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 NOBUMICHI HOZUMI IN SUPPORT OF MERCK'S REPLY TO PATENT OWNER'S RESPONSE

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

I. INTRODUCTION

I, Nobumichi Hozumi, hereby declare and state as follows:

1. This declaration is submitted on behalf of Merck Sharp & Dohme Corp. ("Merck") in 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 AND RELEVANT EXPERIENCE

3. As further detailed in my CV, attached as Exhibit A to this declaration, I graduated from the School of Medicine at Keio University in 1967

and received my M.D. degree in 1968. In 1972, I obtained a Ph.D. in Medical Science from Keio University, where I majored in Molecular Biology.

4. I lectured at the Keio School of Medicine from 1972 until 1975, when I became a member of the Basel Institute for Immunology in Basel, Switzerland. Afterwards, I was a postdoctoral Fellow at the University of Toronto's Ontario Cancer Institute, part of the Department of Medical Biophysics. In 1979, I became an assistant professor for the department, then in 1984 an associate professor, and finally in 1988 a professor for the department.

5. During the time I was a professor, I was also a senior staff member at the Ontario Cancer Institute until 1985. In 1985, I was hired as a Senior Scientist at the Samuel Lunenfield Research Institute at Mount Sinai Hospital. I continued in that role, as well as becoming a member of the institute in 1998, until 2000. From 1996 through the present, I have been a professor at the Research Institute for Biological Sciences in the Tokyo University of Sciences.

6. In 1983, I won the David Pressman Memorial award. In 1984, I won the Boehringer Mannheim Canada Prize of Canadian Biochemical Society.

7. Finally, I am a member of the American Association of Immunologists, the Japanese Society of Immunologists. I was a member of the advisor board for the Journal of Biochemistry from 1997-2001, and from 2005-

2008 was a member of the advisory board for the Japanese Society of Immunologists.

8. I am a named inventor on U.S. Patent No. 5,663,481, entitled "Animal model of the human immune system."

III. COMPENSATION

9. I am being compensated for my work on this case at my standard consulting rate of $500/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 ON RECOMBINANT EXPRESSION OF ANTIBODIES

10. In the early 1980s, I began collaboration with Marc Shulman, one of my colleagues at the University of Toronto. Among the projects that our labs undertook was the recombinant expression of an antibody molecule. Our initial work focused on transferring and expressing the light (κ) chain of an antibody specific for the hapten TNP; however our ultimate goal was to transfer and express both a heavy and a light chain.

11. In connection with this work, I obtained the pSV2-neo vector from Richard Mulligan, a member of Paul Berg's lab. I was familiar with the Berg lab's

prior work describing the pSV2 vector and I chose the pSV2-neo vector because it was well-suited to expressing exogenous genes in mammalian cells. When I selected the pSV2-neo vector, I believed that it would be capable of accepting genes for both the heavy and light chains on a single vector.

12. Our work transferring and expressing the antibody light chain was primarily carried out by Atsuo Ochi, one of the researchers in my lab. In particular, Dr. Ochi was responsible for performing protoplast fusion whereby a bacterial cell containing the pSV2-neo vector was fused with a mammalian host cell. Our work expressing the antibody light chain is 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")).

13. After we successfully transferred and expressed the antibody light chain, we began work to transfer and express the heavy and light chains together in a single host cell. This was the clear and natural next step of our recombinant antibody research.

14. I understand that Patent Owners have alleged that the "prevailing mindset" as of April 1983 was that the antibody heavy and light chains should be expressed in separate host cells. We never contemplated such an approach. To the contrary, we determined that expressing the heavy and light chains in a single host

DOCKET ALARM

Explore Litigation Insights

Docket Alarm provides insights to develop a more informed litigation strategy and the peace of mind of knowing you're on top of things.

Real-Time Litigation Alerts

Keep your litigation team up-to-date with **real-time alerts** and advanced team management tools built for the enterprise, all while greatly reducing PACER spend.

Our comprehensive service means we can handle Federal, State, and Administrative courts across the country.

Advanced Docket Research

With over 230 million records, Docket Alarm's cloud-native docket research platform finds what other services can't. Coverage includes Federal, State, plus PTAB, TTAB, ITC and NLRB decisions, all in one place.

Identify arguments that have been successful in the past with full text, pinpoint searching. Link to case law cited within any court document via Fastcase.

Analytics At Your Fingertips

Learn what happened the last time a particular judge, opposing counsel or company faced cases similar to yours.

Advanced out-of-the-box PTAB and TTAB analytics are always at your fingertips.

API

Docket Alarm offers a powerful API (application programming interface) to developers that want to integrate case filings into their apps.

LAW FIRMS
Build custom dashboards for your attorneys and clients with live data direct from the court.

Automate many repetitive legal tasks like conflict checks, document management, and marketing.

FINANCIAL INSTITUTIONS
Litigation and bankruptcy checks for companies and debtors.

E-DISCOVERY AND LEGAL VENDORS
Sync your system to PACER to automate legal marketing.