AWARD OF MEDALS

The Eighty-sixth Annual Award of Medals was held on Monday, June 10, 1996, 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. This year, the fifth presentation of the Duke of Edinburgh Prize for the Japan Academy also took place at the same time.

The Medals and Prizes were presented to the following recipients:

Imperial Prize and Japan Academy Prize to:

Tasuku HONJO
for "Studies on Regulation of Immunoglobulin Class Switching"

Japan Academy Prizes to:

Yutaka HIRATA
for *The Era of Buddhist Painters*

Junjiro KANAMORI
for "Theory of Ferromagnetic Transition Metal Alloys"

Shinzo WATANABE
for "Study of Stochastic Analysis"

Masatoshi TAKEICHI
for "Discovery of Cadherins Indispensable for Cell-cell Adhesion in Animals, and Elucidation of their Function"

Mamoru HOSAKA and Toshio SATA
for "Collaborative Research on Integration of Design and Manufacturing"

Tadashi INAGAMI and Kazuo MURAKAMI
for "Biochemical and Molecular Biological Studies of Renin-angiotensin System"

Morio IKEHARA and Eiko OHTSUKA
for "Synthesis and Functional Studies on Nucleic Acids—Synthetic c-Ha-*ras* Gene and Related Subjects"

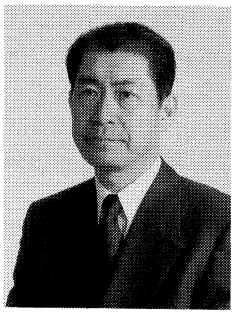
Duke of Edinburgh Prize to:

Hiroya KAWANABE
for "Ecological Studies on the Maintenance and Conservation of Biological Diversity in Freshwater Fishes"

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

The function was closed at 11:20 a.m.

Imperial Prize and Japan Academy Prize to:



Tasuku HONJO
Professor,
Graduate School of Medical Science,
Kyoto University

for "Studies on Regulation of Immunoglobulin Class Switching"

Outline of the Work:

Elucidation of molecular mechanism for immunoglobulin (Ig) production is central to immunology. Human and mouse can produce 9 and 8 immunoglobulin isotypes, respectively, that are determined by the primary structure of the constant region of the Ig heavy chain. Each isotype has its unique strategy to eliminate antigens recognized by the variable region. In 1970's it remained an intriguing question in molecular biology as well as immunology how a single antigen stimulation can induce production of a variety of isotypes recognizing the same antigen, the phenomenon known as class switching. Dr. Honjo found that DNA deletion is involved in class switching and elucidated its molecular and regulatory mechanism.

In 1978, Dr. Honjo discovered that specific constant region genes of the Ig heavy chain locus were deleted in malignant plasma cells, *i.e.* myelomas and proposed a gene deletion model for class switching. Subsequently, he isolated both germline and rearranged Ig heavy chain genes and demonstrated, by comparison of the gene structure, that deletional DNA rearrangement is the basic mechanism for class switching. Dr. Honjo also identified a unique repetitive region called S region as target of switch recombinatin. In 1990 he further showed that looping-out deletion takes place in class switch recombination.

In 1978 Dr. Honjo also proposed the order of Ig heavy chain constant genes based on their deletion profile in various myeloma cells. By isolation of 200 kilo base-pair DNA containing the complete murine Ig constant region genes he has proved the proposed order of the mouse Ig heavy chain locus; V, μ, δ, $\gamma 3$, $\gamma 1$, $\gamma 2b$, $\gamma 2a$, ε and α. He then almost completed the physical mapping of the human heavy chain variable-region locus, which provided the basis for identification of autoantibodies and production of humanized antibodies.

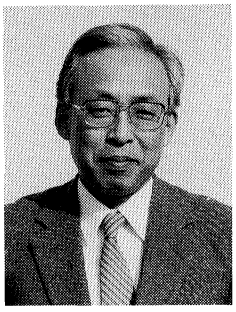
In 1986, Dr. Honjo developed a new strategy for cloning cDNA for proteins in scarce supply such as lymphokines without the knowledge of their primary structures. Using this method Dr. Honjo isolated cDNAs for interleukin (IL)-4 and IL-5 and determined their structures and functions. Prior to 1986, more than 10 factors were proposed to regulate differentiation and activation of B cells. IL-4 directs class switching to IgG1 and IgE. IL-5 augments production of IgA.

In 1992 Dr. Honjo showed that the self-antigen can kill self-reactive B lymphocytes using an Ig gene transgenic mouse model and that CD40 stimulation by helper T cells can rescue apoptotic death of antigen stimulated B cells and rather activate them using an *in vitro* cell line. Taken together with results by many other groups, combination of antigen stimulation and CD40 signaling activates B cells, leading to class switching to particular isotypes by the direction of lymphokines produced by helper T cells.

In 1994 Dr. Honjo established an *in vitro* system to induce differentiation of embryonic stem cells into B lymphocytes by coculture with a stroma cell line OP9. He also found a unique transcription factor called RBP-Jκ (vertebrate homologue of Suppressor of Hairless) that interacts directly with the Notch receptor involved in cell fate determination of the nervous and muscular systems. RBP-Jκ is also essential to immortalization of human B lymphocytes by Epstein-Barr virus.

Dr. Honjo thus elucidated most important molecular events in Ig production by B lymphocytes after encounter with antigens. His contribution is not confined to immunology but also had strong impact to other fields including genetics, embryology and oncology.

Japan Academy Prize to:



Yutaka HIRATA
Professor, Nagasaki Junshin
Catholic University
Emeritus Professor, Kyushu University

for *The Era of Buddhist Painters*

Outline of the Work:

Professor Hirata, the author of this work, has published important research on the history of Japanese painting, especially Buddhist genres, during his tenures at the Nara National Cultural Properties Research Institute and at the Faculty of Literature, Kyushu University. The present tome, which represents one summary of that research, is the first to elucidate the role and significance of Buddhist painters in the history of art.

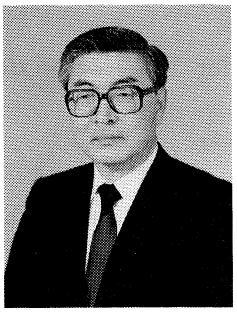
The work consists of two volumes, historical documents and research. The volume of documents records nearly all the historical evidence on painters across a five century span, from the reorganization of the Official Bureau of Painters in 808, through the production by Buddhist painter Ryosen of a Nirvana painting in 1328. Five hundred and forty-seven historical documents as well as twenty supplementary documents and other materials make up the volume. Here we are given a clear view, through documentation of the painters' movements, of the variations in Japanese art history throughout the Heian and Kamakura periods.

The research volume attempts to clarify these variations and movements according to the systems, functions and painting styles of Buddhist painters, who formed the nexus of painting production. The production of lavish Buddhist painting in the early half of the eleventh century under Fujiwara no Michinaga's and Yorimichi's patronage culminates in the honoring of Buddhist painters with the title of Sōgō-i in 1068, and it was from this point on that the painters' titles as well as social status were recognized widely. This period was followed by an era of beautiful Buddhist painting using minute coloring techniques, during the reigns of Retired Emperors Shirakawa and Toba (1072–1156).

We find changes in artistic styles and in the status of the Buddhist painter according to changes in polity and in the hereditary succession of Sōgō-i titles under the reigns of Retired Emperors Goshirakawa and Gotoba (1156–1221). At this point Buddhist painters find themselves in the position of head painters at the monastic guilds of prominent temples, hence securing their social statuses. At the same time they disperse into groups; factions are created, and artists establish unique styles developed through their spiritual affiliations with high monks. The reception of water and ink painting in the latter thirteenth century strengthens this tendency toward dispersal, and produces a multiplicity of painting themes and styles; it is at this moment that the Buddhist painter's role in painting history, nurtured in a strong tradition from the eleventh century, ends.

The present work delineates the centrality of the Buddhist painter in the formation of Japanese painting history through historical documents spanning nearly two hundred and fifty years, from the eleventh century on. Its success in clarifying the aspects and causes of temporal change in Japanese painting has deepened our understanding of the history of Japanese art and cultural history; it is to be highly evaluated for precisely this reason.

Japan Academy Prize to:



Junjiro KANAMORI
President, Osaka University

for "Theory of Ferromagnetic Transition Metal Alloys"

Outline of the Work:

Iron, Cobalt, and Nickel are well-known ferromagnetic metals. Prof. Kanamori was the first in the world to incorporate into theory the "electron correlation" between two electrons of antiparallel spins in the 3d band of these metals and to elucidate the origin of ferromagnetism of these metals (1963).

Binary alloys among Fe, Co, Ni, and between one of these metals and a lighter transition metal or the heavier copper have been studied "experimentally" for a long time in the world because of their importance in pure and applied physics. Prof. Kanamori studied these materials theoretically and clarified some of their peculier properties. He also studied alloys of Fe (also of Ni) and an element that ranges from H through B, C, N, to Ba. All these alloys (mostly dilute alloys) have been objects of experimental nuclear magnetism or of industrial importance. He made these studies with the cooperation of a number of his students during the period from 1964 up to the present time. Very detailed study of the electronic structures of these alloys has been made, and precise numerical results have been obtained. These results could predict all the corresponding experimental data. Some of mystic experimental results have been interpreted theoretically as will be described below.

The ferromagnetic magnetization of Fe is 2.3 Bohr magnetons per atom, which is higher than that of Co (1.75 Bohr magnetons per atom). However, when Co is added to Fe, the magnetization increases initially with the concentration of Co and attains a maximum value of 3 Bohr magnetons at 25% Co. This was known experimentally. Prof. Kanamori's interpretation through his analysis of the electronic structure is the following. The 3d orbitals of a Co atom imbedded in Fe combine with the 3d orbitals of the surrounding Fe atoms in the way that a 3d level of Fe is pushed up above the Fermi level and as a consequence the electrons in that 3d level fall down to lower 3d levels of Fe, with spin reversal, to increase the magnetic moment of these Fe atoms.

Another example is the dilute Fe-B alloy. The boron atoms occupy interstitial positions of the iron. The sp orbitals of a boron atom hybridize with the 3d orbitals of the surrounding Fe atoms, and these Fe atoms play a similar role as that of Co in Fe, and cause an increase in the magnetic moments of the farther-neighboring Fe atoms. The strongest permanent magnet ever found, by Dr. Sagawa in Sumitomo Metal Co., is iron diluted by boron and a rare-earth metal. The role of boron to increase the magnetization of such a magnet must be that predicted by Prof. Kanamori.

Japan Academy Prize to:

Shinzo WATANABE
Professor, Graduate School of Science,
Kyoto University

for "Study of Stochastic Analysis"

Outline of the Work:

Stochastic integration was introduced to represent the random orbit of a diffusion process by the solution $X_t = X_{t,x}(w)$ of a stochastic differential equation

$$dX_t = a(X_t)dt + \sigma(X_t)dw_t,\ X_0 = x.$$

This is the origin of stochastic analysis. It can be verified that the transition probability distribution of the diffusion process $X_{t,x}$ satisfies the Fokker-Planck equation in the weak sense.

In 1978 P. Malliavin introduced the concept of smooth functionals on the Wiener space and brought about the epoch-making progress in stochastic analysis. In this theory it is proved that if the coefficients a and σ are smooth and σ is non-degenerate, then $X_{t,x}$ is a non-degenerate smooth functional and the transition probability distribution has smooth density $p(t,x,y)$, which turns out to be the fundamental solution of the Fokker-Planck equation in the strong sense.

In 1984 Dr. Shinzo Watanabe introduced the concept of generalized functionals on the Wiener space, established its theory and applied it to solve the problem of the asymptotic expansion in t of the transition

density $p(t,x,y)$.

Since 1962 Watanabe has devoted himself to studying stochastic processes, stochastic differential equations and stochastic analysis, and published mathematical papers on martingale stochastic integrals (with H. Kunita), additive functionals (with M. Motoo), branching processes (with N. Ikeda and M. Nagasawa), construction of solutions of stochastic differential equations with boundary conditions, excursion point processes and diffusion processes and many others. All of these papers are full of new ideas and are highly appreciated by the researchers in the field. Also his joint work with N. Ikeda: Stochastic Differential Equations and Diffusion Processes is a well-organized book covering fundamental concepts through recent results and has very much influenced a large number of researchers in the fields.

The most outstanding work of Watanabe's is his establishment of the theory of generalized functionals. He defined a generalized functional on the Wiener space to be a linear functional on the polynomials following the Schwartz idea for distributions, and introduced the Sobolov norms of a negative differentiation index. According to this theory the composition $T \circ F$ is a generalized functional, if T is a Schwartz tempered distribution and F is a non-degenerate smooth functional.

This theory can be applied to numerous fields, as is illustrated below by the problem of an asymptotic expansion of the transition density $p(t,x,y)$. Observing that

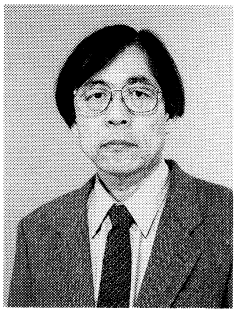
$$p(t,x,y) = <\delta_y \circ X_{t,x}, 1> = \mathrm{E}(\delta_y \circ X_{t,x}),$$

Watanabe first proved that $\delta_y \circ X_{t,x}$ has an asymptotic expansion in t whose coefficients are generalized functionals and then took the average to obtain an asymptotic expansion of $p(t,x,y)$.

The theory of generalized functionals is extremely powerful in solving the problems related to elliptic operators in analysis, geometry and mathematical physics, as can be seen in recent papers by Watanabe himself, N. Ikeda, S. Kusuoka, I. Shigekawa, and H. Sugita. In 1989 Dr. Watanabe was awarded the Autumnal Prize of the Mathematical Society of Japan.

Japan Academy Prize to:

Masatoshi TAKEICHI
Professor, Graduate School of Science,
Kyoto University



for "Discovery of Cadherins Indispensable for Cell-cell Adhesion in Animals, and Elucidation of their Function"

Outline of the Work:

Cell-cell adhesion is fundamental to the construction of the multicellular animal body. Early studies revealed that animal cells are capable of self-assembly; during this process the cells selectively adhere to particular cell types, as known as "cell sorting" phenomenon. These properties of cells are thought to be

crucial for their ability to organize complex body structures. Dr. Takeichi investigated the molecular basis for cell-cell adhesion, and discovered a molecular family termed "cadherin," which plays a central role in the association of cells, selective cell adhesion, and tissue organization.

In his early studies, Dr. Takeichi found that the cell-cell adhesion mechanism comprises of two distinct systems, Ca^{2+}-dependent and Ca^{2+}-independent ones. Subsequently, he succeeded in identification of molecules involved in each mechanism. The one for the Ca^{2+}-dependent mechanism was designated as cadherin. Studies by use of antibodies and cDNAs showed that the cadherin plays a key role for connecting cells; without this molecule, cells forming tissues tend to fall apart. Dr. Takeichi then found that there exist many molecules similar to the cadherin, constituting a molecular family. Members of the family were thus designated as E-cadherin, N-cadherin and so on. Importantly, each cadherin is expressed in different tissues, and its expression pattern dynamically changes with development, being associated with morphogenetic events. Moreover, each of the molecules exhibits a specific, homophilic binding nature; and this property of cadherins confers selective adhesiveness on cells. On the basis of these findings, Dr. Takeichi proposed that cadherins are factors responsible for the cell sorting phenomena classically discovered. His recent work revealed that the cadherin family is present not only in the vertebrate but also in invertebrate species, suggesting its universal role in the generation of multicellular animals.

The mechanism of how cadherins function in cell-cell adhesion was also pursued. Dr. Takeichi found that the cytoplasmic domain is necessary for the cell adhesion activity of cadherins. Furthermore, he cloned α-catenins, proteins associating with the cytoplasmic domain of cadherin, and provided evidence that these molecules are indispensable for cadherins to function. This was the first demonstration that cell-cell adhesion is controlled by cytoplasmic machinery.

Dr. Takeichi's research also contributed to medical problems. Through collaborations with other investigators, he found that cadherin activity is down-regulated in many tumor cells, and this down-regulation facilitates their dispersion, and invasiveness. It is now believed that this is a key process for cancer cells to be released from the original tumor sites, leading to their metastasis. This idea has been supported by observations from many other laboratories. Recently, Dr. Takeichi began to study the role of cadherins in brain morphogenesis, and found that a number of cadherin subtypes are expressed in developing brains, each delineating specific subdivisions of the brain or specific subsets of neurons. These findings are opening a new field for shedding light on the cellular and molecular basis of brain organization.

In conclusion, Dr. Takeichi's discovery of cadherins has made an enormous contribution to our understanding of how the animal body forms.

Japan Academy Prize to:

Mamoru HOSAKA
Board of Directors,
Tokyo Denki University
Emeritus Professor,
University of Tokyo

and

Toshio SATA
Vice President, Toyota
Technological Institute
Emeritus Professor,
University of Tokyo

for "Collaborative Research on Integration of Design and Manufacturing"

Outline of the Work:

Prof. Mamoru Hosaka, whose speciality is information systems and CAD (Computer Aided Design) and Prof. Toshio Sata, whose speciality is product engineering and CAM (Computer Aided Manufacturing) had agreed in early 1970s to work on a theme "integration of design and manufacturing activities based on computer internal model of objects". Since then, they had worked collaboratively to develop an experimental integrated system and individually have solved successfully problems associated to CAD and CAM. Their works during these 30 years have not only lead the research activities in these fields, but also made great contribution on the progress of mechanical manufacturing industry of Japan.

Prof. Hosaka had considered in late 1960s that engineering design was a process to construct information model of an object to be designed and its construction process could be aided by computer. To test his idea on design, he built an experimental system with a language system called GIL for treating model building and processing. In it, a solid body is represented in a computer as a set of names of surrounding faces with their geometric as well as their topological data. Since its other geometrical information could be deduced from them, the information model of a solid was well be considered to consist of these two kinds of information at any stages of its model processing. This was quite different from CAD systems at that time, which only supported making of engineering drawings or cutter path calculation from their description.

Prof. Hosaka made an invited lecture at the conference of the Japan Society of Precision Engineering in 1972, in which he said, referring his research work, that computer internal model would be the key of the future CAD system that supports whole design processes. This was the first case that the solid model was introduced in computer aided design field.

Prof. Sata had been working since 1965 on application of computer in production process, especially adaptive control of machining process based on its mathematical model in the computer.

After he learned Prof. Hosaka's research on solid model in spring of 1972, he proposed Prof. Hosaka to work together on its application on manufacturing. Prof. Hosaka also learned importance of technological information attached to the model, which was to be used in subsequent manufacturing processes. Then they began their collaboration.

Then Prof. Hosaka's initial modelling system, which was built on a small laboratory made computer, had evolved into a full scale software system called GEOMAP (Geometric Modelling And Processing) compatible with a powerful computer system. To assist all the activities from design to process planning, manufacturing data was attached to the model in GEOMAP system at Prof. Sata's laboratory. Then from the model produced by design, automatic generation of control instructions was achieved for processes: machining by numerical control machines, measurements of shape by 3D measuring machines, assembly process by robot, etc.

The results of this research were presented at PROLAMAT (Programming Language for Machine Tool) conference in 1982 and got special admiration from many of the attendants that this was the first realization of integration of design and manufacturing. This spurred researches on the integration of CAD/CAM in the world. Prof. Stata organized a committee in the Japan Society of Precision Engineering for further promotion of GEOMAP system as an integrated system and the participant companies received fruits of the research work.

As for engineering products with freeform surfaces, owing to lack of appropriate theories applied to their design and evaluation, their full integration by computer had not be considered. Since 1965 Prof. Hosaka had been studying expressions of freeform surface. Finally in 1975 he introduced shift operators working on control points of freeform curve segments and surface patches. This method simplified the expressions of Bézier curve and surface, and clarified the disposition of control points for their smooth connection. He also developed methods of evaluation of freeform surfaces and solved the problem of their interference. With these results, constructing information model of objects with freeform surfaces had realized, and they became the basis of advanced CAD/CAM systems in car industries in Japan. Prof. Hosaka published a book on his developed theories from Springer Verlag in 1992.

Using appropriate modelling techniques, Prof. Sata also performed various researches: simulation of cutting process, monitoring technique of machining operation by using cutting sound, and intelligent control of production processes, whose functions were diagnoses of and recoveries from failures. He also proposed a concept of virtual manufacturing based on product modelling and the results of their research works, in which design and manufacturing planning with their evaluation are to be performed in a computer in advance.

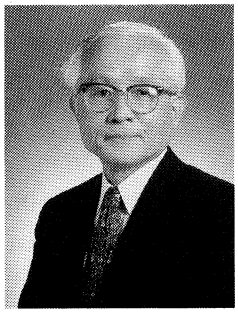
Values of these research results of Prof. Hosaka and Prof. Sata are high not only from academic, but also from practical application point of view. Their works have contributed on the fact that manufacturing industry of our country have attained the highest position in the world in their short product development period together with high quality and production efficiency.

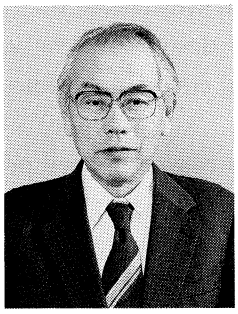
Japan Academy Prize to:

Tadashi INAGAMI
Professor,
Department of Biochemistry,
School of Medicine,
Vanderbilt University
(U.S.A.)

and

Kazuo MURAKAMI
Professor,
Institute of Applied
Biochemistry,
University of Tsukuba





for "Biochemical and Molecular Biological Studies of Renin-angiotensin System"

Outline of the Work:

Enzyme (renin)-hormone (angiotensin I, II) system plays an important role in the control of blood pressure and electrolyte balance. Renin-angiotensin system was studied extensively from molecules to the whole body by Dr. T. Inagami and Dr. K. Murakami. Their achievements are classified into three parts.

1) Molecular level

a) Renins were purified from the organs of various species and their cDNAs and genes were cloned. As a consequence, primary structure of renins and their genes has been determined completely.

b) Angiotensin II receptor (type 1a and 1b) cDNAs were cloned and their all nucleotide and amino acid sequences were determined. The molecular model of angiotensin II receptor (type 1a) was constructed as shown in Fig. 1.

The type 1a receptor gene was expressed in many tissues but the type 1b receptor gene was expressed specifically in adrenal and brain. A new angiotensin II receptor (type 2) cDNA was also cloned.

2) Cell and organ level

Dr. Inagami demonstrated renin-angiotensin system in adrenal gland and cells (neuronal cell and hormone-producing cells in pituitary). He presented a new hypothesis that angiotensin II participates not only in the blood pressure control in circulation but also in local specific function in various organs and cells.

3) Whole body level

a) Based on the above molecular and cellular studies, transgenic mice carrying human renin and human angiotensinogen genes were created. Their systolic blood pressure was about 30 mmHg higher than that of control mice. The elevated blood pressure was decreased to the normal level by a human renin specific inhibitor and other inhibitors of renin-angiotensin system.

b) Angiotensinogen-deficient mice were created by gene targeting method. Their systolic blood pressure was about 30 mmHg lower than that of control mice. Moreover, two kinds of mice lacking

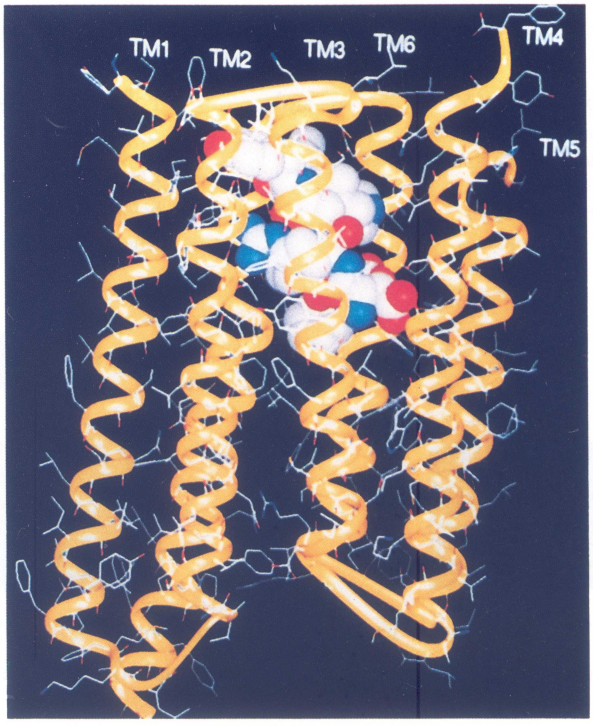


Fig. 1. Molecular Model of Angiotensin II Receptor (type 1a).
Transmembrane (TM) helices are represented by the yellow solid ribbon. space-filled model: angiotensin II, white: carbon, red: oxygen, blue: nitrogen.

angiotensin II receptor-type 1a or -type 2 were created. The analysis of their blood pressure indicated a very interesting result that angiotensin II increased the blood pressure via the type 1 receptor and decreased the blood pressure via the type 2 receptor.

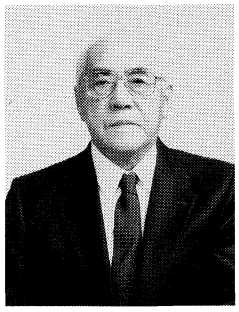
In summary, Dr. Inagami and Dr. Murakami have elucidated the molecular structure of renin and angiotensin II receptors and their genes, and demonstrated that the main function of renin-angiotensin system is the control of blood pressure in heart and blood vessel.

Japan Academy Prize to:

Morio IKEHARA
Advisor,
Biomolecular Engineering
Research Institute
Emeritus Professor,
Osaka University

and

Eiko OHTSUKA
Professor,
Faculty of Pharmaceutical
Sciences,
Hokkaido University



for "Synthesis and Functional Studies on Nucleic Acids
—Synthetic c-Ha-*ras* Gene and Related Subjects"

Outline of the Work:

Dr. Ikehara started his studies of nucleosides in 1960 and succeeded in the synthesis of a novel series of compounds, 8-cyclonucleosides, which opened new routes in the modification of carbohydrate and base moieties of nucleosides. A new method for the introduction of bromine atom at the 8-position of purines led to the synthesis of 7, 8-dihydro-8-oxoguanine (8-oxyguanine) derivatives which were later found to be a major type of DNA lesion and are presently used in studies of the *ras* oncogene by Dr. Ohtsuka.

1. Development of new synthetic methods for RNA and total synthesis of tRNA

For the synthesis of larger RNA molecules, Dr. Ikehara and Dr. Ohtsuka developed aromatic phosphoramidates and o-nitrobenzyl groups for the protection of the phosphate and 2′-hydroxyl groups, and the selective removal of these groups was performed. Using these methods, they succeeded in the total synthesis of formylmethionine tRNA in 1979. They also used synthetic RNA fragments to identify the tRNA active sites by the replacement of natural molecules. These synthetic approaches were applied to studies for the structure-function relationship of RNA enzymes (ribozymes) by Dr. Ohtsuka.

2. New synthetic approaches for DNA and gene constructions

The phosphoramidate protection method was then applied to DNA synthesis in solution, and the operator DNA fragments thus produced were used to elucidate the interactions with proteins. The deoxyinosine method developed by Drs. Ikehara and Ohtsuka has proved to be more advantageous than any other methods, and deoxyinosine probes were successfully used to elucidate the base sequences of the genes encoding various proteins such as cholecystokinin and glycoproteins. The genes for human growth hormone, c-Ha-*ras*, RNase T1, human lysozyme and T4 endonuclease V were synthesized and expressed in sufficient quantities for structural studies. Indeed, the synthesis of the normal and activated *ras* genes led to the determination of the 3D structure of the first oncogene product.

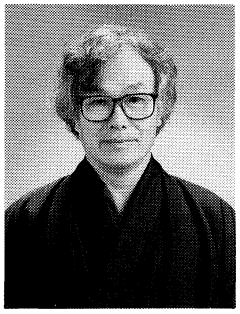
3. Expression and mutagenesis of synthetic *ras* genes

The activated synthetic *ras* genes were shown to transform cultured mammalian cells, indicating that the product of the activated gene is responsible for the malignant growth of these cells. The expression of these activated genes was inhibited by using designed ribozymes that selectively cleave ras mRNA.

The synthetic *ras* genes were also used to investigate the mutagenesis of damaged bases, such as 8-oxyguanine and thymine photodimers, by introducing the damaged bases in hot spots of the oncogene. These unnatural bases in the *ras* gene were found to be mutagenic and to cause malignant growth of cultured cells. The mechanism of G to T transversion caused by 8-hydroxylation of deoxyguanosine was proposed in these studies.

The synthetic approaches developed by Dr. Ikehara and Dr. Ohtsuka have contributed to progress in the chemistry and biology of nucleic acids.

Duke of Edinburgh Prize to:



Hiroya KAWANABE
Director General, Lake Biwa Museum
Emeritus Professor, Kyoto University

for "Ecological Studies on the Maintenance and Conservation of Biological Diversity in Freshwater Fishes"

Outline of the Work:

Today the conservation of biological diversity and the sustainable use of bioresources is receiving global attention; the Convention on Biological Diversity was signed at Rio de Janeiro in 1992 and went into effect in 1993. Studies on the origin and maintenance of biological diversity are indispensable to its conservation. Way before biodiversity conservation and maintenance issues became internationalized, Prof. Hiroya Kawanabe had begun his studies in the field. Using aquatic ecosystems as his medium, he began his monumental work on the social structure and population dynamics of Ayu, a dominant fish in Japanese rivers; and he explored mechanisms for maintaining species diversity of fishes in various fresh water ecosystems. His major findings can be divided into the following three categories.

(1) Social structure and population dynamics of Ayu

In the 1950's Prof. Kawanabe studied the relationship between the social structure and population dynamics of Ayu (*Plecoglossus altivelis*) which feeds on algae attached to stones in the rivers of Japan. He found Ayu to be territorial when its population density is low, but gregarious, forming schools, when its population density is high. He observed that social structure influences the growth rate of each individual. This was a momentous work that innovatively combined animal sociology and population ecology, two disciplines which previously tended to be treated independently.

Prof. Kawanabe played a pioneering role in the development of behavioral ecology, or sociobiology as it later became known. In the 1960's and 1970's. Prof. Kawanabe explored the historical and evolutionary

aspects of the Ayu's social structure, paying particular attention to the effect of size and role of its territory on population regulation. Many rivers in Japan are stocked with Ayu. A widely applied criterion for determining the amount of fry to be released into them is based on his studies.

(2) Food segregation in river fishes

Prof. Kawanabe extended his studies to the food web structure in river ecosystems, and identified the habitat and food niche shift in various species of fishes as influenced by the presence or absence of the dominant fish, Ayu. This became a remarkable piece of work on community organization in the late 1950's. He emphasized the importance of flexible relationships among species in community organization, imbuing the concept of ecological niche with a new dimension. Furthermore, he developed the concept of biological production with special reference to the relationship among species.

(3) Maintenance of biological diversity in Lake Tanganyika

Since the 1970's, Prof. Kawanabe has been conducting an international cooperative research project on mechanisms that maintain biological diversity in Lake Tanganyika in Africa. He discovered a new relationship—that of "competitive cooperation" among fish species which, having similar resource requirements, were conventionally thought to be competitive. He showed that the foraging success of a fish species sometimes increases when another apparently competing species is present. He proposed the idea that this competitive cooperation behaviour plays an important role in the maintenance of fish species diversity in Lake Tanganyika, in place of the traditional competitive exclusion principle. His pioneering work led to various studies dealing with the importance of indirect effects in community organization.

In 1992, he proposed and began an international cooperative research project, Symbiosphere, within the framework of a project on biological diversity, DIVERSITAS, organized by IUBS, SCOPE and UNESCO. It attempts to clarify how biological diversity was formed in the past and is maintained through various interactions in the present, with an aim at contributing to the conservation of biological diversity. Furthermore, in 1993, he organized the International Network of DIVERSITAS Western Pacific and Asia (DIWPA) to promote studies of biological diversity and to exchange information in the Western Pacific and Asia.

PROCEEDINGS AT THE 900TH GENERAL MEETING

The 900th General Meeting of the Academy was held on Tuesday, June 11, 1996, at 1:05 p.m., Dr. Yoshio FUJITA, President, taking the chair. Eighty-eight members were present, and the following communications were made:

The state in the historical perspective of ideas . . . . . Kan'ichi FUKUDA, M. J. A.
Medical care and government. . . . . Ryuichiro TACHI, M. J. A.
From Fermer to Wiles. . . . . Shokichi IYANAGA, M. J. A.
Topological saponification of oriented poly(vinyl trifluoroacetate) to poly(vinyl alcohol) with gaseous ammonia. . . . . Shuji MATSUZAWA, Tetsuya TANIGAMI, and Qi WANG
Communicated by Seizo OKAMURÀ, M. J. A.
A remark on Jeśmanowicz' conjecture . . . . . Kei TAKAKUWA
The schur indices of the cuspidal unipotent characters of the finite unitary groups . . . . . Zyozyu OHMORI
Orbits in the flag variety and images of the moment map for $U(p,q)$ . . . . . Atsuko YAMAMOTO
Elliptic curves related with triangles . . . . . Soonhak KWON
Above four, communicated by Shokichi IYANAGA, M. J. A.
Peridotites from the Parece Vela Rift in the philippine sea. Upper mantle material exposed in an extinct back-arc basin . . . . . Yasuhiko OHARA, Shigeru KASUGA, and Teruaki ISHII
Communicated by Yoshibumi TOMODA, M. J. A.
On the solvability of linear partial differential equations . . . . . Hiroshi KOSHIMIZU and Kiyoshi TAKEUCHI
Eigenvalues of the Laplacian under singular variation of domains—The Robin problem with obstacle of general shape . . . . . Shin OZAWA
Geometric measure theory and manifolds of nonnegative Ricci curvature. . . . . Yoe ITOKAWA and Ryoichi KOBAYASHI
Determination of the Harish-Chandra C-function for $SU(n, 1)$ and its application to the construction of the composition series. . . . . Masaaki EGUCHI and Shin KOIZUMI
Above four, communicated by Kiyosi ITÔ, M. J. A.
Rheological behavior of volcanogenic deformations . . . . . Izumi YOKOYAMA, M. J. A.
Hydrodynamic properties of water in myoplasm in resting and active states . . . . . Michi-hiko OGATA
Communicated by Setsuro EBASHI, M. J. A.
Magma distribution in island arc mantle in three dimensions . . . . . Hiroki SATO, Kenichi MURO, Akira HASEGAWA, and Ko HASHIZUME
Communicated by Ikuo KUSHIRO, M. J. A.
Origin of cratonic peridotite and komatiite: evidence for melting the wet Archean mantle. . . . . Eiji OHTANI, Kenji MIBE, and Takumi KATO
Communicated by Shun-iti AKIMOTO, M. J. A.

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

First, the President announced that Dr. Katsuma DAN, M. J. A., had passed away on May 18, 1996; Dr. Yuzo YAMADA, M. J. A., had passed away on May 25, 1996; Dr. Hisao KUMAGAI had passed away on June 11, 1996. The members rose from their seats in silence, expressing profound sense of grief.

Next, Dr. Teruaki MUKAIYAMA, M. J. A., paid a tribute of admiration to the late Dr. Tetsuo NOZOE's meritorious services to academic circles.

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

Then, the President reported that the Twenty-fourth meeting of the Japan Academy Public Lectures was opened to the public in the Kyodai-Kaikan, Kyoto, at 2:00 p.m. on Sunday, May 26, 1996, with Dr. Chihiro HOSOYA, M.J.A., and Dr. Yoshikazu MIYAZAKI, M.J.A., as speakers, whose respective subjects were:

"The Asia-Pacific War—In Various Perspectives—"

"Beyond the National Economy".

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: Atsushi KOBATA, Sueo IKEHARA, Ryuichiro TACHI, Saburo NAGAKURA, Hiroshi TSUJI, Masanao MATSUI, Tamio YAMAKAWA.

The Meeting adjourned at 4:52 p.m.

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PROCEEDINGS OF THE JAPAN ACADEMY

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