

UNITED STATES BOARD OF PATENT APPEALS  
AND INTERFERENCES

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Ex parte GEETHA VASANTHAKUMAR  
and JOHN A. MONTGOMERY

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Appeal No. 1994-1573  
Application No. 07/552,744

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ON BRIEF

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Before McKELVEY, Senior Administrative Patent Judge, and  
SCHAFFER and TORCZON, Administrative Patent Judges.

TORCZON, Administrative Patent Judge.

DECISION ON APPEAL

Appellants seek review under 35 U.S.C. § 134 of the final  
rejection of claims 1-7<sup>1</sup> (Paper No. 13 (Notice of Appeal)).

We affirm in part.

BACKGROUND

Appellants filed the subject application for patent on  
16 July 1990 (Paper No. 1).

The claimed subject matter relates to an enzyme present  
in *Plasmodium falciparum* parasites. These parasites cause  
malaria in mammalian hosts. *P. falciparum* parasites are

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<sup>1</sup>Claim 8 was withdrawn from consideration by the examiner  
when Appellants elected claims 1-7 in response to the  
examiner's restriction requirement (Paper No. 6 (Rej.) at 2).  
See 37 CFR § 1.142. Claims 1-7 are reproduced in an Appendix  
to this decision.

incapable of de novo purine synthesis within the red blood cells of the host and must rely upon the host's cells as a source for needed purines (Paper No. 1 at 1 and 2).

The *P. falciparum* enzyme hypoxanthine-guanine phosphoribosyl transferase (HGPRT) is present in blood-stage *P. falciparum* parasites at high levels. The enzyme scavenges purines from host cells to form nucleotides for the parasites' own use. Specifically, the enzyme catalyzes the phosphoribosylation of hypoxanthine and guanine to yield the nucleotides inosine monophosphate (IMP) and guanosine (Paper No. 1 at 2 and 3).

Appellants report that they have isolated the cDNA sequence of the protein *Plasmodium falciparum* HGPRT and have successfully expressed this protein in *E. coli* (Paper No. 1 at 6 and 7).

#### The rejections

The examiner made the following rejections:

1. Claims 2-4 and 6 under 35 U.S.C. § 102(a) as anticipated by-

G. Vasanthakumar, R.L. Davis, Jr., M.A. Sullivan, & J.P. Donahue, Nucleotide sequence of cDNA clone for hypoxanthine-guanine phosphoribosyltransferase from

Plasmodium falciparum, 17 Nucleic Acids Res. 8382  
(1989) (Vasanthakumar I);

2. Claims 2-4 under 35 U.S.C. § 102(b) as anticipated

by-

A. King & D.W. Melton, Characterization of cDNA Clones for hypoxanthine-guanine phosphoribosyltransferase from the human malarial parasite, Plasmodium falciparum: Comparisons to the mammalian gene and protein, 15 Nucleic Acids Res. 10469-10481 (1987) (King); and

3. Claims 1-7 under 35 U.S.C. § 103 as unpatentable

over the combination of King and the following additional references-

D.B. Smith, M.R. Rubira, R.J. Simpson, K.M. Davern, W.U. Tiu, P.G. Board, & G.F. Mitchell, Expression of an enzymatically active parasite molecule in Escherichia coli: Schistosoma japonicum glutathione S-transferase, 27 Molecular & Biochemical Parasitology 249-256 (1988) (Smith),

G. Vasanthakumar & R.L. Davis, Jr., Cloning and expression of the hypoxanthine-guanine phosphoribosyltransferase gene from Plasmodium falciparum in E. coli, J. of Cellular Biochem., Abstracts of the 18th Annual Meetings, Supp. 13 E at 125 (1989) (Vasanthakumar II),

P. Marsh, Ptac, an E. coli Vector for Expression of Non-Fusion Proteins, 14 Nucleic Acids Res. 3603 (1986) (Marsh), and

C.N. Remy & M.S. Smith, Metabolism of 2,6-Diaminopurine Conversion to 5'-Phosphoribosyl-2-Methylamino- 6-Aminopurine by Enzymes of

Escherichia coli, 228 J. Biol. Chem. 325-338 (1957)  
(Remy).

DISCUSSION

35 U.S.C. § 102(a)

Appellants state that claims 2-4 and 6 stand or fall together for purposes of the § 102(a) rejection over Vasanthakumar I (Paper No. 14 (App. Br.) at 12). They do not dispute that Vasanthakumar I teaches the complete nucleotide sequence of *P. falciparum* HGPRT (Paper No. 14 at 13) or that the *P. falciparum* HGPRT nucleotide sequence defined in claim 4 corresponds to the HGPRT sequence described in Vasanthakumar I (Compare claim 4 with Vasanthakumar I at 8382). Instead, they argue that Vasanthakumar I is not a proper reference against their claims because it reports the work of the Appellants (Paper No. 14 at 12-14). Counsel argues that co-applicant Vasanthakumar was responsible for naming the authors and that she named them in accordance with conventional protocol for authorship of scientific papers. Therefore, counsel argues that Davis was named because he was the technician most responsible for conducting the testing that led to the sequencing of the HGPRT and that Sullivan and Donahue were named because they were the scientific directors of the

project. Counsel explains the omission of co-applicant Montgomery from the paper as an oversight (Paper No. 14 at 12-13). Counsel argues that arguments in the record explaining why the authors of the reference article were not the inventors should be sufficient to overcome the 102(a) rejection (Paper No. 14 at 13).

"It was incumbent ... on [Appellants] to provide a satisfactory showing which would lead to a reasonable conclusion that [they are] the [true] inventor[s]" of the subject matter disclosed in the article and claimed in the application. In re Katz, 687 F.2d 450, 455, 215 USPQ 14, 18 (CCPA 1982). Such showings should be in the form of sworn affidavits or declarations by the applicants filed in accordance with 37 CFR §§ 1.131 and 1.132. No such declarations or affidavits are currently of record.<sup>2</sup> The argument of counsel cannot take the place of evidence lacking in the record. E.g., Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 595, 44 USPQ2d 1610, 1615 (Fed. Cir. 1997). The

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<sup>2</sup>Appellants state in their Brief on Appeal filed 26 July 1993 that they will file declarations under 37 CFR § 1.131 or § 1.132 "within the next thirty days" (Paper No. 14 at 13), but there is no evidence of record that such declarations were ever received.

preponderance of evidence currently of record supports the § 102(a) rejection over Vasanthakumar I.

35 U.S.C. § 102(b)

Appellants request independent consideration of each of claims 2-4 for the rejection under 35 U.S.C. § 102(b) over King (Paper No. 14 at 19). King describes isolated cDNA clones for *P. falciparum* HGPRT. The clones were identified using full-length mouse HGPRT cDNA clones as probes (King at 10470). Sequencing of the *P. falciparum* HGPRT clones revealed a nucleotide sequence identical to the sequence set forth in Appellants' claim 4 except that at one point King's sequence contains a thymine instead of the cytosine of Appellants' claim 4 sequence. The substitution of thymine for cytosine results in a codon in King (ATG) that encodes the amino acid methionine in the same location where a codon in Appellants' sequence (ACG) encodes the amino acid threonine. King states that "all attempts to express the protein product of P. falciparum HGPRT cDNA were unsuccessful" (King at 10478).

Claim 2 is limited to "A cDNA sequence encoding for *Plasmodium falciparum* HGPRT". The claim requires a cDNA sequence that directs the production of a protein exhibiting

hypoxanthine-guanine phosphoribosyltransferase (HGPRT) activity in *P. falciparum*. King was unable to express the protein product and did not detect and characterize the activity of any protein product of King's sequence. It follows that King does not establish with any degree of certainty that King's cDNA sequence would encode a protein exhibiting HGPRT activity. One skilled in the art might conclude that King's cDNA could express a protein exhibiting HGPRT activity. Inherency, however, may not be established by probabilities or possibilities. The fact that a result might occur in a specific set of circumstances is not sufficient. Mehl/Biophile Int'l Corp. v. Milgraum, \_\_\_ F. 3d \_\_\_, \_\_\_, 52 USPQ2d 1303, 1305 (Fed. Cir. 1999).

The examiner has not established that King's cDNA inherently encodes a protein that would exhibit HGPRT activity, so the rejection of claim 2 under § 102(b) is reversed. Claim 3 requires the same HGPRT activity as claim 2, and claim 4 depends from claim 3, so the rejection of these claims must be reversed as well.

35 U.S.C. § 103

Appellants request independent consideration of each of claims 1-7 for § 103 rejection over King, Smith, Vasanthakumar II, Marsh, and Remy (Paper No. 14 at 30). The examiner recognizes that King does not teach expression of the cDNA it describes but notes King's statement that "[i]f this protein could be expressed in some convenient host, there are totally non-homologous regions in the *P. falciparum* enzyme which could be used as potential drug therapy targets" (King at 10480). The examiner found King's statement to provide ample motivation for a person having ordinary skill in the art to look to the prior art for a suitable host for expression (Paper No. 15 (Ex. Ans.) at 4-5).

The Smith, Vasanthakumar II, Marsh, and Remy references describe expression of parasitic enzymes, including *P. falciparum* HGPRT (Vasanthakumar II), in *E. coli*. Based on these references, the examiner finds that one skilled in the art would have been motivated to select *E. coli* as a suitable host for expression of the *P. falciparum* HGPRT cDNA described by King.

There is no evidence of record to indicate 1) that King's cDNA sequence would be successfully expressed in *E. coli* or 2) that the encoded polypeptide would exhibit HGPRT activity upon successful expression. Without further evidence, a person having ordinary skill in the art might have found it obvious to try expressing the King cDNA in *E. coli* to see if any resulting protein exhibited HGPRT activity, but this is not the standard under 35 U.S.C. § 103. E.g., In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987).

King, in explaining how codon usage problems may hamper the study of *P. falciparum* HGPRT, discourages the selection of *E. coli* as a suitable host. King speculates that a preference in *P. falciparum* for TTA as a codon for leucine expression could be a problem in hosts that rarely use the TTA codon for leucine. King reports that human  $\beta$ -globin genes never use, and highly expressed *E. coli* genes rarely use, the TTA codon for leucine (King at 10478-10479). The prior art references must be considered in their entirety, including portions that would lead away from the claimed invention. W.L. Gore & Associates, Inc. v. Garlock, Inc., 721 F.2d 1540, 1548, 220 USPQ 303, 309 (Fed. Cir. 1983). A person having ordinary

skill in the art reading King's specific teachings would have been led away from the selection of *E. coli* as a host for expression of King's cDNA because of potential codon usage problems regardless of what the other more general references might have suggested. E.g. Tec Air, Inc. v. Denso Manufacturing Michigan, Inc., \_\_\_ F.3d \_\_\_, \_\_\_, 52 USPQ2d 1294, 1298 (Fed. Cir. 1999) (apparently inoperative combination teaches away). Since there is no motivation to modify King and since King discourages the selection of *E. coli* as a host for expression of the described cDNA, the § 103 rejection over the combination of King and the other references is reversed.

DECISION

We affirm the § 102(a) rejection of claims 2-4 and 6 over Vasanthakumar I. We reverse the § 102(b) rejection of claims 2-4 over King and the § 103 rejection of claims 1-7 over King and the other references. The period for taking any subsequent action in connection with this appeal will be

extended only under the limited circumstances provided in 37  
CFR § 1.136(b).

AFFIRMED

FRED E. McKELVEY, Senior	)	
Administrative Patent Judge	)	
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RICHARD E. SCHAFER	)	) BOARD OF PATENT
Administrative Patent Judge	)	APPEALS AND
	)	INTERFERENCES
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	)	
RICHARD TORCZON	)	
Administrative Patent Judge	)	

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Appendix

1. An isolated and purified dimeric protein having a molecular weight of about 52,000 daltons and having substantially the following amino acid residue sequence:

Met Pro Ile Pro Asn Asn Pro Gly Ala Gly Glu Asn Ala Phe  
Asp Pro Val Phe Val Lys Asp Asp Asp Gly Tyr Asp Leu Asp  
Ser Phe Met Ile Pro Ala His Tyr Lys Lys Tyr Leu Thr Lys  
Val Leu Val Pro Asn Gly Val Ile Lys Asn Arg Ile Glu Lys  
Leu Ala Tyr Asp Ile Lys Lys Val Tyr Asn Asn Glu Glu Phe  
His Ile Leu Cys Leu Leu Lys Gly Ser Arg Gly Phe Phe Thr  
Ala Leu Leu Lys His Leu Ser Arg Ile His Asn Tyr Ser Ala  
Val Glu Thr Ser Lys Pro Leu Phe Gly Glu His Tyr Val Arg  
Val Lys Ser Tyr Cys Asn Asp Gln Ser Thr Gly Thr Leu Glu  
Ile Val Ser Glu Asp Leu Ser Cys Leu Lys Gly Lys His Val  
Leu Ile Val Glu Asp Ile Ile Asp Thr Gly Lys Thr Leu Val  
Lys Phe Cys Glu Tyr Leu Lys Lys Phe Glu Ile Lys Thr Val  
Ala Ile Ala Cys Leu Phe Ile Lys Arg Thr Pro Leu Trp Asn  
Gly Phe Lys Ala Asp Phe Val Gly Phe Ser Ile Pro Asp His  
Phe Val Val Gly Tyr Ser Leu Asp Tyr Asn Glu Ile Phe Arg  
Asp Leu Asp His Cys Cys Leu Val Asn Asp Glu Gly Lys Lys  
Lys Tyr Lys Ala Thr Ser Leu.

2. A cDNA sequence encoding for *Plasmodium falciparum* HGPRT.

3. A purified isolated DNA sequence consisting essentially of a DNA sequence coding for the protein having the amino acid residue sequence according to Claim 1 or for a protein having substantially the same amino acid sequence and substantially the same HGPRT activity as the protein defined in Claim 1.

4. A purified isolated DNA sequence according to Claim 3 wherein one such sequence is:

ATG CCA ATA CCA AAT AAT CCA GGA GCT GGT GAA AAT GCC TTT  
GAT CCC GTT TTC GTA AAG GAT GAC GAT GGT TAT GAC CTT GAT  
TCT TTT ATG ATC CCT GCA CAT TAT AAA AAA TAT CTT ACC AAG  
GTC TTA GTT CCA AAT GGT GTC ATA AAA AAC CGT ATT GAG AAA  
TTG GCT TAT GAT ATT AAA AAG GTG TAC AAC AAT GAA GAG TTT  
CAT ATT CTT TGT TTG TTG AAA GGT TCT CGT GTT TTT TTC ACT

GCT CTC TTA AAG CAT TTA AGT AGA ATA CAT AAT TAT AGT GCC  
GTT GAG ACG TCC AAA CCA TTA TTT GGA GAA CAC TAC GTA CGT  
GTG AAA TCC TAT TGT AAT GAC CAA TCA ACA GGT ACA TTA GAA  
ATT GTA AGT GAA GAT TTA TCT TGT TTA AAA GGA AAA CAT GTA  
TTA ATT GTT GAA GAT ATT ATT GAT ACT GGT AAA ACA TTA GTA  
AAG TTT TGT GAA TAC TTA AAG AAA TTT GAA ATA AAA ACC GTT  
GCC ATC GCT TGT CTT TTT ATT AAA AGA ACA CCT TTG TGG AAT  
GGT TTT AAA GCT GAT TTC GTT GGA TTC TCA ATT CCT GAT CAC  
TTT GTT GTT GGT TAT AGT TTA GAC TAT AAT GAA ATT TTC AGA  
GAT CTT GAC CAT TGT TGT TTG GTT AAT GAT GAG GGA AAA AAG  
AAA TAT AAA GCA ACT TCA TTA TAA.

5. An isolated and purified protein which is *Plasmodium falciparum* HGPRT enzyme.

6. An expression vector comprising a DNA sequence encoding for an enzyme selected from the group consisting of (1) *P. falciparum* HGPRT enzyme; and (2) a HGPRT active mutant of *P. falciparum* HGPRT enzyme or a fragment thereof having substantially the same activity as the enzyme wherein an amino acid residue has been inserted, substituted or deleted in or from the amino acid sequence of the enzyme or its fragment.

7. A purified protein isolated from a recombinant organism transformed with a vector that codes for the expression of *Plasmodium falciparum* HGPRT said protein having substantially the same amino acid sequence and substantially the same HGPRT activity as the protein according to Claim 1.

Appeal No. 94-1573  
Application No. 07/552,744

Paper No. 24  
Page 14

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