UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

MYLAN PHARMACEUTICALS, INC., and
MERCK SHARP & DOHME CORP.,
Petitioners

v.

GENENTECH, INC. AND CITY OF HOPE
Patent Owners

U.S. Patent No. 6,331,415

"Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein"

Inter Partes Review No. 2016-0710[1]

DECLARATION OF ATSUO OCHI IN SUPPORT OF MERCK'S REPLY TO PATENT OWNER'S RESPONSE

[1] Case IPR2017-00047 has been joined with this proceeding.

I, Atsuo Ochi, hereby declare and state as follows:

I. INTRODUCTION

1. I have been asked by counsel for Merck Sharp & Dohme Corp. ("Merck") to submit this declaration in connection with IPR No. 2016-00170, regarding U.S. Patent No. 6,331,415, "Methods of Producing Immunoglobulins, Vectors and Transformed Host Cells for Use Therein," owned by Genentech, Inc. and City of Hope (collectively, "Patent Owners").

2. I have been asked to provide information on my scientific work related to recombinant expression of immunoglobulin heavy and light chains in mammalian cells, which took place in the early 1980s, in response to statements made in Patent Owners' Response (Paper 31) and the opinions expressed by Patent Owners' expert Dr. John Fiddes (Ex. 2019). Specifically, I have been asked to explain how the work I performed prior to April 1983 refutes Patent Owners' and Dr. Fiddes' arguments regarding the alleged uncertainties surrounding recombinant expression of antibodies in April 1983 and their arguments that the "prevailing mindset" in April 1983 was to express only one exogenous protein per host cell.

II. BACKGROUND

3. As further detailed in my curriculum vitae, attached hereto as Exhibit A, I graduated from Tokyo Medical and Dental University in 1978 with a degree in Dentistry. Afterwards, I matriculated to Tokyo University, where I graduated with

a Ph.D. in Immunology in 1982. I completed Postdoctoral training at the Ontario Cancer Institute and University of Toronto, in Dr. Nobumichi Hozumi's lab, in 1986.

4. After my Postdoctoral training, I was hired as a Staff Scientist and Assistant Professor at the Mt. Sinai Hospital Research Institute at the University of Toronto from 1986 to 1994. In 1994, I transferred to the John P. Robarts Research Institute and the University of Western Ontario, where I was a Staff Scientist and Assistant Professor until 1999. In 1999, I was promoted to Associate Professor, a position I held until 2005. My work, through this point, was entirely in the departments of Microbiology, Medical Genetics, and Immunology.

5. In 2003, I stopped working as a Staff Scientist at the John P. Robarts Research Institute, and instead was hired as an Associate Scientist in Research in 2004. I held that position until 2010, when I transferred to the Mt. Sinai Hospital Research Institute in Toronto, where I had the same title. I continued in that role until 2011, when I took positions with the New York University Medical Center as a Scientist in Research and Assistant Professor, both in the Department of Surgery.

6. I have authored over 50 journal articles and contributed 48 abstracts and presentations.

7. I have received multiple grants and an award for my research. I received the National Institute of Canada Research Scholarship for the term of

1986 through 1990. I have received over $1.5 million in grant money for my research.

8. I am also a member of various professional societies. I was a member of the Canadian Association of Immunologists from 1994 to 2004 and a member of the American Association of Immunologists from 1996 to 2004. I served on the committee for the CIHR senior Investigator Awards committee in 2002 and 2003.

III. COMPENSATION

9. I am being compensated for my work on this case at my standard consulting rate of $500 per hour. My compensation is not contingent upon the results of my analysis or the substance of my testimony. I have no stake in the outcome of this proceeding or any related litigation or administrative proceedings. I have no financial interest in Merck, and similarly have no financial interest in the '415 patent or its owner.

IV. MY WORK EXPRESSING THE ANTIBODY LIGHT CHAIN

10. I moved to Canada and joined Dr. Hozumi's lab in June 1982. Immediately thereafter, I began working to express an antibody light chain using recombinant DNA techniques. My work on this project and the follow-on project to express the heavy and light chains is reflected in a series of lab notebooks that I kept in the ordinary course of my research and that have remained in my possession since then. True and accurate copies of these notebooks are attached as

Exhibits 1137, 1138, and 1146. My work expressing an antibody light chain is also described in Ochi et al. "Transfer of a cloned immunoglobulin light-chain gene to mutant hybridoma cells restores specific antibody production," *Nature* 340-342 (1983) (Ex. 1021 ("Ochi I")).

11. Upon joining Dr. Hozumi's lab, my first task was to construct a vector containing the κ gene for a IgM(κ) antibody specific for the hapten TNP. Dr. Hozumi selected the pSV2-neo vector. Throughout the months of June and July 1982, I worked to insert the κ gene into a pSV2-neo vector. By August 1, 1982, I had successfully created two vectors containing the κ_{TNP} gene, one containing the κ gene in a tandem orientation and a second containing the gene is a reversed orientation. Ex. 1137 at 69. These vectors are referred to as PT-*Tκ1* and PR-*Tκ1*, respectively, in Ochi I. Ex. 1021 at 340.

12. Thereafter, I sought to transform the vectors that I created into a eukaryotic host cell, specifically a mutant form of the Sp603 hybridoma. Implementing the techniques needed to transform foreign DNA into a eukaryotic host cell was the most technically challenging aspect of our work. Dr. Hozumi and I decided to use a protoplast fusion technique, which requires growing the plasmid in a bacterial cell and then fusing that bacterial cell with the host cell in this case, the mutant form of Sp603. The protoplast fusion technique is derived from the

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