SEQ ID NO: 11 were known in the art (*id.* at 6). In support, the Examiner cites Smirnoff, which "describes an L-galactose dehydrogenase discovered in the pea plant and *A. thaliana* as a 'newly discovered NAD^+-dependent L-galactose dehydrogenase' and further states that the enzyme is 'as far as we know, the only plant dehydrogenase acting on a non-phosphorylated sugar'" (*id.*).

The Examiner concludes that "[g]iven the very large genus of sequences encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to their common sequence motifs/structures, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims" (*id.*). "Therefore, the skilled artisan

would have reasonably concluded that Appellants were not in possession of the claimed invention (*id.* at 7).

We agree with the Examiner that the Specification does not adequately describe the genus of "L-galactose dehydrogenase (LGDH) enzyme[s] having at least about 90% identity with SEQ ID NO: 11" recited in claim 13. Claim 13 is directed to a method of using a nucleic acid encoding a protein defined by two properties: (1) it is at least 90% identical to SEQ ID NO: 11 and (2) it has the activity of the enzyme L-galactose dehydrogenase (LGDH).

To describe a genus of functional variants, a specification must provide guidance regarding which variants within the genus have the recited function. On facts similar to those here, the U.S. Court of Appeals for the Federal Circuit has held claims to lack adequate description. In *University of California v. Eli Lilly and Co.*, 119 F.3d 1559 (Fed. Cir. 1997), the court held that claims generically reciting cDNA encoding vertebrate or mammalian insulin were not adequately described by the disclosure of cDNA encoding rat insulin. *Id.* at 1568. The court held that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus.

Id. The court held that a

> description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by

> nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus.

Id. The court has since clarified that the complete structure of the representative species does not necessarily have to be described. *See Enzo Biochem v. Gen-Probe*, 323 F.3d 956, 964-65 (Fed. Cir. 2002).

Eli Lilly supports our conclusion that the instant Specification does not adequately describe the recited genus of nucleic acids. The *Eli Lilly* court held that a fully described genus is one for which a person skilled in the art can "visualize or recognize the identity of the members of the genus." Here, as the Examiner has pointed out, the Specification does not provide guidance regarding what structural features are responsible for the enzymatic activity of LGDH, nor does it describe what amino acid changes can be made in the wild-type sequence without affecting the enzymatic activity of the protein.

Thus, the Specification does not describe the recited genus sufficiently to allow a person skilled in the art to determine whether a given protein that is 90% identical to SEQ ID NO: 11 is within the scope of the instant claims. Since the Specification does not describe the recited genus adequately for those skilled in the art to distinguish the SEQ ID NO: 11 variants that are within the claims from other variants of SEQ ID NO: 11, the Specification does not adequately describe the recited genus under the standard of *Eli Lilly*.

The court also addressed similar facts in *University of Rochester v. G.D. Searle & Co.*, 358 F.3d 916 (Fed. Cir. 2004). In that case, the patent claimed a method of selectively inhibiting the enzyme PGHS-2 (also known as COX-2) by "administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product to a human." *Id.* at 917. The

patent "describe[d] in detail how to make cells that express either COX-1 or COX-2, but not both . . . , as well as 'assays for screening compounds, including peptides, polynucleotides, and small organic molecules to identify those that inhibit the expression or activity of the PGHS-2 gene product.[']" *Id.* at 927.

The court held that the disclosure of screening assays and general classes of compounds was not adequate to describe compounds having the desired activity: without disclosure of *which* peptides, polynucleotides, or small organic molecules have the desired characteristic, the claims were not adequately described. *See id.* ("As pointed out by the district court, however, the '850 patent does not disclose just 'which "peptides, polynucleotides, and small organic molecules" have the desired characteristic of selectively inhibiting PGHS-2.' . . . Without such disclosure, the claimed methods cannot be said to have been described.").

Just as in *University of Rochester*, the present application discloses a genus of chemical compounds (proteins having amino acid sequences at least 90% identical to SEQ ID NO: 11). According to Appellants' calculations, the genus encompasses 3.4×10^{41} different proteins (App. Br. 6). But the claims are limited to only those compounds having a desired characteristic (having LGDH enzymatic activity). Just as in *University of Rochester*, the present Specification does not guide the skilled artisan to the subset of proteins within the genus of 3.4×10^{41} proteins that are at least 90% identical to SEQ ID NO: 11 that have the recited enzymatic activity.

Granted, those skilled in the art could make libraries of SEQ ID NO: 11 variants and screen them to identify specific proteins that are at least 90%

identical to SEQ ID NO: 11 and that have LGDH enzymatic activity. That, however, does not make up for the deficiency of the Specification's description. The *University of Rochester* court specifically noted that the patent at issue there disclosed screening assays to identify compounds having the desired characteristic, but nonetheless held that the description was inadequate. The same holds true here.

Appellants argue that *Eli Lilly* "is not applicable to the facts of the present case," because the claims in *Eli Lilly* were directed to cDNA, while the present claims are not (Reply Br. 4). Appellants' argument does not persuade us that the *Eli Lilly* court's holding with respect to describing a chemical genus, discussed above, does not apply to this case.

Appellants also argue that the claimed genera in *Eli Lilly* were distinguished from other genera only by their function (encoding mammalian or vertebrate insulin), while the genus recited in claim 13 "distinguishes over other genera by *both* the LGDH function *and* structural features commonly possessed by members of the genus that distinguish them over others (i.e., the limitations to particular sequences recited by the claims)." (Reply Br. 5.) Along the same line, Appellants argue that they have provided "relevant, identifying characteristics sufficient to show they were in possession of the claimed genus"; specifically, a correlation between LGDH enzymatic activity and the amino acid sequence of SEQ ID NO: 11. (*Id.* at 3-4.)

These arguments are not persuasive. Certainly SEQ ID NO: 11 is adequately described. We can also assume, for present purposes, that a description of SEQ ID NO: 11 is adequate to describe amino acid sequences that are 90% identical to SEQ ID NO: 11: Given a computer and sequence-

comparison software, a skilled artisan may well be able to visualize or recognize the identity of members of that genus. That is not the issue here, however.

The issue raised by this case is whether the Specification describes the subgenus of proteins that have 90% sequence identity to SEQ ID NO: 11 *and also have LGDH enzymatic activity*. That is, does the Specification describe the subgenus of proteins within the "90% identical to SEQ ID NO: 11" genus that also have LGDH activity?

To describe the subgenus of "functional variants" within the genus of "variants," the Specification can describe a representative number of functional variants, or it can describe structural features that are common to functional variants that distinguish them from the rest of the genus (i.e., structural features that correlate with enzymatic activity regardless of other variations from SEQ ID NO: 11). *See Eli Lilly*, 119 F.3d at 1568. Maybe a functional subgenus can be described in other ways as well; the case law is a little hazy in this area. But, in our view, the case law makes clear that a functional subgenus is not adequately described by disclosure of a single functional embodiment – SEQ ID NO: 11 itself – within a genus of 3.4×10^{41} variants of SEQ ID NO: 11.

Appellants also argue that it would be impossible to list all of the vast number of potential proteins having at least 90% identity to SEQ ID NO: 11, and that *Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005), held that "there is no *per se* rule that a sequence listing must be presented for every biological sequence claimed in a patent application" (App. Br. 6).

This argument does not persuade us that the rejection should be reversed. It is true that there is no per se rule that every nucleic acid encompassed by a claim must be recited in the Specification. *See Falkner v. Inglis*, 448 F.3d 1357, 1366 (Fed. Cir. 2006). And it is true that different inventions can be described in different ways. *See Capon*, 418 F.3d at 1358. But a chemical genus must be described in some way that demonstrates to those of skill in the art that the applicant was in possession of the claimed genus at the time the application was filed. Appellants have not shown that the genus recited in claim 13 was described – either in one of the ways laid out in *Eli Lilly* or in some other way – in a manner that would show possession of the claimed genus to those skilled in the art. Without such a description, claim 13 must be held to lack adequate written description in the Specification.

Finally, Appellants argue that the claims do not encompass use of all proteins having at least 90% identity to SEQ ID NO: 11, but "are plainly drawn to *L-galactose dehydrogenases, wherein the LGDHs* have the recited levels of similarity or identity to SEQ ID NO:11 or 12. The skilled artisan would have a reasonable expectation that an LGDH . . . would be operable in the claimed methods" (App. Br. 7).

Again, Appellants' argument is not directed to the issue that is raised by this appeal. The Examiner has not questioned whether the claimed method could be practiced with nucleic acids that encode functional LGDH enzymes other than that of SEQ ID NO: 11. The lack of an enablement rejection, in fact, suggests that the Examiner has concluded that the claimed method could be practiced with nucleic acids encoding functional LGDH

enzymes (that are at least 90% identical to SEQ ID NO: 11), *if such nucleic acids were adequately described in the Specification*. The problem with claim 13, in other words, is not that the method could not be practiced with other LGDH-encoding nucleic acids, if they were possessed, but that Appellants' description of such nucleic acids does not show that they were in possession of them at the time this application was filed.

SUMMARY

Because the Specification does not describe the genus of nucleic acids encoding functional LGDH enzymes at least 90% identical to SEQ ID NO: 11, we affirm the rejection of claim 13 under 35 U.S.C. § 112, first paragraph. Claims 12 and 14 fall with claim 13. 37 C.F.R. § 41.37(c)(1)(vii).

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

AFFIRMED

Ssc:

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