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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MERCK SHARP & DOHME CORP.,
Petitioner,

v.

GENENTECH, INC. and CITY OF HOPE,
Patent Owner.

Case IPR2016-01373
Patent 6,331,415 B1

Before TONI R. SCHEINER, LORA M. GREEN, and SUSAN L. C. MITCHELL, *Administrative Patent Judges*.

GREEN, *Administrative Patent Judge*.

DECISION
Denying Institution of *Inter Partes* Review
37 C.F.R. § 42.108

I. INTRODUCTION

Merck Sharp & Dohme Corp. ("Petitioner") filed a Petition requesting an *inter partes* review of claims 1–4, 11, 12, 14–20, and 33 of U.S. Patent No. 6,331,415 B1 (Ex. 1001, "the '415 patent"). Paper 1 ("Pet."). Genentech, Inc. and City of Hope (collectively, "Patent Owner") filed a Preliminary Response. Paper 24.

We have jurisdiction under 35 U.S.C. § 314, which provides that an *inter partes* review may not be instituted "unless . . . there is a reasonable likelihood that the petitioner would prevail with respect to at least 1 of the claims challenged in the petition." Upon considering the Petition and the Preliminary Response, we exercise our discretion under 35 U.S.C. § 325(d) and decline to institute an *inter partes* review.

A. Related Proceedings

Petitioner identifies four petitions for *inter partes* review challenging the '415 patent. Pet. 62. A trial in IPR2016-01624 was instituted on February 5, 2016, to which the trial in IPR2016-00460 was joined. That joined proceeding settled on September 2, 2016. The petition in IPR2016-00383 was denied institution on June 23, 2016. Pet. 63. Petitioner identifies also IPR2016-00710 (*id.*), which was instituted on September 8, 2016.

In addition, Petitioner has filed a second Petition for *inter partes* review of some of the same claims of the '415 patent, IPR2017-00047, in which Petitioner seeks joinder to IPR2016-00710. A trial in IPR2017-00047 has been instituted and joined to IPR2016-00710 concurrently with the instant decision.

Patent Owner identifies also several district court and PTO proceedings related to the '415 patent. Papers 15, 25.

B. The '415 Patent (Ex. 1001)

The '415 patent issued on December 18, 2001, and claims priority to an application filed on April 8, 1983, now U.S. Patent No. 4,816,567. *See* Ex. 1001, Title Page. Shmuel Cabilly, Herbert L. Heyneker, William E. Holmes, Arthur D. Riggs, and Ronald B. Wetzel are the listed co-inventors. *Id.*

The '415 patent relates generally to processes for producing immunoglobulin molecules in a host cell transformed with a first DNA sequence encoding the variable domain of the heavy chain and a second DNA sequence encoding the variable domain of the light chain, as well as vectors and transformed host cells used in such processes. *Id.*, Abstract. More specifically, the first and second DNA sequences are present either in different vectors or in a single vector, and independently expressed so that the immunoglobulin heavy and light chains are produced as separate molecules in the transformed single host cell. *See id.*, Claims 1, 15, 18, 21, and 33.

According to the Specification of the '415 patent, prior to the invention, there were two major sources of vertebrate antibodies—they could be generated *in situ* by the mammalian B lymphocytes or in cell culture by B-cell hybrids (hybridomas). *Id.* at 1:42–45. The Specification notes, however, that monoclonal antibodies produced by these two sources suffer from disadvantages, including contamination with other cellular materials, instability, production of an undesired glycosylated form, high cost, and an inability to manipulate the genome. *Id.* at 2:40–66. The Specification recognizes that "recombinant DNA technology can express entirely heterologous polypeptides—so-called direct expression—or

alternatively may express a heterologous polypeptide fused to a portion of the amino acid sequence of a homologous polypeptide." *Id.* at 4:33–37.

The Specification states that "[t]he invention relates to antibodies and to non-specific immunoglobulins (NSIs) formed by recombinant techniques using suitable host cell cultures," which can "be manipulated at the genomic level to produce chimeras of variants which draw their homology from species which differ from each other." *Id.* at 4:53–59. The Specification further indicates that "[t]he ability of the method of the invention to produce heavy and light chains or portions thereof, in isolation from each other offers the opportunity to obtain unique and unprecedented assemblies of immunoglobulins, Fab regions, and univalent antibodies." *Id.* at 12:52–62.

C. Illustrative Claims

Petitioner challenges claims 1–4, 11, 12, 14–20, and 33 of the '415 patent. Claims 1, 15, 18, and 33 are independent. Independent claim 1 is illustrative, and is reproduced below:

> 1. A process for producing an immunoglobulin molecule or an immunologically functional immunoglobulin fragment comprising at least the variable domains of the immunoglobulin heavy and light chains, in a single host cell, comprising the steps of:
>
> (i) transforming said single host cell with a first DNA sequence encoding at least the variable domain of the immunoglobulin heavy chain and a second DNA sequence encoding at least the variable domain of the immunoglobulin light chain, and
>
> (ii) independently expressing said first DNA sequence and said second DNA sequence so that said immunoglobulin heavy and light chains are produced as separate molecules in said transformed single host cell.

D. The Asserted Grounds of Unpatentability

Petitioner challenges the patentability of claims 1–4, 11, 12, 14–20, and 33 of the '415 patent on the following grounds (Pet. 12–13):

References	Basis	Claims Challenged
Mulligan Papers[1] and Axel[2]	§ 103	1, 3, 4, 11, 12, 14–17, 19, and 33
Mulligan Papers, Axel, and the Nobel Article[3]	§ 103	1, 3, 4, 11, 12, 14–17, 19, and 33
Mulligan Papers, Axel, and Builder[4]	§ 103	1, 3, 4, 11, 12, 14–17, 19, and 33
Southern[5] and Axel	§ 103	1, 2, 11, 12, 14, 18–20, and 33
Southern, Axel, and Builder	§ 103	1, 2, 11, 12, 14, 18–20, and 33

Petitioner relies also on the Declarations of Roger D. Kornberg, Ph.D. (Ex. 1009) and Richard A. Lerner, Ph.D. (Ex. 1008). Pet. 13.

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[1] R.C. Mulligan and P. Berg, *Expression of a Bacterial Gene in Mammalian Cells*, 209 SCIENCE 1422–27 (1980) (Ex. 1002); R.C. Mulligan and P. Berg, *Selection for Animal Cells that Express the Escherichia coli Gene Coding for Xanthine-Guanine Phosphoribosyltransferase*, 78 PNAS 2072–76 (1981) (Ex. 1003) (collectively, the "Mulligan Papers"),

[2] Axel et al., U.S. Patent No. 4,399,216, issued Aug. 16, 1983 (Ex. 1006) ("Axel").

[3] Paul Berg, *Dissections and Reconstructions of Genes and Chromosomes*, 213 SCIENCE 296–303 (1981) (Ex. 1004) ("the Nobel Article").

[4] Builder et al., U.S. Patent No. 4,511,502, issued Apr. 16, 1985 (Ex. 1007) ("Builder").

[5] P.J. Southern and P. Berg, *Transformation of Mammalian Cells to Antibiotic Resistance with a Bacterial Gene Under Control of the SV40 Early Region Promoter*, 1 J. MOLECULAR AND APPLIED GENETICS327–341 (1982) (Ex. 1005) ("Southern").

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