AWARD OF MEDALS

The Eighty-first Annual Award of Medals was held on Monday, June 10, 1991, at 10:30 a.m., in the presence of Their Majesties the Emperor and Empress.

The function was opened with an address by the President, in which he made a brief statement of each award.

The Medals and Prizes were presented to the following recipients.

Imperial Prize and Academy Prize to Yoshinori KOBAYASHI
for "Linguistico-Philological Investigations in the *Kakuhitsu* Documents"

Imperial Prize and Academy Prize to Akira TONOMURA
for "The Development of Electron Holography and the Verification of the Aharonov-Bohm Effect"

Academy Prize to Yuichi SHIONOYA
for "The Structure of Value: Utility vs. Rights"

Academy Prize to Satio HAYAKAWA
for "Researches on Radiation in the Universe"

Academy Prize to Yoshihiko SAITO
for "Determination of Absolute Configurations and Electron-density Distribution of Transition Metal Complexes"

Academy Prize to Masatane KOKUBU
for "Influences of Compositing of Admixtures on Workability, Durability, and Strength of Concrete"

Academy Prize to Yasuyuki YAMADA
for "Functional Expression of and Secondary Metabolite Regulation in Cultured Plant Cells"

Academy Prize to Tomisaku KAWASAKI
for "Identification, Epidemiology and Treatment of Kawasaki Disease"

Academy Prize to Michio UI
for "Studies on the Role of GTP-binding Proteins in Cellular Signaling"

After this, congratulatory addresses were given by the Prime Minister and the Minister of Education, Science and Culture.

The function was closed at noon.

THE OUTLINES OF THE RECIPIENS' WORKS

Yoshinori KOBAYASHI

Linguistico-Philological Investigations in the *Kakuhitsu* Documents

Kakuhitsu is a kind of pencils, made of ivory, bamboo, or antlers, with which they wrote annotating *kana* and other marks between the *kanji* lines. The purpose was just for memorandum, so that the written things were visible only to the writer himself. Therefore, *kakuhitsu* documents remained unnoticed for a long time.

On the 13th of September 1961, Professor Hiroshi Tsukishima found that something was written between the *kanji* lines, through the glass window of a department store in Ueno in Tokyo, where the *Kanjo Shūboku Retsuden* was exhibited. This was the first *kakuhitsu* document found. Since then similar *kakuhitsu* documents were found in succession, and No. 104 was found on the 12th of February 1983.

The dates of the found *kakuhitsu* documents begin in the Nara period (2 documents) and end in the Edo period (35 documents). They are Chinese books (17 d.), Buddhistic books (76 d.) and Japanese books (6 d.).

Professor Y. Kobayashi classifies them as follows: (1) books, in which *kakuhitsu* marks and *kana* play the same subsidiary role as the marks and *kana* written in white, red, or yellow ink; (2) books, in which only *kakuhitsu* marks and *kana* are used playing the subsidiary role; (2. 1.) no other marks nor *kana* are written; (2. 2.) marks and *kana* in white or red ink are added later; (2. 3.) the lines in black ink are not in Chinese but in Japanese; (3) books, in which *kakuhitsu* marks and *kana* are written independently of the *kanji* lines in black ink.

Professor Y. Kobayashi investigated the *kakuhitsu* documents in accordance with these classifications, and for that matter, the groups and the subgroups separately. He is of the opinion that no revealing conclusion will be obtained if one investigates all the documents ensemble without classifying them.

As the result, he has found that in the *kakuhitsu* writings, (1) there appear linguistic phenomena which are outside of the customs and traditions of the writings written with *fude* (i.e. writing brushes), (2) the results of historical linguistic changes appear earlier than in the writings written with *fude*, and (3) slangy expressions are projected.

On the other hand, *kakuhitsu* documents contribute also in the fields of the history of the Japanese literature, the history of Japan, and the bibliography. However, the most conspicuous contribution is the fact that Professor Y. Kobayashi's investigations in the *kakuhitsu* documents have revealed that the results of histrical changes of Japanese appear earlier here than in the writings written with *fude*.

Akira TONOMURA

The Development of Electron Holography and the Verification of the Aharonov-Bohm Effect

The principle of holography was discovered in 1947 by Gabor (who was awarded the 1971 Nobel Prize), but its experimental realization was difficult at that time. With the invention of lasers it was embodied in the technique of laser holography, which is now well established. Gabor's original idea was intended for application to electron microscope, but that was not possible, until several decades later.

A key difficulty for this application was to generate an electron beam with a high degree of coherence. Dr. Akira Tonomura, however, succeeded in producing such an electron beam by using the field emission of electrons from a very sharp metallic point, to which a strong electric field was applied. He produced an electron hologram, which, by projection of laser beam, allows reconstruction of the image of the object under the electron microscope. This technique, now called the electron holography, has opened a wide range of possibilities for the application of electron microscopes as interference microscopes utilizing the full information carried by the electron wave interacting with the object under observation. Thus Dr. Tonomura and his coworkers have made a great breakthrough in realizing the dream of Gabor. Furthermore they have added numerous ingeneous ideas and techniques, such as the amplification of the phase difference by using the pair of real and virtual images produced by holography. In fact, the resolving power of electron microscopes can now be improved to the atomic scale. These achievements are regarded as leading the world.

One remarkable contribution of Dr. Tonomura is the application of electron holography to the study of a very basic problem of physics, namely the experimental verification of the AB effect, which is a quantum effect predicted in 1959 by Aharonov and Bohm: it asserts that the vector potential describing electromagnetic fields is a physical observable determining the phase of an electron wave function. Even when an electron passes through a spatial region where there is no magnetic field, the electron feels the existence of the magnetic flux that produces the vector potential in the region. This is intuitively difficult to understand from a classical picture since it is purely a quantum-mechanical effect. Therefore its experimental verification is particularly fundamental for quantum physics. There were many previous attempts to check the AB predictions, but none were satisfactorily decisive. Tonomura succeeded in giving a very clear cut and conclusive demonstration of the AB effect. He performed two distinct experiments. The first experiment used a tiny ring of ferromagnetic permalloy which was toroidally magnetized. This was placed under an electron microscope and a holograph was made using a highly coherent electron beam. An interference pattern was produced between the wave

going through the hole of the toroid and that passing outside. The AB effect was clearly seen through the shifts of the interference fringes.

The second experiment was carried out to answer any remainig doubts of cautious critics. In order to prevent any leakage of magnetic flux, the permalloy toroid was covered by a niobium layer and then the surface was covered by a copper layer to prevent infiltration of the electron beam into the sample. The electron holographic image of this sample again exhibited the AB effect leaving no room for doubt. Furthermore, the abrupt change of the interferogram seen at the onset of superconductivity in the niobium at 9°K directly reflected the quantization of magnetic flux in superconducting states.

It should be mentioned that the method of electron holography has made it possible to observe mesoscopic distributions of magnetic flux directly via the interference fringes. This is a powerful new technique for the study of superconductors and ferromagnets.

In conclusion, Dr. Tonomura's work is a major breakthrough in the technology of electron microscopy and has had a great impact on the most basic studies of quantum physics.

Yuichi SHIONOYA

The Structure of Value: Utility vs. Rights

This work is a philosophical study of foundations of normative economics. Presupposing scarcity of resources, it is natural to set up as performance criteria of economic systems the equity of distribution of the result of productive efforts as well as efficiency in the allocation of scarce resources. Efficiency and equity are the dual problems which arise in the world of scarcity, and normative economics must solve these two problems at the same time.

It is a well-known fact, however, that the contemporary normative economics separates the problem of efficiency from that of equity, and concentrates only on the former. The basis of the efficiency-oriented normative economics lies in the supposition of homo economicus, that is, of the man who seeks to maximize his own utility. And it is difficult to explain the concept of distributional justice on the basis of this supposition.

Starting from the above consideration, Shionoya insists that it is necessary to study first the structure of value in order to treat properly the problem of "efficiency vs. justice." And to investigate the principle of justice, Shionoya seeks to have recourse to the Kantian concept of "moral personality" as interpreted and developed by John Rawls, and tries to associate the concept of rights to this image of the person. And so the problem of efficiency vs. equity in normative economics can be transformed into the problem of "utility vs. rights" in terms of philosophical foundations.

Part I of the work is devoted to a survey of methodological approaches

to ethical problems historically contemplated and arranged. In this way, the author formulates his method of model-building and justification in moral theory as refinement and extension of "reflective equilibrium" in the Rawlsian sense.

Part II and III take up Sidgwick's utilitarianism and Rawls' version of the social contract doctrine respectively as modern systems of thought representing the antagonism of "utility vs. rights." They are critically examined by applying the method developed in Part I. In this process of argument, the author introduces a series of concepts called "a framework of normative reasoning" which facilitates the comparative study of different systems of thought.

Part IV develops the problem of "utility vs. rights" in a more extended perspective. The conventional way of thinking which bases social value judgment on individual utility contains a grave error. Some of individual utility may be satisfaction in bad or mean matters. It can not be said that it is socially desirable to satisfy individual's want unconditionally. To overcome the principle of utility, it is necessary not only to make clear the limitations of the image of man as a mere utility-seeker, but also to introduce "resources" as non-utility concept and to develop a theory of just economic system in terms of the rights to resources. It is to be noted that Shionoya's "resources" thus introduced roughly correspond to Rawls' "primary social goods" which include rights and liberties, opportunities and powers, income and wealth. Shionoya's own design of a just economic system, however, is not fully developed in this work.

Satio HAYAKAWA
Researches on Radiation in the Universe

Prof. Hayakawa is known as one of the leading theoretical physicists and astrophysicists who has contributed to many fields of physical sciences, particularly, astrophysical researches based on his deep understandings of particle and nuclear physics. In this report, his contributions to researches on the origin of cosmic-ray and X-ray and infrared astronomy are emphasized and summarized.

Origin of Cosmic-Ray

Since cosmic-ray was discovered in 1912, its origin had been a puzzle as it consists of charged particles whose paths are deflected by any magnetic field including terrestrial one. Prof. Hayakawa investigated its origin by recognizing that it consists of more heavier particles than general cosmic abundances and concluded that heavier particles come from supernovae erupted and lighter ones are produced by their interactions with interstellar matters. In fact he made detailed studies on probabilities of eruptions of the supernovae and the total energies produced to obtain the results. At the

same time Ginzburg, a Russian physicist, who is known as his contribution to the understanding of cosmic radio emission, reached at the same conclusion by a different way of study. Now every astrophysicist believes that the cosmic-ray is originated mainly by eruptions of the supernovae according to the researches by Profs. Hayakawa and Ginzburg.

As cosmic-ray consists of various particles like high-energy positron, atomic nucleus and high-energy electron as well as γ-ray, Prof. Hayakawa estimated their respective intensities based on the theories of the supernova eruptions and their interactions with interstellar matters and emphasized the importance of observations of the γ-ray which is not charged, to study structure of the Galaxy. His study is one of the main researches which encouraged to open the field of γ-ray astronomy which is now active by using scientific satellites and ground-based facilities.

X-ray Astronomy

His interests in X-ray sources started from theoretical investigations on their properties and origins in early days of X-ray astronomy. In his series of pioneering papers he proposed both thermal radiations from neutron stars and X-ray emission from close binaries as possible mechanisms, and discussed on very compact stars like neutron stars, exchange of masses in binary star systems to create accretion discs and high temperature plasma. Such ideas which he introduced appear now in every paper connected with X-ray astronomy. In fact he is one of leading astrophysicists who has explored theoretical side of X-ray astronomy. He has participated also in observational side of X-ray astronomy, particularly, Japanese space projects as one of the leaders, who have contributed to the great success of the three X-ray satellites.

Infrared Astronomy

Professor Hayakawa has payed much attention to infrared astronomy, a new and now very active field, from early days and started to make infrared observations with use of balloons and rockets in Japan and by collaboration with Australian scientists. One of his achievements in this field is survey of the Galaxy by near-infrared wavelength which exhibits active star-forming regions near the center of the Galaxy and very high activities in the Galactic center.

With his group he was engaged in measuring the intensity of the cosmic black-body radiation in sub-millimeter region by rockets, the first attempt in this wavelength, and this investigation encouraged NASA to launch COBE satellite which is mainly for measuring the cosmic black-body radiation.

He published more than 300 papers in various fields and he is recognized as a theoretical astrophysicist who suggested several new kinds of observations to understand more precisely the structure of the Galaxy, early evolution of the Universe and so on.

Yoshihiko SAITO

Determination of Absolute Configurations and Electron-density Distribution of Transition Metal Complexes

In 1955 Saito first applied anomalous scattering of X-rays to the determination of the absolute configuration of a transition metal complex. He used crystals of $(+)_{589}2[Co(en)_3]Cl_3 \cdot NaCl \cdot 6H_2O$(en=ethylenediamine) and succeeded in detecting slight but discernible differences in intensities of a reflection and its counter reflection by Cu Kα radiation. Moreover, he showed that the observed inequality relations are reversed for the enantiomeric crystal. Thus it was firmly established that the complex ion $(+)_{589}[Co(en)_3]^{3+}$ has Λ (delta) absolute configuration. This first discovery of the absolute configuration of a chiral transition metal complex was achieved almost forty years after Alfred Werner resolved this complex into optical isomers by chemical method and established "coordination theory." Saito determined the absolute configurations of a number of metal chelate complexes with diamines such as R-propylenediamine, trimethylenediamine and many other related ligands. The results shed light on the complicated isomerism of these complexes. Structural information of these complexes together with their chiroptical properties has established empirical rules for the assignment of the absolute configuration of metal complexes on the basis of circular dichroism spectra. The successful applications of the method of circular dichroism spectroscopy have relied to a large degree on the results of X-ray structural studies by Saito and his students and colleagues. This is a particularly valuable contribution to the field.

In 1973 Saito attempted to determine the electron density distribution in crystals of $[Co(NH_3)_6][Co(CN)_6]$ as accurately as possible. At that time it was generally believed that heavy metal atoms would make the detection of bonding electrons extremely difficult owing to a very small valence/metal electron ratio. A breakthrough was attained by constructing a newly designed four-circle diffractometer and by utilizing a spherically shaped specimen of a good quality. Every care was taken to avoid systematic errors in the data collection. He succeeded in detecting not only the bonding electron peak on the deformation maps, but also the asphericity of 3d electron distribution placed in a ligand field for the first time. The arrangement of positive and negative peaks around the cobalt nucleus indicated the excess electron density in the direction of t_{2g} orbitals and the deficiency in the direction of e_g orbitals, which agree well with the expectation based on the ligand field model. Saito extended his work to $K_2Na[Co(NO_2)_6]$, γ-Ni_2SiO_4, $CoAl_2O_4$, chromium metal and other inorganic crystals. The results of electron-density determination of coordination compound was of a great help to gain deeper insight into the question of

what happens when ligating atoms are coordinated to the central metal atom to form a complex.

His work on both subjects has been cited in most of the textbooks and reference books on inorganic and coordination chemistry.

Saito received the Award in Pure Chemistry of the Chemical Society of Japan in 1968, and the Asahi Award in 1977.

Masatane KOKUBU

Influences of Compositing of Admixtures on Workability, Durability, and Strength of Concrete

The quality of concrete may be enhanced through appropriate compositing with admixtures. Dr. Kokubu perceived the promising future of this technology from the outset of its development (1950), and carried out a great number of experiments to explain the mechanisms of compositing these admixtures. Firstly, he explained the composite effect of air-entraining admixtures and water-reducing admixtures on workability and durability of concrete, and particularly, with regard to water-reducing admixtures which also work to disperse cement particles, he showed that especially advantageous effects could be attained, and established standards for mix proportioning when using these admixtures.

With regard to fly ash, Dr. Kokubu, using electron microscopy, firstly revealed physically the mechanism of still continuing increases in water-tightness, strength, and durability of concrete even at long-term ages when pozzolanic reactions have become weakened. In effect, a water gap of thickness about 0.5 to 1 micron exists at the surface of a fly ash particle during mixing of concrete and this remains as a boundary layer even after placement of the concrete, and with the progress of pozzolanic reaction, there are reaction products precipitated inside the layer. This theory was published at an International Symposium on the Chemistry of Cement and left a considerable impression on participants. He went on further to point out that when fly ash is used in air-entrained concrete, the uncombusted carbon contained in it causes air-entraining admixture to be adsorbed so that the air content of the concrete is varied and thus workability is also varied, and originated a two-stage mixing method for elimination of this drawback. It was in this way that he successively spurred on numerous technological improvements.

As Chairman of the Committee on Rationalized Construction of Concrete Dams, Dr. Kokubu developed a construction method for large dams which takes advantage of the features of admixtures, in particular, the reduction of heat of hardening and inhibition of cracking of concrete by fly ash, and the retarding effect of water-reducing admixtures, named this the RCD Method, and published it at a meeting of the International Commission on Large Dams in 1984. The RCD Method makes possible reduction in

construction costs and shortening of work periods and has won high acclaim internationally.

Furthermore, Dr. Kokubu has been exposing a total of 75 large concrete specimens containing admixtures in natural conditions of severe cold since 1961, and has been periodically measuring dynamic moduli of elasticity and other properties. This program has already been going on for 28 years and the durabilities of the concretes have been ascertained. This long-term research is highly regarded at an international level.

As described in the foregoing, the research concerning compositing of admixtures by Dr. Kokubu has induced a great many technological improvements in concrete engineering which may be recognized as accomplishments worthy of the highest esteem.

Yasuyuki YAMADA

Functional Expression of and Secondary Metabolite Regulation in Cultured Plant Cells

Based on the concept that cultured cells of the same plant are heterogeneous in potential, Dr. Yamada succeeded in selecting specific cells that express special plant functions and in establishing an experimental system for large scale culture of these cells. With this system, for the first time it became possible to determine the actual functional expression of secondary metabolites in higher plants and the regulation of these metabolites. This had been difficult or impossible using plants themselves or noncellular systems derived from higher plants.

Working with this original experimental system, Dr. Yamada has opened up a new area of plant research and has made several outstanding contributions to our understanding of functional expression and secondary metabolite regulation in higher plants. His extensive body of research are divisible into four categories, which briefly summarized are

I. Cell fusion in plants and plant regeneration from cultured rice cells

Dr. Yamada was the first to successfully regenerate plants from cultured rice cells and protoplasts, the production of which had been the subject of intensive study for several decades. These successes were obtained through comprehensive examinations of the various species of rice and the conditions necessary for the isolation of protoplasts and of the culture of rice cells and protoplasts. He also succeeded in fusing cells of different plant species using an improved method of electrofusion which he developed. With this method he obtained cybrid rice plants through asymmetric cell fusion of protoplasts of a cytoplasmic male-sterile rice and cultivar rice.

The results of his research in this area have made a significant contribution to fundamental research in the agricultural sciences and are making possible a new technology with which to produce improved plant

species, including those of rice.

In addition, Dr. Yamada isolated four plasmid-like DNAs from the mitochondria of cytoplasmic male-sterile rice and analysed their complete DNA sequences, which he found contain sequences homologous to those in the plasmid-like DNA of maize mitochondria. His research results provide evidence that the plasmid-like DNAs of rice and maize are very closely related and may have evolved from a common ancestral sequence.

II. Photoautotrophic cultured plant cells and photosynthesis

Cultured green cells of tobacco (a C_3 plant) were selected continuously during callus induction and cell subculture, by which method a photoautotrophic tobacco cell line was developed. In these cultured cells (C_3), C_1-C_3 carboxylation by phosphoenolpyruvate carboxylase, which is a characteristic of C_4 plants, is present—an unusual functional expression for photoautotrophic C_3 plant cells. The phosphoenolpyruvate carboxylase from these cultured green C_3 cells was purified to homogeneity, after which the nucleotide sequence of the gene was determined.

In addition, a new type of mutant tobacco cell that has resistance to the photosynthesis-inhibiting herbicide atrazine was obtained by selection from cultured photoautotrophic cells. In these mutant cells, the 264th serine, codon AGT in the wild *psb*A gene encoding D-1 protein, had been changed to threonine, ACT. This new type of mutant also has moderate cross-resistance to phenylurea herbicides. The results of this part of his research have led to the proposal of new herbicide-binding models.

III. Selection and applications of high secondary metabolite-producing cells

Having observed that individual cells of calli have different potentials for the production of specific compounds, as well as having different functions, Dr. Yamada developed a specific method for the selection of cells with high capabilities for producing a particular desired compound in high yield. His results have provided the basis for the industrial production of the following useful compounds: anthocyanin from cultured *Euphorbia milli* cells, berberine from cultured *Coptis japonica* cells, aromoline from cultured *Stephania cepharantha* roots, shikonin from cultured *Lithospermum erythrorhizon* cells, reserpine from cultured *Rauwolfia serpentina* cells and scopolamine from cultured *Hyoscyamus* and *Duboisia* roots.

IV. Analysis of the regulatory mechanism of secondary metabolite production in cultured plant cells and roots

Using isotope tracing in higher plants or in noncellular systems derived from such plants, scientists previously could only speculate about what metabolic pathways actually function when seeking to establish production processes for obtaining secondary metabolites and when studying the mechanisms of their metabolic pathways. But, with the system of Dr. Yamada (described previously), it has now become possible to determine what the reaction mechanisms are that operate in the various pathways of biosynthesis. In particular, he has been able to study the biosynthesis of

berberine (an isoquinoline alkaloid) in cultured *Coptis japonica* cells, aromoline (a bisbenzylisoquinoline alkaloid) in cultured *Stephania cepharantha* roots, and scopolamine (a tropane alkaloid) in cultured *Hyoscyamus* and *Duboisia* roots.

The reports he has made on the sequential bioconversion from the initial precursor, ornithine, to the end product, scopolamine, have been highly evaluated internationally for the uniqueness of their perceptions. Specifically, he has shown the steps in the pathway from [S]-hyoscyamine to scopolamine—one of the most important reaction sequences in scopolamine biosynthesis: [S]-hyoscyamine is first converted to 6β-hydroxyhyoscyamine by a 2-oxoglutarate-dependent dioxygenase (designated hyoscyamine-6β-hydroxylase). This 6β-hydroxyhyoscyamine then is epoxidized to scopolamine by the same enzyme. Dr. Yamada next purified this enzyme to homogeneity, then determined the gene nucleotide sequence. Transformation into tobacco cells confirmed the expression of the gene. Publication of these results established the primary determination of a reaction mechanism by an enzyme related to alkaloid biosynthesis and confirmed that a transformed gene can have enzyme activity.

Through his extensive and diverse research, Dr. Yamada has demonstrated clearly the functional expression of secondary metabolites and how these metabolites are regulated. His novel experimental system incorporates methods from biochemistry, organic chemistry, and molecular biology. The results of his broad and varied investigations have opened up new areas of research and contributed greatly to the broad spectrum of plant sciences.

Tomisaku KAWASAKI

Identification, Epidemiology and Treatment of Kawasaki Disease

I. Identification of the new disease

The first patient, a 4-year 3-month old male child, visited the hospital on January 5, 1961. The main symptoms were fever lasting two weeks, swelling of cervical lymph nodes, polymorphous exanthema, diffuse erythema of the palms and soles, indurative edema of the hands and feet, bilateral ocular conjunctival injection, redness and cracked lips, diffuse erythema in the oral mucosa and desquamation from the fingertips during the convalescent phase. Due to the unusual symptoms, no definitive diagnosis could be made. Since then, five to ten patients associated with the above mentioned symptoms have been found every year. The examination of four autopsy cases resulted in diagnosing infantile periarteritis nodosa.

The clinical features of a total of 50 patients who visited the hospital from 1961 to 1966, were summarized. The first paper in Japanese entitled "A new acute febrile mucocutaneous lymph node syndrome" was reported in the Japanese Journal of Allergology, March 1967 and the same material was

published in the English journal "Pediatrics," September 1974, in collaboration with Dr. Itsuzo Shigematsu. The new disease was called the "Kawasaki disease."

II. Epidemiology

Since then new cases began to be frequently reported throughout Japan, the Ministry of Health and Welfare organized the Kawasaki Disease Research Committee in 1970. The Committee carried out the first nationwide survey of Kawasaki disease conducted by Drs. Itsuzo Shigematsu and Tomisaku Kawasaki. From 1970 to 1988, the survey has been carried out 10 times at about two-year intervals as of the end of December 1988 with the total number of patients studied amounting to 94,330. During the term, three epidemics of this disease were reported at intervals of 3 to 4 years, namely in 1979, 1982 and 1986. One survey was further extended to Japanese immigrants in Hawaii. Children of Japanese ancestry showed the highest morbidity rate compared to those of other Asian, African or Caucasian descent. The study indicated that Kawasaki disease may be related to industrialization in a country, because it was found most frequently in the more developed countries.

III. Treatment

Antiinflammatory and antithrombotic agents such as aspirin had been used for therapy. In 1983, treatment with a high dose of gamma globulin was introduced in therapy. A Research Committee of the Ministry of Health and Welfare, under Dr. Kawasaki, established guidelines for gamma globulin treatment in 1990.

Michio UI

Studies on the Role of GTP-binding Proteins in Cellular Signaling

Extracellular signals that are brought to mammalian cells as neurotransmitters, hormones or autacoids are translated into intracellular signals mostly at the membrane sites termed receptors. GTP-binding proteins (G proteins) play a pivotal role in the receptor-coupled signal translation (or transduction). The roles of G proteins in a variety of cellular signaling systems have been identified by successful application to these systems of pertussis toxin which was introduced by Dr. Ui, as an islet-activating protein (IAP), based on his original and extensive work in the field of metabolic physiology and autonomic neurology.

Epinephrine (adrenaline) exerts its diverse effects on mammals because it interacts with dual α- and β-adrenergic receptor systems. Dr. Ui first found that hyperglycemia (the increase in blood glucose level) observed in epinephrine-injected rats was a reflection of well-balanced stimulation of both α- and β-adrenergic receptors. Epinephrine failed to cause hyper-

glycemia during alkalosis, acidosis or exercise (forced swimming) or in hyper- or hypothyroidism, because, according to his discovery, the relative functions of α- to β-adrenergic receptors are altered under these pathological conditions. The injection of pertussis vaccine into rats afforded additional unique conditions under which β-adrenergic receptor functions were predominant over the α-receptor ones, as revealed by the failure of epinephrine *in vivo* to cause hyperglycemia in vaccinated rats and by the reversal of α-receptor-mediated inhibition of insulin secretion *in vitro* from perfused pancreases isolated from these rats.

Dr. Ui and his colleagues soon succeeded in purification of this unique factor from the culture medium of *Bordetella pertussis*, and analyzed the complicated subunit composition of this protein, IAP or pertussis toxin. Pertussis toxin interacted with most of the mammalian cells as well as pancreatic islets responsible for insulin secretion via cyclic AMP, one of the intracellular signaling substances or second messengers. Stimulation of certain types of receptors including α-adrenergic receptors resulted in inhibition, rather than activation, of adenylate cyclase, the enzyme producing cyclic AMP from ATP. The receptor-mediated inhibition of adenylate cyclase was GTP-dependent and was reversed by the action of pertussis toxin. Dr. Ui's conclusion was that the adenylate cyclase inhibition is directly mediated by a new pertussis toxin-susceptible G protein (Gi) distinctly different from the only one G protein (Gs susceptible to cholera toxin instead of pertussis toxin) thus far known to mediate the adenylate cyclase stimulation.

Pertussis toxin can enter the intact mammalian cells owing to its complicated subunit structure and then ADP-ribosylates Gi located on the intracellular side of the cell membranes. The ADP-ribosylated Gi is incapable of being coupled to receptors any longer. Thus, pertussis toxin proved to be an ideal probe for G protein involvement in cellular signaling systems; if a signaling system is blocked by exposure of the cells to the toxin *in vitro* or *in vivo*, it does afford convincing evidence for the involvement of the toxin-susceptible G protein(s) in the system. Taking advantage of this strategy worked out by himself, Dr. Ui made an important expansion of G protein role; *i.e.*, receptor-coupled activation (or inhibition) of phospholipase C, phospholipase A_2 and certain Ca^{2+} and K^+ channels proved to be mediated by pertussis toxin-susceptible G proteins in a variety of cell types. These newly discovered G proteins have been purified as the substrates of the toxin-induced ADP-ribosylation, their cDNAs (and genomic DNAs in some cases) have been cloned and the constituent amino acids sequenced.

Because of his such brilliant contributions to the analysis of the role of G proteins in cellular signaling, Dr. Ui's publications took the high rank in the "Citation Index" in 1984–6. He was awarded "Paul Ehrlich and Ludwig Darmstaedter" Prize, the international medical award in Germany in 1991 for his outstanding contributions to the research field of Dr. Paul Ehrlich, the Nobel Prize winner in 1908, who established the currently accepted concept leading to the identification of membrane receptor at the beginning of the 20th century.

PROCEEDINGS AT THE 850TH GENERAL MEETING

The 850th General Meeting of the Academy was held on Tuesday, June 11, 1991, at 1:00 p.m., Dr. Yoshitaro WAKIMURA, President, taking the chair. Eighty-one members were present, and the following communication were made:

"Peace-keeping operations" of the United Nations..... Shigejiro TABATA, M.J.A.
On the convergence of socio-economic systems..... Shigeto TSURU, M.J.A.
On the Cauchy-Kowalevskaya theorem for systems ..... Waichiro MATSUMOTO and Hideo YAMAHARA
An ill-posed estimate for a class of degenerate quasilinear elliptic equations..... Kazuya HAYASIDA
The initial boundary value problems for linear symmetric hyperbolic systems with characteristic boundary ..... Mayumi OHNO, Yasushi SHIZUTA, and Taku YANAGISAWA
L^p estimate for abstract linear parabolic equations ..... Mariko GIGA, Yoshikazu GIGA, and Hermann SOHR
Above four, communicated by Kunihiko KODAIRA, M.J.A.
Isolation and structure of diapause hormone of the silkworm, *Bombyx mori*..... Kunio IMAI, Takamichi KONNO, Yoshitaka NAKAZAWA, Takashi KOMIYA, Minoru ISOBE, Kazushi KOGA, Toshio GOTO, Toshinobu YAGINUMA, Kiyoshi SAKAKIBARA, Kinsaku HASEGAWA, and Okitsugu YAMASHITA
Communicated by Seijiro MOROHOSHI, M.J.A.
Sequence variation of human platelet membrane glycoprotein IIIa associated with the Yuk^a/Yuk^b alloantigen system ..... Li WANG, Takeo JUJI, Yoichi SHIBATA, Shoji KUWATA, and Katsushi TOKUNAGA
Communicated by Setsuro EBASHI, M.J.A.
On invariant eigendistributions on $U(p, q)/(U(r)\times U(p-r, q))$ ..... Shigeru AOKI and Suehiro KATO
Centralizers of Galois representations in pro-l pure sphere braid groups..... Hiroaki NAKAMURA
On solutions of the Poincaré equation..... Katsunori IWASAKI
A note on multivalent functions..... Tadayuki SEKINE and Shigeyoshi OWA
Tuboids of C^n with cone property and domains of holomorphy..... Giuseppe ZAMPIERI
Above five, communicated by Shokichi IYANAGA, M.J.A.
Ion cyclotron waves generated by the entry of solar wind plasma into the magnetospheric boundary layer..... Yoshio KATO, M.J.A., and Yutaka TONEGAWA

After a recess during which the members present met in their respect Sections, the General Meeting was resumed for business transactions.

First, the President announced that Dr. Takesi Nagata, M.J.A., had passed away on June 3, 1991. The members rose from their seats in silence, expressing profound sense of grief.

Next, Dr. Atsushi KOBATA, M.J.A., paid a tribute of admiration to the late Dr. Masao SUENAGA's meritorious services to academic circles.

Then, the Chairmen of both Sections made reports of the matters dealt with at the respective Sectional Meetings.

After that, it was reported on the result of election of half the members of the Administrative Committee, which had taken place at the Sectional Meetings. The Committee members elected are: Tatsuro YAMAMOTO, Shigemitsu DANDO, Tsutomu OUCHI, Takeo NAGAMIYA, Masao YOSHIKI, Naohide HIRATSUKA, and Kyosuke TSUDA.

Finally, the President reported that the fourteenth meeting of the Japan Academy Public Lectures was opened to the public at Kyodai-Kaikan, Kyoto, at 2:00 p.m. on Saturday, May 25, 1991, with Dr. Chushiro HAYASHI M.J.A., and Dr. Osamu HAYAISHI, M.J.A., as speakers, whose respective subjects were:

"Formation of the Solar System"

"Secrets of Sleep".

The Meeting was adjourned at 4:40 p.m.

日本学士院紀要
平成三年六月　第六十七巻A　第六号

平成三年七月五日　印刷
平成三年七月八日　発行

編集兼発行者　日本学士院
東京都台東区上野公園七の三十二

印刷所　株式会社東京プレス
東京都板橋区桜川二丁目二十七の十二

印刷者　依田高夫
東京都板橋区桜川二丁目二十七の十二

Printed by
TOKYO PRESS COMPANY LIMITED
No. 27-12, Sakuragawa 2-chome, Itabashi-ku,
Tokyo 174 Japan
Tel.: (3932) 9291~4