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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte CORRADO FOGHER, SERENA REGGI, and
KIRIL PERFANOV.¹

Appeal 2015-006080
Application 12/377,085
Technology Center 1600

Before DEMETRA J. MILLS, JEFFERY N. FREDMAN, and
JOHN E. SCHNEIDER, *Administrative Patent Judges*.

SCHNEIDER, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134(a) of the Examiner's Final Rejection involving claims 9–17 to a genetically modified plant which have been rejected as obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

The present invention is directed to plants transformed to produce Apolipoproteins in oligomeric form. Spec. 1. The novel proteins are

¹ Appellants identify the Real Party in Interest as Plantechno S.r.l. Br. 3.

muteins of human ApoA-1 and exhibit increased stability and capacity to transport cholesterol. *Id.*

Claims 9–17 are on appeal. Claim 9 is illustrative and reads as follows:

9. A genetically transformed plant with one or more expression vectors comprising a seed-specific expression cassette and a nucleotide sequence encoding a mutein of human apolipoprotein (Apo) A-1, expressing in the seed's storage tissue one or more of said muteins, and forming oligomers comprising three or more monomers, in an essentially oligomeric form, said one or more muteins characterised in that they show in their oligomeric forms biological activities equal to or higher than the activities shown by apolipoprotein (Apo) A-1 Milano in its dimeric form in the following tests:
a') measurement of the reverse cholesterol transport capacity evaluated by calculation of the association kinetics of equal quantities of said oligomer, and of the said dimer of Apo A-1 Milano with dimyristoylphosphatidylcholine (DMPC); and
b') measurement of the plasma half life of said oligomer by a plasma half life test in comparison to a calibration curve obtained performing the same test with the purified Apo A-1 Milano dimer.

The claims stand rejected as follows:

Claims 9–17 stand rejected under 35 U.S.C. § 103(a) as unpatentable over Moloney² in view of Zhu³.

² Moloney et al., US 2005/0172359 A1, published Aug. 4, 2005 (“Moloney”).

³ Zhu et al., *Cysteine mutants of human apolipoprotein A-1: a study of secondary structural and functional properties*, 46 JOL. LIPID RES. 1303 (2005) (“Zhu”).

THE REJECTION UNDER 35 U.S.C. § 103(a)

Issue

In rejecting the pending claims as obvious, the Examiner finds that Moloney teaches expression of apolipoproteins in plants. Final Act. 4. The Examiner finds that Moloney specifically teaches the Apo A-1 “Milano” and “Paris” muteins. *Id.* The Examiner finds that expression of the “Milano” mutein would inherently lead to dimers that have equal activities shown by Apo A-1 Milano dimers. *Id.* The Examiner goes on to find that Zhu teaches seven different muteins of Apo A-1, each having a cysteine substitute at a defined position in one of the alpha helices of the protein. Final Act. 4. The Examiner finds that each of these mutations form dimer and oligomers and possessed different characteristics regarding association with lipids. *Id.* The Examiner concludes that

[a]t the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to generate double mutants that would comprise the cysteine substitution found in Apo A-1 "Milano" and also the cysteine substitution found in Apo A-1 "Paris". One would have been motivated to do so, because beneficial effects have been observed with each of these mutations, and it would have been obvious to combine the mutations to achieve the benefits of both mutations in one mutein. Introducing two cysteines would result in formation of oligomers with more than two monomer subunits, because additional cysteines would be available for forming di-sulfide bonds.

Final Act. 4–5.

Appellants contend that the cited references teach muteins with only one free cysteine and that they are not capable of forming oligomers.

Appeal Br. 8. Appellants argue that the muteins disclosed in Moloney

cannot reach the storage organs of the plant and cannot form oligomers without further processing. Appeal Br. 9. Appellants point out that Zhu only discloses the formation of dimers and does not teach the formation of oligomers. Final Act. 9–10. Appellants go on to argue that the Examiner failed to consider Appellants’ evidence of unexpected results. Appeal Br. 12–13. Appellants also argue that the Examiner has failed to establish that one skilled in the art would have a reasonable expectation of success in producing oligomeric forms of Apo A-1 muteins. Appeal Br. 8–9.

The issue with respect to this rejection is whether the Examiner has established by a preponderance of the evidence that claims 9–17 would have been obvious over Moloney combined with Zhu as defined by 35 U.S.C. § 103(a).

Principles of Law

“Where claimed subject matter has been rejected as obvious in view of a combination of prior art references, a proper analysis under § 103 requires, inter alia, consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have had a reasonable expectation of success. Both the suggestion and the reasonable expectation of success must be founded in the prior art, not in the applicant’s disclosure.” *In re Vaeck*, 947 F.2d 488, 493 (Fed. Cir. 1991) (citation omitted).

Analysis

We agree with Appellants that the Examiner has failed to put forth persuasive evidence that one skilled in the art would have a reasonable expectation of success in combining the teachings of the references. Appeal Br. 8–9, Reply Br. 5–7. As Appellants point out, the Examiner has failed to explain why introducing two cysteine substitution at the locations cited by the Examiner would produce an oligomer as opposed to forming an intra-chain disulfide bond. Reply Br. 6–7. Thus one skilled in the art would not have a reasonable expectation of success in producing oligomers as required by the claims.

The Examiner argues that the introduction of two mutations into the same Apo A-1 mutein would have been *prima facie* obvious since the prior art taught that each mutation would be useful for the same purpose. Ans. 5–6. While the Examiner has correctly cited the general proposition regarding combining two compositions with the same known properties, we find the *per se* argument unpersuasive in the present case. As Appellants point out, in the present case,

[O]ne of ordinary skill would have basic knowledge from protein engineering and known that mutant residues may interact when introduced into the same protein AND their beneficial effects may not be additive, especially where Zhu showed residues R151C (Apo A-1 Milano) and R173C (Apo A-1 Paris) occupy similar positions in helix 5 and helix 6, respectively (see Figure 1's legend at page 1305). Under these circumstances, one of ordinary skill would not have had a reasonable expectation of whether the substituted cysteines interact with each other OR their effects on Apo A-1 activity are additive.

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Conclusion of Law

We conclude that the Examiner has failed to establish by a preponderance of the evidence that claims 9–17 would have been obvious over Moloney combined with Zhu under 35 U.S.C. § 103(a).

DECISION

We reverse the rejection under 35 U.S.C. § 103(a).

REVERSED