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ADDRESS AT THE 50TH ANNIVERSARY
OF THE RESEACH INSTITUTE FOR
MICROBIAL DISEASES OSAKA
UNIVERSITY

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The Osaka University Research Institute for Microbial Diseases was established just 50 years ago, on September 17th, 1934. Previous to this, from the fact that Osaka and Kobe were becoming the entrance ports for such infectious diseases as cholera and plague, and further the fact that the Tokyo University Institute for Infectious Diseases, which at the time was the main organization for preventive measures for epidemics of infectious diseases, could not produce sufficient vaccines and anti-serums due to damage caused by the Kanto Great Earthquake in 1923, Dr. Chozaburo Kusumoto, President of the Osaka Medical College and Dr. Tenji Taniguchi, Professor of the Department of Bacteriology and Serology, Medical School of Osaka University, realizing the need for a microbiological research organization in West Japan equivalent to the Institute for Infectious Diseases in Tokyo, made claims upon the Governor of Osaka Prefecture and Financial Circles of Osaka. As a result, a gift of two hundred thousand yen was received from Mr. Gendo Yamaguchi, and combining the Takeo Tuberculosis Institute which was established by a gift of many thousand yen from Mr. Takeo and the Osaka Special Skin Disease Institute which was established by a gift of many thousand yen from charitable citizens of Osaka, the Research Institute for Microbial Diseases was established as an attached institute to the Osaka University. The people of Osaka take pride in the fact that this institute was established due to the efforts and financial aid of its citizens.

Initially this institute was comprised of 5 departments: the Bacteriology and Serology Department (Bacteria Section, Serum Section and Bacterial Chemistry Section), Immunology Department, Parasitology Department, the Takeo Tuberculosis Institute and the Leprosy Therapy Department, the total staff being under 20 people. Thereafter, although there were the difficult war and post-war years, this institute has developed to where there are now 15 departments with a

staff of 170 people, the location also changed from Dojima, Osaka City to the present Senri, Suita City in 1978, and it has become known not only in Japan but worldwide.

The first Director was Dr. Yashiro Kotake, the second Director Dr. Arao Imamura, and from 1943 for the following 12 years Dr. Taniguchi was the director. The talented young Dr. Taniguchi, who came to Osaka Medical College, which developed to the present Medical School of Osaka University, as professor of Bacteriology and Serology from the Tokyo University Institute for Infectious Diseases, was a magnanimous, farseeing and progressive scholar who trained many excellent researchers and through his activities during his directorship established the basis of the present Biken.

During his initial period as Director, Dr. Taniguchi recognized the Importance of studies on virus, or filterable pathogens as they were known at that time, and as this was before the event of the electron microscope, his discovery of the elementary body of pox virus under the optical microscope became the dawn of Virology in Japan. Another important work was his isolation and identification of the pathogen of Dengue Fever, a strategically important disease during the war. There is an episode on the devoted cooperation on the part of the young researchers and medical students during this important work. During the postwar years, much effort was put into isolation of the pathogen of viral hepatitis and Izumi fever. The work itself was unfruitful, but research on the ectromelia virus, developed as a by-product and led to the discovery of A and B type inclusion bodies by Dr. Juntaro Kama-hora, professor of the Pathology Department, and Dr. Shiro Kato. Subsequently, Dr. Hidesaburo Hanafusa who joined the department later, came the discovery of the reactivation phenomena between pox viruses.

Research on isolation of the Izumi Fever pathogen led to isolation of the so-called HVJ virus from mice which was named the

Z strain. The use of this virus to infect Ehrlich ascites tumor cell led to Dr. Yoshio Okada's discovery of the cell fusion phenomenon. Later, this was utilized as a method for cell hybridization and is a basis for the development of today's cell engineering. To further research in this field, Osaka University had recently established the Institute for Molecular and Cellular Biology.

After the World War II Dr. Taniguchi put much effort into the development of a measles vaccine. This work was taken over by Dr. Yoshiomi Okuno with the establishment of a Measles Department, and after much effort led to the development of a live measles vaccine, which was followed by development of rubella and mumps vaccines. Dr. Takahashi, who took over the department, has developed the live varicella vaccine first in the world. These works have led to world-wide recognition of Biken in the field of live viral vaccines.

Dr. Taniguchi was also active in the field of Public Health. The work of Dr. Teishiro Seki with diphtheria toxin and the research by Dr. Konosuke Fukai on purification of influenza and Japanese encephalitis virus greatly contributed to the improvement of these vaccines. Dr. Fukai's morphological studies on virus using the electron microscope played a pioneering role in this field in Virology research in Japan, and this work is being carried on by Dr. Yasuhiro Hosaka and Dr. Akira Igarashi.

The progress in viral research in this Institute, led to establishing a Tumor Viruses Department in 1964. Dr. Kamahora, chief of this department, together with Dr. Takeo Kakunaga were successful in transformation of cultured rodent cells with 4NQO. Dr. Kakunaga, during his stay at the National Cancer Institute, U.S.A., was successful in further developing this research to human cultured cells, and his present work on the genetics in human cancer cells is world famous. He returned to Biken to become professor of the Chemotherapy Department and this year became professor of the newly established

Oncogene Department.

A further development in the Tumor Virus Department was Dr. Kumao Toyoshima's work on temperature sensitive mutant of Rous Sarcoma virus. Dr. Toyoshima has since become professor of the Tokyo University Institute for Medical Sciences, and Dr. Hakura, who is now head of the department, is working on cellular factors of virus transformation and also carcinogenesis of papiloma virus. Dr. Shiro Kato, who took over the Department of Pathology from Dr. Kamahora, has performed distinguished works on the Marek's disease virus.

Dr. Tsunesaburo Fujino, who was in charge of research on serology and bacteriology under Dr. Taniguchi, performed excellent works on the action mechanism of sulfonamides. On the occasion of the Shirasu food poisoning incident in 1950, Dr. Fujino made the great discovery of the causative agent "Vibrio Parahaemolyticus". Dr. Toshio Miwatani, who took over the Department after Dr. Fujino, and Dr. Takeda have further developed this work with studies on the toxin of this vibrio. Dr. Takeda is now professor at the Tokyo University Medical Institute. This department, as the center of clinical bacteriology in Kansai, is contributing greatly in the field of public health of this area.

Dr. Taniguchi's work in serology was carried on by Dr. Tsunehisa Amano, whose research on the immunochemistry of lysozymes is of world standard, and this work is being carried on by Dr. Mitsuo Torii and Dr. Kei Fujio.

Dr. Taniguchi always attached importance to chemical research on bacteria and during the difficult post-war years this work bloomed in the form of Dr. Masami Suda's famous research on adaptive enzymes. Dr. Osamu Hayaishi, a member of this group, established the basis of his world famous work on the discovery of oxidative enzymes here, and later completed it during his stay in the U.S.A.

Development of chemical research led to the establishment of a Chemotherapy Department, where such work as discovery of the carcinogenicity of actinomycin by Dr. Jun-ichi Kawamata can be mentioned, which developed to the recent research of Dr. Atsuo Nakata on genetic control of *E. coli* alkaline phosphatase. Dr. Kawamata's experience in his chemical carcinogenesis work led him to recognize the importance of experimental animals, and from his efforts Biken has excellent facilities for experiments with infected animals. Dr. Yamanouchi is active as head of this facility.

The Parasitology Department before the war was working on *Ascaris* which was an important public health problem in Japan, and Dr. Sadao Yoshida's research on the ecology in the human body is well known. Also, due to a request from the Army, Dr. Taniguchi started research on Malaria which led to Dr. Shouzo Inoki's discovery of the monkey Malaria Plasmodium. This led to the establishment of the Protozoology Department where Dr. Inoki made many contributions to research on the genetics of Protozoa. Another member of this department Dr. Aizo Matsushiro in his research on genetics in microorganisms discovered the *E. coli* $\phi 80$ phage. With the establishment of the Microbial Genetics Department, Dr. Matsushiro and Dr. Fumio Imamoto obtained many noteworthy results on the molecular biology of this virus.

In the Takeo Tuberculosis Research Department, studies by the former president Dr. Imamura on BCG are the basis of today's BCG vaccination in Japan. Dr. Mitsuo Hori, who took over after Dr. Imamura, performed many notable works on the resistance of tubercule bacilli. Dr. Masahiko Yoneda, who came from Nagoya City University in 1960, performed many prominent works on diphtheria toxin, biosynthesis of *M. tuberculosis* antigen, etc. This work on diphtheria toxin was later taken into Dr. Takeshi Uchida's work on cell fusion to give interesting

results, and also led to development of research on tetanus toxin by Dr. Morihiro Matsuda, who took over after Dr. Yoneda.

In the Protozoology Department Dr. Toshio Nakabayashi, who took over after Dr. Inoki, is performing genetical works on the Malaria Protozoa, and also contributing in the field of international cooperation.

The Leprology Department was taken over by Dr. Tonetaro Ito after Dr. Shinji Nishimura. Dr. Ito's group are not only known for their studies on the murine Leprosy Mycobacterium and success in transplantation of human leprosy bacteria to nude mice, but is contributing in international cooperation in the control of leprosy.

The Clinical Department was established in 1935 and the Cancer Therapy Department in 1936. In that year, a gift of Radium was received from the Osaka Cancer Therapy Research Association, this being the only Radium in Japan at the time, and radiation therapy of cancer was started. On the retirement of Dr. Shigeru Shiba, Dr. Tetsuo Taguchi became Director of this Department. Dr. Taguchi is an expert in the chemotherapy of cancer. In the field of Internal Medicine, Dr. Teruo Kitani has taken over from Dr. Shigeyuki Ishigami, and is steadily promoting studies on treatment of leukemia.

As can be seen, the unique originality of research performed at Biken is not something that was born individually, but is the result of human relations starting from Dr. Taniguchi, and it is not something closed but a very open relationship. This relationship, through being passed on and through a mechanism of organic binding is bearing more relationships, and I am certain that this will continue in the future.

To give the characteristic points of the attitude toward research at our Institute, one could say that 1) the researchers had the foresight to be ahead of times, 2) the cooperation between the researchers was very close and 3) importance was attached not only to basic re-

search but also to practical research. Needless to say our main aim is to attain achievements in research, but I believe another important mission is the training of specialists in various areas, not only to contribute in the field of public health in Japan, but also to cooperate in international aid programs. In 1969, in cooperation with the Japanese International Cooperation Agency, we undertook the training course in Microbiology, we have accepted 98 trainees from 23 countries in the past 15 years. On their return to their respective countries, these trainees are each playing an active part in the field of public health.

The future fields of research in this institute are:

1. Although the prevention and control of infections has been the aim of this institute since its establishment, most infectious diseases can now be controlled by vaccines and antibiotics. However, new infections still

appear one after another and overseas there are still many infections which are causing much trouble. Furthermore, genetic engineering which has its origin in research on microbial diseases, is now becoming the driving force of the industrial revolution. It is my belief that we must put still more effort in this field and in a broad sense, including basic research, drive forward in research on infections.

2. Research on treatment of cancer has been carried out since this Institute started. Particularly with establishment of the Department of tumor virus, and with the newly established Department of Oncogenes, much effort has been put into basic research on cancer. The other Departments also have been contributing to cancer research, and I believe that in order to meet the request of the people, further effort both in basic and clinical research must be made in this field.