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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte TAIMOUR LANGAEE and PETER W. STACPOOLE¹

Appeal 2015-005006
Application 13/703,990
Technology Center 1600

Before DONALD E ADAMS, ERIC B. GRIMES, and
RACHEL H. TOWNSEND, *Administrative Patent Judges*.

TOWNSEND, *Administrative Patent Judge*.

DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to an array for determining a GSTZ1/MAAI haplotype of a subject, which have been rejected as anticipated and obvious. We have jurisdiction under 35 U.S.C. § 6(b).

We reverse.

STATEMENT OF THE CASE

“DCA [dichloroacetate] has long been used as an investigational drug for the treatment of several acquired or congenital disorders.” (Spec. 14–15.) “Dichloroacetate (DCA) . . . is dehalogenated by the bifunctional

¹ Appellants identify the Real Party in Interest as University of Florida Research Foundation, Inc. (Appeal Br. 3.)

enzyme glutathione transferase zeta (GSTz1)/maleylacetoacetate isomerase (MAAI).” (Spec. 14.) “DCA inhibits GSTz1/MAAI, which leads to a marked decrease in its plasma clearance.” (Spec. 15.) Moreover, “[e]nzyme inhibition by DCA also results in the accumulation of the potentially hepatotoxic tyrosine intermediates maleylacetoacetate and maleylacetone and of delta-aminolevulinate, a precursor of heme synthesis that has been associated with neurotoxic effects.” (*Id.*)

Different haplotypes for GSTz1/MAAI show different activity towards DCA kinetics and biotransformation of DCA in humans. (Spec. 18–22). The claimed invention concerns an array for determining a GSTz1/MAAI haplotype of a subject.

Claims 18–28 are on appeal.² Claim 18 is representative and reads as follows:

18. An array for determining a GSTZ1/MAAI haplotype of a subject comprising:

a first target substrate that can detect the presence of the KGM allele in the GSTZ1/MAAI haplotype, wherein the first target substrate comprises a polynucleotide having a sequence corresponding to a Val99Met mutation in GSTZ1/MAAI;

a second target substrate that can detect the presence of the EGM allele in the GSTZ1/MAAI haplotype, wherein the second target substrate comprises a polynucleotide having a sequence corresponding to a Thr82Met mutation in GSTZ1/MAAI;

a third target substrate that can detect the presence of the EGT allele in the GSTZ1/MAAI haplotype, wherein the third

² Claims 1–17 are also pending, but stand withdrawn from consideration. (Appeal Br. 5.)

target substrate comprises a polynucleotide having a sequence corresponding to a wild-type GSTZ1/MAAI;

a fourth target substrate that can detect the presence of the KGT allele in the GSTZ1/MAAI haplotype, wherein the fourth target substrate comprises a polynucleotide having a sequence corresponding to a Glu32Lys mutation in GSTZ1/MAAI;

and

a fifth target substrate that can detect the presence of the KRT allele in the GSTZ1/MAAI haplotype, wherein the fifth target substrate comprises a polynucleotide having a sequence corresponding to a Gly42Arg mutation in GSTZ1/MAAI.

(Appeal Br. 30.)

The following grounds of rejection by the Examiner are before us on review:

Claim 18 under 35 U.S.C. § 102(b) as anticipated over Fodor.³

Claims 18–28 under 35 U.S.C. § 103(a) as unpatentable over Fodor and Ahern.⁴

DISCUSSION

Anticipation

The Examiner finds that Fodor anticipates the claimed invention because Fodor “exemplifies . . . a comprehensive nucleic acid array comprising every 10-mer probe sequence” and that array “includes target substrates that meet the limitations of the five target substrates required by

³ Fodor et al., US 2001/0053519 A1, published Dec. 20, 2001.

⁴ Holly Ahern, *Tools & Technology: Biochemical, Reagent Kits Offer Scientists Good Return on Investment*, *The Scientist*, July 24, 1995, at 20.

the claims.” (Ans. 3; Final Action 3.) The Examiner finds “[f]or example, the array of Fodor et al includes: 5’-ggccagcatg-3’, relevant to the first target substrate; 5’-tagaggagat-3’, relevant to the second target substrate; 5’-tagaggagac-3’, relevant to the third target substrate; 5’-atcgactaca-3’, relevant to the fourth target substrate; and 5’-ataaaggata-3’, relevant to the fifth target substrate.” (*Id.*)

We disagree with the Examiner’s finding of anticipation over Fodor because reading the claim language in light of, and consistent with, the Specification, the broadest reasonable interpretation of the structural requirements of the target substrates does not encompass Fodor’s array.

A. Claim Construction

1. Preamble

According to the Examiner, the language “for determining a GSTZ1/MAAI haplotype of a subject” recited in the preamble is “an intended use of the claimed array” that is not “necessary to give life, meaning, and vitality to the claim.” (Ans. 7–8.) We disagree. Here, the body of claim 18 recites that each of five separate target substrates “can detect the presence of” a particular “allele in the GSTZ1/MAAI haplotype” if the allele is present. (Claim 18 (emphasis added).) Consequently, as Appellants noted, “the preamble of claim 18 recit[ing], ‘a GSTZ1/MAAI haplotype,[’] . . . establishes antecedent basis for the ‘GSTZ1/MAAI haplotype’ recited five times in the body of the claim.” (Reply Br. 6.) Moreover, because the polynucleotide substrates are able to detect a particular allele in “the GSTZ1/MAAI haplotype,” the array is able to “achieve its purpose of ‘determining a GSTZ1/MAAI haplotype.’” (Reply

Br. 7.) As such, we find the preamble “act[s] as a necessary component of the claimed invention.” *Eaton Corp. v. Rockwell Int’l Corp.*, 323 F.3d 1332, 1339 (Fed. Cir. 2003). That is, we find that the claimed array must be able to determine the GSTZ1/MAAI haplotype of the subject.

2. *Structural Requirement of the Target Substrate*

According to the Examiner, because “a sequence” only requires a minimum of two nucleotides, and “corresponding to” reasonably can be interpreted to mean “identical or complementary to” each target substrate, which has “the limitation that it ‘comprises a polynucleotide having a sequence corresponding to a’ mutation or wild-type sequence,” requires only that there be two contiguous nucleotides that are identical or complementary to any portion of the amino acid mutation recited or wild-type sequence. (Ans. 2–3, 7; Final Action 7.) In other words, according to the Examiner, the target sequence does not require an entire codon sequence, e.g., a sequence corresponding to a Val99Met mutation is not a limitation requiring an entire ATG methionine codon, but rather, includes any two contiguous nucleotides from ATG. (Ans. 2–3, 9–10; Final Action 9–10.) Moreover, according to the Examiner, the functionality of the target substrates does not require “that different alleles are somehow distinguished from one another” just that a particular allele can be detected “when that allele is in a sample.” (Ans. 7; Final Action 7.) We disagree with the Examiner’s interpretation of what is required structurally and functionally by the claimed “target substrates.” First, as we noted above, the claim preamble requires that the array be able to determine the GSTZ1/MAAI haplotype of a subject. In order for that to occur, the target substrate must be able to distinguish the

recited alleles one from another, not just be capable of detecting an amino acid that is in one allele that might also be in another allele.

Claim 18 requires that target substrates can detect a particular allele in the GSTZ1/MAAI haplotype, i.e., the KGM allele, the EGM allele, the EGT allele, the KGT allele, and the KRT allele, which if detected allows for the array to be able to determine the GSTZ1/MAAI haplotype of the subject. The Specification teaches that these alleles of GSTZ1/MAAI have particular defining amino acids at particular positions in GSTZ1/MAAI.

The Specification teaches that certain single nucleotide polymorphisms (“SNPs”) in the GSTZ1/MAAI gene result in particular amino acid changes in the enzyme encoded by the GSTZ1/MAAI gene at one or more of positions 32, 42, 82, and 99, as compared to the “wild-type” haplotype “EGT.” (Spec. 10, 17–19, 21.) These amino acid changes affect the kinetics of the investigational drug dichloroacetate (“DCA”). (Spec. 17, 19, 22, 31.)

The wild-type EGT allele has the amino acid Glutamic Acid (“Glu”) at position 32, the amino acid Glycine (“Gly”) at position 42, the amino acid Threonine (“Thr”) at position 82, and the amino acid Valine (“Val”) at position 99. (Spec. 19, 31.) The EGM allele has an SNP of C to T that results in a substitution of Methionine (“Met”) for Thr at position 82. (Spec. 18, 31.) At amino acid positions 32 and 42, however, the EGM allele has the same amino acids as the EGT wild-type, namely, Glu at 32 and Gly at 42. (Spec. 31.) The KGT allele has an SNP of G to A that results in a substitution of Lysine (“Lys”) for Glu at position 32. (Spec. 17–18, 31.) At amino acid positions 42 and 82, however, the KGT allele has the same

amino acids as the EGT wild-type, namely, Gly at 42 and Thr at 82. (Spec. 31.) The KRT allele has an SNP of G to A that results in a substitution of Arginine (“Arg”) for Gly at position 42. (Spec. 18, 31.) At amino acid position 82, however, the KRT allele has the same amino acid as the EGT wild-type, namely, Thr82. (Spec. 31.) It has another substitution from the wild-type at position 32, the same substitution that the KRT allele has, namely Lysine. (Spec. 31.) The KGM allele has a missense mutation from G to A in an exon that results in the substitution of Met at position 99 for the wild-type amino acid Val. (Spec. 19.)

While the Specification teaches that SNPs are the cause of these amino acid substitutions (Spec. 17–19), claim 18, nevertheless, requires the target substrates to include polynucleotide sequences that correspond to “Val99Met,” “Thr82Met,” “Glu32Lys,” and “Gly42Arg,” i.e., the amino acids that result from the mutations at the particular locations of the GSTZ1/MAAI gene. (Claim 18.) As Appellants point out, “[i]f all that is required to identify MET[, for example,] is ‘AT’ then not only any MET within the GSTZ1/MAAI be identified by [the first target substrate, but] any Isoleucine, Histidine, Aspartate, and Tyrosine present [may be detected] as well.” (Appeal Br. 23.) That is because Isoleucine is encoded by “ATA,” Histidine is encoded by “CAT,” Aspartate is encoded by “GAT,” and Tyrosine is encoded by “TAT.” (*Id.*) Thus, as Appellants note, a polynucleotide of only two nucleotides that encodes part of the amino acid substitution at a particular position of the GSTZ1/MAAI enzyme that results from a SNP is not sufficient for the target to detect the allele of import. Thus, regardless of the fact that the Specification teaches the recited amino

acid substitution results from a SNP, the claim is directed to sequences that can detect the presence of specific polymorphisms in the GSTZ1/MAAI gene, not the presence of a particular codon in any context.

Claim 18 requires that the target substrates can detect a particular allele. As noted above, these alleles are differentiated by what amino acids are encoded at positions 32, 42, 82, and 99 compared to the wild-type GSTZ1/MAAI amino acids at these positions. Thus, for example, the EGT (wild-type) haplotype has Glu32/Gly42/Thr82, whereas the KGT haplotype has Lys32/Gly42/Thr82, the EGM haplotype has Glu32/Gly42/Met82, and the KRT haplotype has Lys32/Arg42/Thr82. (Spec. 31.) The Examiner has not provided persuasive evidence to show that a sequence that contains two contiguous nucleotides that are part of the triplet codon encoding one of the recited amino acids of positions 32, 42, 82, or 99 is capable of detecting any of the claimed alleles. That is, a dinucleotide sequence does not detect the substituted amino acid of import at the requisite position, much less determine whether one of the recited alleles is present. Thus, we conclude that the Examiner's interpretation of claim 18 is beyond what is a reasonable interpretation in light of, and consistent with, Appellants' Specification.

We find, instead, that the language "a second target substrate that can detect the presence of the EGM allele in the GSTZ1/MAAI haplotype, wherein the second target substrate comprises a polynucleotide having a sequence corresponding to a Thr82Met mutation in GSTZ1/MAAI" requires that the second target substrate must be able to detect the presence of the EGM allele of the GSTZ1/MAAI gene by recognizing a codon for Met at position 82, not simply any ATG (Met) codon in the subject, as well as the

codons in the GSTZ1/MAAI gene for Glu at position 32 and Gly at position 42, because the Specification defines the EGM allele as having those codons at those positions (Spec. 31). Likewise, the Specification defines the KGM, EGT, KGT, and KRT alleles that are recited in the claims to require specific codons at specific position of the GSTZ1/MAAI gene, not generic codons regardless of context.

B. Anticipation

The Examiner contends that because the 10-mer array of Fodor includes: 5'-ggccagcatg-3'; 5'-tagaggagat-3'; 5'-tagaggagac-3'; 5'-atcgactaca-3'; and 5'-ataaaggata-3', it anticipates claim 18. (Ans. 3; Final Action 3). In light of our claim construction above, we disagree. The Examiner has not pointed to evidence showing that the 10-mers in Fodor's array "can detect the presence of" the specific alleles of GSTZ1/MAAI that are recited in the claims on appeal. As discussed above, the claims require more than detecting the presence of a single codon, regardless of context; the claims require detecting the presence of specific alleles, which are defined in the Specification as encoding specific amino acids at specific positions in the GSTZ1/MAAI gene. The Examiner has not shown that the 10-mers of Fodor's array have that ability.

For the foregoing reasons, therefore, we reverse the Examiner's finding that claim 18 is anticipated by Fodor.

Obviousness

The Examiner has rejected claims 18–28 under 35 U.S.C. § 103(a) as unpatentable over Fodor and Ahern. The Examiner relies on Ahern regarding limitations in the dependent claims 19–28, not for any further

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teaching regarding the first through fifth target substrates of claim 18.
Therefore, for the reasons set forth above, we reverse the rejection of claims 18–28 under 35 U.S.C. § 103(a) as unpatentable over Fodor and Ahern.

SUMMARY

We reverse the rejection of claim 18 under 35 U.S.C. § 102(b) as anticipated by Fodor, as well as the rejection of claims 18–28 under 35 U.S.C. § 103(a) as unpatentable over Fodor and Ahern.

REVERSED