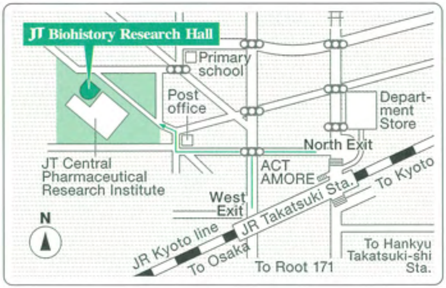
The image of Biohistory

This picture illustrates the history and diversity of life which came into being over the course of this 3.8 billion years period.

Original idea by Keiko Nakamura (Ph.D.) with consultation of Marina Dan (Ph.D.) / Illustrated by Ritsuko Hashimoto



JT Biohistory Research Hall

1-1 Murasaki-cho, Takatsuki, Osaka 569-1125, Japan
Tel. 81-72-681-9750 Fax. 81-72-681-9743
E-mail: eng@brh.co.jp URL: http://www.brh.co.jp/en/index.html

Open	10:00 AM to 4:30 PM Admission: Free
Closed	Sundays and Mondays / Year-end holidays (Dec.29-Jan.4) The Hall may be closed on days in addition to the above due to preparations for new exhibits, etc.
Access	10-minute walk from Takatsuki Station on JR Kyoto Line 18-minute walk from Takatsuki-shi Station on Hankyu Kyoto Line (Access from the JR station is more convenient.)

BIOHISTORY JOURNAL
Special International Edition 2005

JT Biohistory Research Hall
Science Communication and Production sector

Director Keiko Nakamura
Chief editor Mitsuko Kudo
Editor Mari Toyama

Hidekatsu Murata, Tomoko Kuwako, Atsushi Yamagishi, Naoko Kitaji, Noriko Kato, Asuka Bando (student)

Design Keisuke Saka
Printing Okamura Printing Industries co., ltd.

Published in March, 2005

BIOHISTORY JOURNAL

Special
International
Edition
2005

Contents

CONCEPT Biohistory through the hall

- The concept of Biohistory
- BRH where Biohistory is practiced
- Challenge for practicing Biohistory
- Pop-up stairs of Biohistory

DIALOGUE Making the concept of Biohistory more concrete through dialogue

- Biohistory with various fields

RESEARCH Biohistory through the latest research

- Researches with a walk through Biohistory
- Medaka—A model animal raised by Japanese
  Hiroyuki Takeda The University of Tokyo
- The potential of the science of the wild—Inuit knowledge and modern science
  Keiichi Omura Osaka University
- Genome imprinting
  Fumitoshi Ishino Tokyo Medical and Dental University

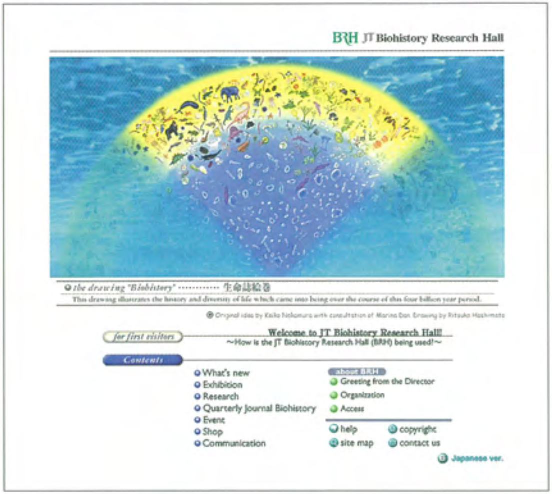
SCIENTIST LIBRARY Biohistory through people

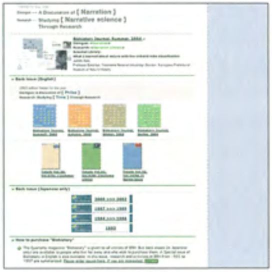
- World map and history of scientist library
- Fascinated by the mechanism of immunity
  Tasuku Honjo Kyoto University
- Observing with the heart—The division of cell and organella
  Tsuneyoshi Kuroiwa Rikkyo University

BIOHISTORY WEBSITE

We have opened
Biohistory Research Hall (BRH)
website to the public
as one way to express
the concept of Biohistory.
The activities, such as
biology research and expression,
are here introduced.
Beside articles in these cards,
a lot of other articles can
also be read on this website.
We regularly update the website.
If you have a good idea,
please tell us by "Contact us" form.

http://www.brh.co.jp/en/





Quarterly Journal Biohistory

The contents are updated once every three months based on quarterly journal Biohistory (Japanese version).

We at BRH

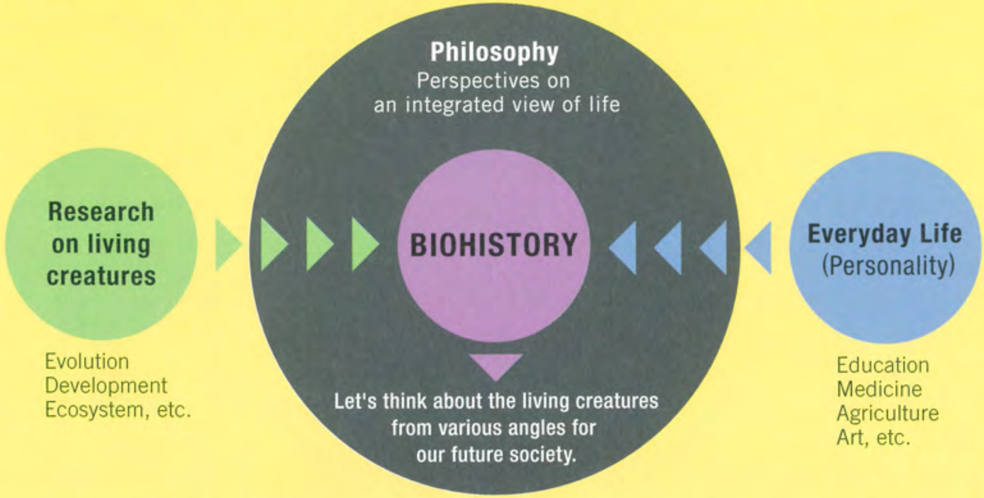
The diary of the members of Science Communication and Production sector are updated once a month.
Their daily works are introduced with their own word.

The concept of Biohistory

Biohistory in society

Where did we come from?
What are we?
Where are we going?

Biohistory is a novel intellectual field based on the research of living creatures. The 21st century is expected to become "The era of life", when people consider that respect of life is truly important in our lives.



In Biohistory Research Hall (BRH), we combine research on living creatures and everyday life. Indeed, the result of research is always exhibited, such as in art, music, symposia and contemporary auditory and visual technologies in BRH. These activities offer an integrated view of life and we can propose new perspectives on the relationship between nature and humanity through collaboration with philosophers, artists, specialists from various fields and the general public, including children. To reconstruct fascinating stories of life using research results is one of the most important activities of Biohistory.

The concept of Biohistory

The challenge understanding living creatures through the genome

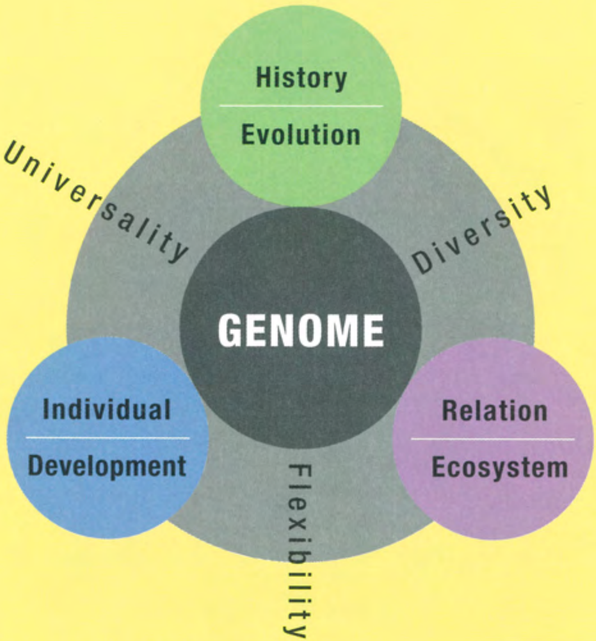
All living creatures on the Earth originated from a common ancestor that appeared some 3.8 billion years ago, most probably in the ancient sea. This 3.8 billion year historical period gave rise to human beings. Biohistory aims to enrich our view of lives by examining this history and the relationships among the wide variety of living creatures of this period. This science has the potential to inspire today's life-based society, we believe, by allowing everyone to learn of the true bounty of nature and enjoy the science of living creatures.

The genome is "DNA in its entirety, present in the nucleus of a cell" and contains all the genetic information needed to form an individual. For example, each human cell contains a human genome and each mouse cell a mouse genome.

The genome has the face of universality because its DNA constituent is present in every living creature, and at the same time, it has the face of diversity because it differs from organism to organism, and it also has flexibility because it changes with environmental interaction.

When genomes are analyzed, we can reveal, for example, how humans became human. Moreover, both similarity and difference between humans and *Escherichia coli* will be found. In this way, we will be able to see the history of life and the relationship of all living creatures on the Earth.

There are three ways by which one can examine the history of life and the relationships of living creatures through genome analysis. To examine the history of living organisms (evolution) and the process of forming individuals (development) and the relationship among the living creatures (ecosystem) is to see living organisms in their entirety and to pay attention to their diversity. We named this field of research into the history of organisms, Biohistory. Biological studies continue to reveal the involvement of genome activity in more phenomena of life, and we will get closer to elucidation of the magnificent history of all living creatures.



Universality

The origin of the various creatures living on the Earth was only one cell with which the genome was born 3.8 billion years ago. The basic structure and function for survival maintained fundamentally without changing through evolution for a long time could be clarified by the examination of the genome.

Flexibility

Living creatures survive somehow through continuous changes according to environmental interaction. We would like to know how not only multicellular organisms but also unicellular organisms regulate the genome function for environmental change.

Diversity

The first cell born 3.8 billion years ago has changed its shape and function, and spread on the Earth. It is said that there are 14 million species of living creatures on the Earth now. We would like to know the relationship among the various living creatures through the comparison of the genome activity.

The concept of Biohistory

Proposal of the novel wisdom and value system

In ancient times, people had "the sense of man in nature" symbolized in myth. Although modern science that separates nature and man has made it possible for us to live conveniently, strains, such as environmental issues occurred in the quest for economic efficiency. Biohistory tries to create a novel value of "the sense of man in nature" with reason that pursues the revival of humans as living creatures and relativizes science and technology.

	Ancient Times	Ancient Greece	The Middle Ages	The Modern Ages	**The 21st Century**
		REASON →			
Basic principle	**LIFE** (Mythology)	**Idea**	**God**	**Enlightening reason**	**LIFE** (A novel myth)
System of knowledge	·Creation ·Totality ·Relation ·Diversity ·Everyday life ·Narrative ·The five senses	·Totality →Natural philosophy →Natural history	·Natural philosophy	·Universality ·Logic ·Objectivity	·Universality—self-reproducing reality—Diversity ·History ·Relation ·Diversity ·Everyday life ·Narrative
Relation between humans and nature	Human Nature	Olympian Gods Human Nature	God Human Nature	Human Artificiality Nature	Artificiality Human Nature

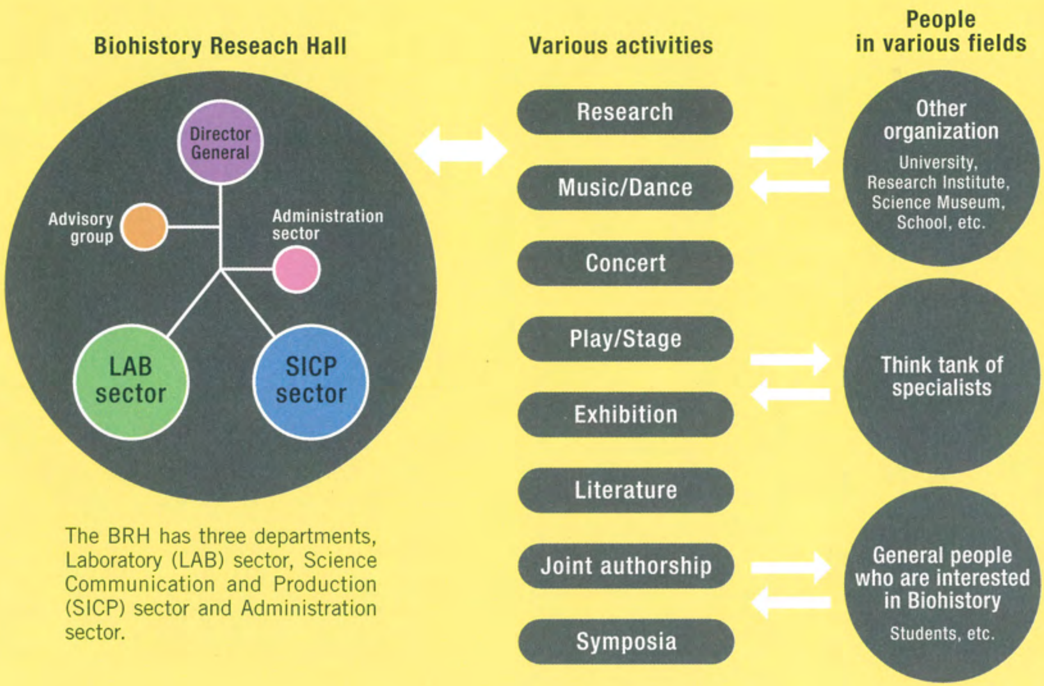
BRH where Biohistory is practiced

Biohistory Research Hall in Japan

The Biohistory Research Hall (BRH) is located in Takatsuki city between Osaka and Kyoto. It takes only about 15 minutes from either of these two cities by train. The exhibition hall and gallery are open to the public five days a week throughout the year.

Situated on 1,320 square meters, the BRH occupies a spacious four-story building, housing an exhibition hall, gallery, lecture hall, research laboratories and other facilities.

The collaboration with various fields



The BRH has three departments, Laboratory (LAB) sector, Science Communication and Production (SICP) sector and Administration sector.

We think that it is important to cooperate with the outside. It is possible to talk about living creatures with many people in other field through various activities in BRH. From these activities, we aim to understand living creatures deeply and to create a new wisdom based on living creatures for better life.

BRH is a unique building which has biological laboratories and a place to express what we know and think about living creatures.

4F Roof Garden

There is a restaurant for butterflies and caterpillers with their host plants on the roof garden.

3F Research Laboratories

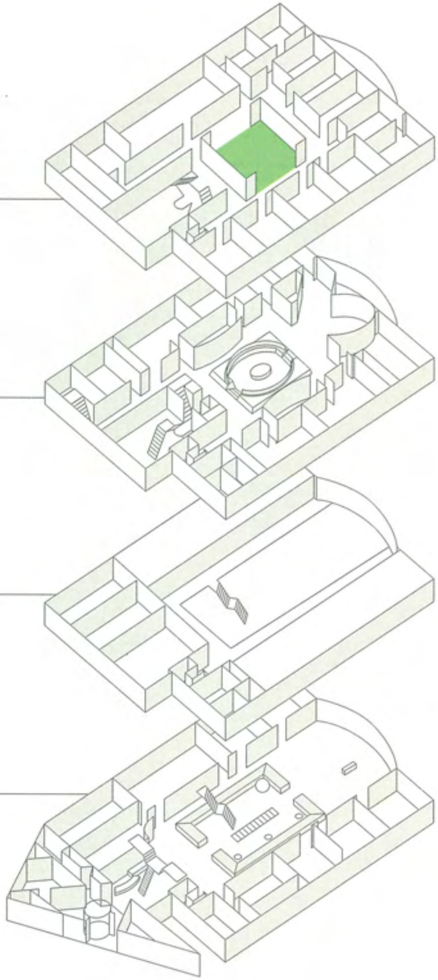
The daily workplace of researchers, where they attempt to unlock the mysteries of living things.

2F Gallery

Fusion of Science and Arts.
The essence of scientific discovery and beauty of science are presented.

1F Exhibiton hall

A variety of approaches are explored to convey the fruits of research and share the joy of these accomplishments.
This is a place to think about and feel Biohistory itself.



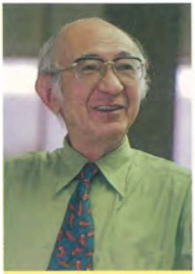
BRH where Biohistory is practiced

Director General and the members of Advisory Group

Director general
Dr. Keiko Nakamura
(Ph.D.)

I love living things, both as a scientist and as a layperson. In Biohistory, I would like to join the knowledge in science and wisdom in everyday life about living creatures including humans.

Keiko Nakamura graduated from the University of Tokyo and obtained her Ph.D. in Molecular Biology. She has served as the director of Mitsubishi-Kasei Institute of Life Sciences, and as a Professor of Waseda University. She advocated the new field "Biohistory" and founded Biohistory Research Hall.



Honorary Adviser
Dr. Tokindo S. Okada
(Ph.D.)

We are proud of the uniqueness of the activities of BRH, which have been admired by visitor from abroad. Please visit us at our website and come when you have a chance to visit Japan, and enjoy science with our presentation.

Tokindo S. Okada was Director General of the BRH (1993-2001). He is a Professor Emeritus of Kyoto University and was Vice-President of the International Union of Biological Sciences (1991-1996). Specializing in developmental biology, he has been awarded the Harrison Prize from the Society (1989). He was Director General of the National Institute of Basic Biology (1984-89), as well as President of Okazaki National Research Institutes (1989-91).

Adviser
Dr. Hiroshi Yoshikawa
(Ph.D.)

About 100 years ago, E. Fabre described the ability of the butterfly to select feeding plants as Instinct. We study it by means of contemporary biology. I enjoy catching butterfly, collecting eggs, raising larvae and doing experiments with them but only when equipped with molecular biology and genome technologies.

Hiroshi Yoshikawa graduated from the University of Tokyo and obtained his Ph.D. in Biochemistry. He has served as an Assistant and an Associate Professor at the University of California, Berkeley in the US and as a Professor of Kanazawa University, Osaka University and Nara Institute of Science and Technology in turn.

Adviser
Dr. Takashi Miyata
(Ph.D.)

Dobzhansky's remark, "Nothing in biology makes sense except in the light of evolution" is my favorite motto.

Takashi Miyata graduated from Waseda University and obtained his Ph.D. in Science. He served as an Assistant Professor Kyusyu University, and a Professor of Kyoto University. And he is a Professor of Osaka University.

Challenge for practicing Biohistory

Collaboration of Laboratory sector and SICP sector

(SICP= Science Communication and Production)

The members of the laboratory have studied about living creatures by scientific methods. The members of SICP have expressed the results of the science research. These two sectors have tried to elucidate new aspects of living creatures in different manners and produce the new concept and field, Biohistory.

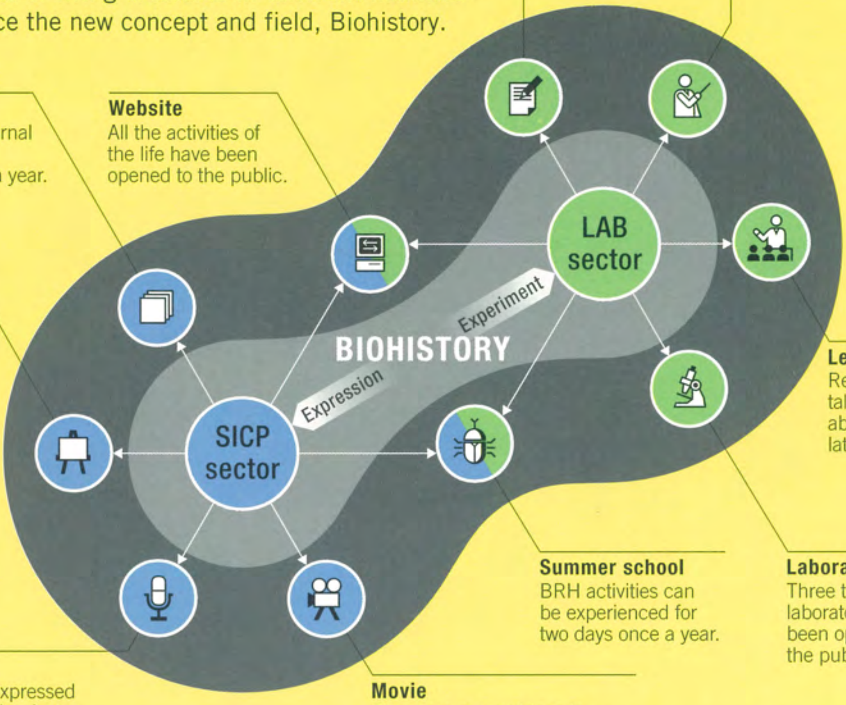
Article
The result of the research is made public through scientific journals.

Presentation
The result of the research is announced at academic societies, etc. and is discussed with other researchers.

Journal
Biohistory Journal is published four times in a year.

Website
All the activities of the life have been opened to the public.

Exhibition
The theme of Biohistory is exhibited.



Lecture
Researchers talk to the public about their latest work

Summer school
BRH activities can be experienced for two days once a year.

Laboratory tour
Three times a year, laboratories have been opened to the public.

Event
Biohistory is expressed in a concert, the dance, and the puppet show, etc.

Movie
There are many videos in which the researcher performs.

Challenge for practicing Biohistory

Research of Science

Laboratory Sector

The members of five laboratories research about evolution, development and ecosystem of living creatures.

How is the brain structure established in vertebrates?

EVO DEVO ECO

The brain morphology of vertebrate species consists of several compartments such as telencephalon and mesencephalon. The basic mechanism for the development of each compartment seems to be consistently the same from fish to mammals. However the size, shape and function of each compartment varies significantly depending upon the species.

Our goal is to understand how this well-patterned morphology of the brain is generated in terms of ontogeny and phylogeny, and how the individual compartment obtains its specific function through the evolutionary process. In order to achieve this goal, we try to define the molecular based developmental mechanisms of the brain by means of experimental biology. Now we are focusing on the formation of the forebrain pattern with the African clawed frog. By studying at which stage of brain formation and to which compartment of diencephalon this operation influences, we can determine how the brain pattern is correctly formed through normal development.

Exploring mutualistic interaction between plants and insects

EVO DEVO ECO

Insects are the most diversified animal group on the Earth. The mutualistic interaction between figs (genus *Ficus*, Moraceae) and the fig-pollinating wasps (family Agaonidae) is the most specialized case. Figs are pollinated by fig wasps in a species-specific way. All figs have a closed inflorescence (syconinum), which is lined with flowers inside. The fig wasps carry the pollen, and enter the syconinum through the narrow entrance (ostiole) in the pointed end of the syconium. In compensation for this, the figs provide the fig wasps with safe oviposition spaces and food for their larvae. The genus *Ficus* includes some 750 species which are mainly distributed in tropical and subtropical regions throughout the world. And it is said that one species of figs is pollinated by only one species of fig wasps. We would like to elucidate the phylogenetic relationships of the figs and the fig wasps by DNA analysis, and explore the mechanisms of their coevolutionary speciation.

Coevolutionaly interaction between insects and plants

EVO DEVO ECO

The swallowtail butterfly feeds exclusively on members of a plant family. Female butterflies lay eggs in response to specific chemical properties contained in their host plants. They perceive a variety of polar compounds as oviposition stimulants through the tarsal chemosensilla of the foreleg by drumming upon the leaf surface. In the last two decades, oviposition stimulants have been extensively identified for swallowtail butterfly species. Based on these facts we have promoted a study to identify genes that are expressed in female foreleg tarsi and function in various steps involved in chemoreception for host plant recognition. Through analysis of 2300 EST cloned from cDNA library prepared from female tarsi of Papilio xuthus, we have identified a seven transmembrane G-protein coupled receptor (7TM-GPCR) expressed specifically in female tarsi and several chemosensory proteins expressed preferentially in tarsi.

Comparative study to understand the common ancestor of flies, spiders and human beings

EVO DEVO ECO

We are vertebrates. Flies and beetles are insects. These two animal groups look similar in that they bear a brain, an anterior-posterior and a dorsal-ventral axis, and segmental structures. Recent studies using *Drosophila* (fly) and vertebrates suggest that these similarities are traits of their common ancestor. However, in most popular phylogenetic trees, many animal groups including starfishes and scallops are placed between the vertebrates and insects. What animals did the vertebrates and insects evolve from? To answer this question, we study the embryonic development of spiders, whose lineage was diverged from the insect lineage more than five hundred million years ago. Molecular-based comparative study of *Drosophila* and the spiders may provide clues for understanding the developmental systems that worked in the ancient animals. We believe that the understanding of the ancient arthropods will help to understand the origin of the vertebrates.

Morphogenesis of butterfly wings

EVO DEVO ECO

A butterfly needs wings to fly as well as to recognize the conspecific one and to protect itself from enemies by threatening or tricking them. How is the wing shape formed? We study the difference in the wing formation mechanism involving cell death among butterflies, and the biological meaning of this mechanism.

Challenge for practicing Biohistory

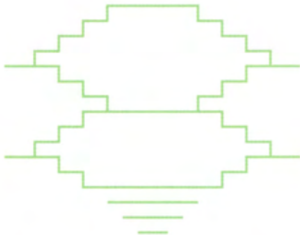
Play of Science

Science Communication and Production sector

Many interesting topics in modern biology are published as academic papers which are full of technical terms. Therefore, even scientists in different fields have difficulty understanding them, not to mention ordinary people.

In music, for example, first-class musicians enjoy not only composing music but also reading and playing it for the public. Why can't scientists do such activities? We present, deliver and share scientific research through the planning of quarterly magazines, exhibitions, a website, pictures, video and so on. We also plan some performances with the artists in various fields and create original souvenirs of BRH (available through our website).

Our aim is to make science exist in the society as culture. We hope you also have fun playing with science through our offers.



Pop-up Stairs of Biohistory

The whole image of the history of the Earth and
the living creatures for 4.6 billion years is introduced
through the Stairs of Biohistory
from the viewpoint of universality and diversity.

Swallowtail butterfly

Ground beetle

Tree shrew

Cambrian animal

Slime mold

Diversity
Illustrated by Utako Kikutani

The stairs of Biohistory

When you enter the BRH, an exhibition "the stairs of Biohistory" will catch your eyes. The bottom of the stairs indicates the birth of the Earth and the top of stairs indicates present time. The universality and diversity of living creatures are illustrated through 56 pictures on the walls. The extension of the abundant living creatures that starts from one cell (diversity) and the relation (universality) can be felt when you climb the stairs up to the fourth floor and while watching these pictures. Please trace, actually feel, and think about the history of the life for 3.8 billion years as your walk through time in BRH.

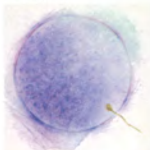
Skelton of reptile

Skelton of fish

The birth of mesoderm

The embryo of 2 germ layer organism

Fertilization



Universality
Illustrated by Hiromi Akashi

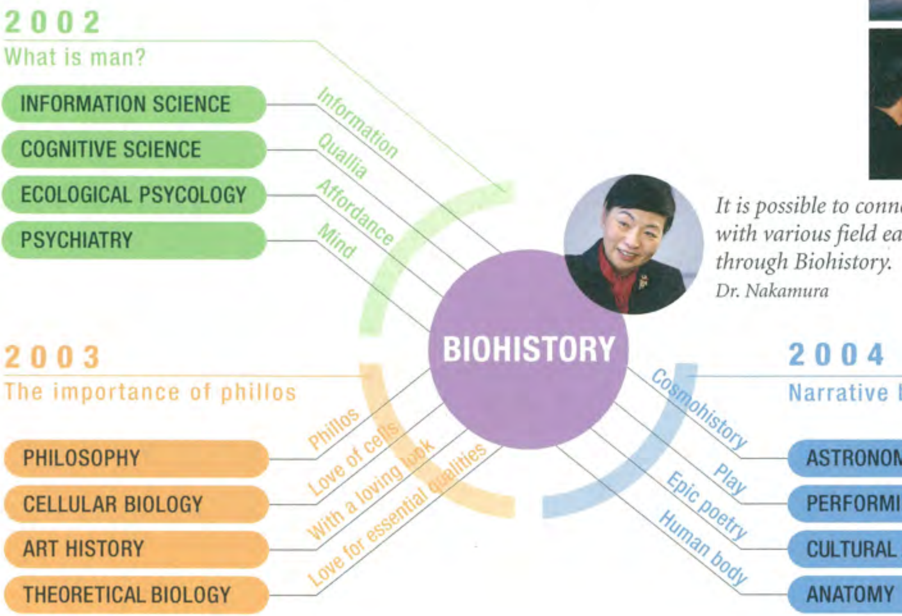
DIALOGUE

Making the concept of Biohistory more concrete through dialogue

A part of the article can be seen in our website.
www.brh.co.jp/en/

Director general Dr. Nakamura has continued to talk with people actively working in various fields (about 40 persons in ten years), and 12 people are introduced here for these three years. The themes for each year's dialogue were : "What is man?" in 2002, "The importance of phillos" in 2003, and "Narrative based science" in 2004. We are trying to generate a novel philosophy for the 21st century based on the understanding of life through these talks. Please join to our challenge to think about a better way of life as humans not only from science but from various angles.

It is possible to connect with various field each other through Biohistory.
Dr. Nakamura



2002 | What is man?

Information science

Humans from the viewpoint of information

Jun-ichi Tsujii

Language and living creatures are systems with diversity and flexibility in spite of keeping strict rules.

Dr. Nakamura | It is important for Biohistory to have the viewpoint that we may need a new methodology different from usual science to elucidate the complicated subject itself.

Cognitive science

Is the human brain special?

Kenichiro Mogi

When we think about the birth of consciousness, we are apt to forget the inconspicuous and essential wisdom, "The brain is also a living organ".

Dr. Nakamura | When we try to understand human beings, we should grasp ourselves as a historical existence and it is necessary to try to know individual history.

Ecological psychology

A new wave of human science – Ecological Psychology

Masato Sasaki

Although it is hard, I would like to try the research of ecological psychology that takes up life of animals with the viewpoint of diversity and universality.

Dr. Nakamura | Although biologists research the function of the brain to find out our minds, I can't help thinking that the mind exists in our whole body and in the relationship between inside and outside of the body. Therefore I am attracted to the concept of affordance.

Psychiatry

Explore the human inside with psychiatry

Kazushige Shingu

Is it natural or not that human society with unreality such as language? It is a big question for me.

Dr. Nakamura | Because the purpose is to make those which are not exist, language exists despite of being imperfect, I think. Although self-consciousness does exist anywhere, we ourselves are created only by language.

2003 | The importance of phillos

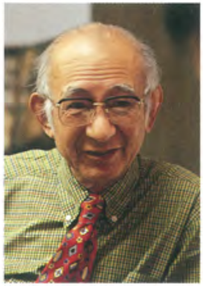
Philosophy

Wonder and tears are the wellspring of creation

Tomonobu Imamichi

Science is just scholarship driven by curiosity, I think. And I hope scientists would have deeper and wider intelligence.

Dr. Nakamura | It is a basic concept of Biohistory to discover the wonder (admiration) in things that seem trivial at a glance.



Cellular biology

The heart of biology

Tokindo S. Okada

The great, basic contradiction of whether one can love the way of biotechnology has recently been on my mind.

Dr. Nakamura | Literature, art, and science expand around nature. We wonder if phillos is the word linking all of these.

Art history

The Perspective of transcribing life

Johei Sasaki

A Japanese painter in the Edo era, Okyo showed the following four phenomena in his sketch. 1) truth 2) falsehood 3) spirit 4) space in which truth and falsehood are integrated.

Dr. Nakamura | Why is this here? Science is explaining things that can be seen using things that can't be seen. I'm surprised to know that Okyo had the same way of thinking as scientists in modern society.

Theoretical biology

Life: The universality lies under diversification

Kunihiko Kaneko

Some people are moved at the marvel of life itself, and some people are interested to see the success of life through the continuous change. I tend to be in the latter group.

Dr. Nakamura | When we think about dynamism of living creatures, it is clear that the essence of living creatures is continuous change. It may be natural to think that DNA has been somehow fixed the living creatures from continuous change.

2004 | Narrative based science

Astronomy

Cosmohistory and Biohistory
Keiichi Kodaira

It is important to create values from the knowledge about nature.
I think science is not free from value.

Dr. Nakamura | I would like to start a new study of "Narrative based science" making the data into knowledge on life phenomena. It will be broader than expression of physics by number and quantity, but narrower than expression of literature.

Performing arts

Build up the world view through plays
Takuo Endo

What am I? Where should I go?
A stage director should show the process to search from such a standpoint, though it's not easy.

Dr. Nakamura | We can discover new facts by narrative based science because when we try to narrate it shows us the whole form. By unifying "finding out" with "Narration", we can learn something new.

Cultural anthropology

The difference among "living creatures", "*Homo Sapiens*" and "humans"
Junzo Kawada

An epic poem is a history and it coheres the past to the present by narration.

Dr. Nakamura | Genomes in our body are the clue to decoding both the history and present day at the same time. To narrate the living creatures with the past as present, it's Biohistory.

Anatomy

The difficulty of both the human body and genome to narrate
Tatsuo Sakai

A lot of things to be cut out are sure to remain if we go back to the original experience before it is cut out in the word.

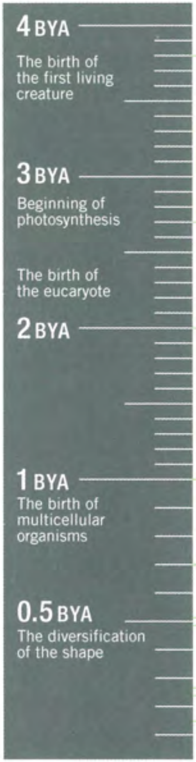
Dr. Nakamura | Living creatures are essentially different from machines. We can grasp the real image of living creatures by searching for their context not by understanding them as machines. I found that anatomy did the same thing for a long time.

RESEARCH

Biohistory through the latest Research

A part of the article can be seen in our website.
www.brh.co.jp/en/

We introduced about biological research of the 3.8 billion year history of living creatures in the quarterly journal Biohistory (Japanese version) since 1993. If there is an interesting biological research, we visit the laboratory, and introduce a new side of living creatures as Research articles. 23 research articles taken up in the past three years were mapped to "A walk through Biohistory" (one of the exhibition in BRH). Three unique research articles are introduced this time from these researches.



EVO DEVO ECO

Primitive life and the condition of the ancient earth
Akihiko Yamagishi

Biological clock in bacteria
Hideo Iwasaki

Research of the rotating molecule, ATP synthetase
Hiroyuki Noji

The creation of form in multicellular organisms as seen through the volvox
Ichiro Nishi

Niche—The cradle of cells
Shin-ichi Nishikawa

Why do we pay attention to the spider now?
Yasuko Akiyama-Oda

Mechanism of appendage diversification reviewed by anatomy
Nao Niwa

Genome imprinting
Fumitoshi Ishino

Severe mass extinction—Accelerator of evolution
Yukio Isozaki

Dialog between the bat and environment—With ultra sonic waves
Sumiko Matsumura

EVO DEVO ECO — **The reason the freshwater fish Arowana lives across the sea**
Yoshinori Kumazawa

EVO DEVO ECO — **The unique form created by the environment: Podostemaceae**
Masahiro Kato

EVO DEVO ECO — **Mechanism of symbiosis**
—Gene network made up of plants and soil microbes
Makoto Hayashi

EVO DEVO ECO — **Relationship among the environment, civilization and the near future elucidated by annually laminated sediment sequence**
Yoshinori Yasuda

EVO DEVO ECO — **Medaka—A model animal raised by Japanese**
Hiroyuki Takeda

human — **The similarity between language and genomes**
Masaaki Nagata

human — **To find out a kind of law hidden in genome sequences**
—Challenge of Bioinformatics
Kiyoshi Asai

human — **Requirements of humans**
—Brain, Language and Music
Tsutomu Nakata

human — **Humanoid Science**
—How can we find out a new understanding of human intelligence?
Minoru Asada

human — **The reconstruction of mind science**
Haruo Kashima

human — **The regeneration of the philosophy of science**
Satoshi Kato

human — **The evolution and development of the mind by the comparison of people, apes, and robots**
Shoji Itakura

human — **The potential of the science of the wild**
—Inuit knowledge and modern science
Keiichi Omura

A walk through Biohistory

Since 3.8 billion years ago, when the first cell was born in the sea, various living creatures have been emerged on the Earth and it has become the present complex and fascinating living world. This living creature's history is expressed by the beautiful laminated 17 glass sheets in the BRH exhibition hall.

Medaka

A model animal raised by Japanese

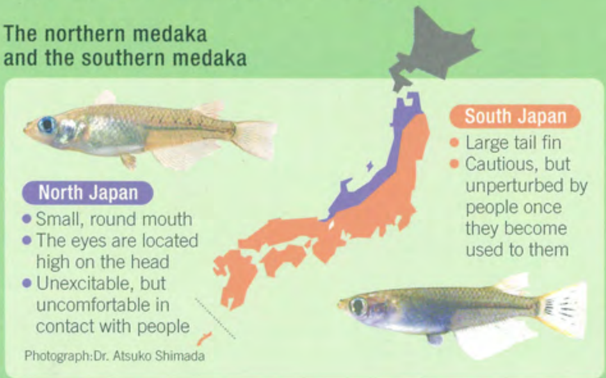
Hiroyuki Takeda School of Science, the University of Tokyo

The medaka (*oryzias latipes*) is a fish well known to the Japanese. Japanese researchers have established pure strains of the medaka in the wild, broadly divided into the northern Japan group and the southern Japan group. These two groups have differences in facial characteristics and physical form.

Although developmental biology research of fish is primarily conducted using the zebrafish, a small tropical fish or blowfish because of their short generation time, the medaka is also interesting and unique for its smaller genome size and its transparency, making their organs visible.

The medaka genome project has gotten underway, and now, we can deal with genetic variants in the pure strain. Therefore, investigations can be made into the relationship among DNA, shape, and ecology.

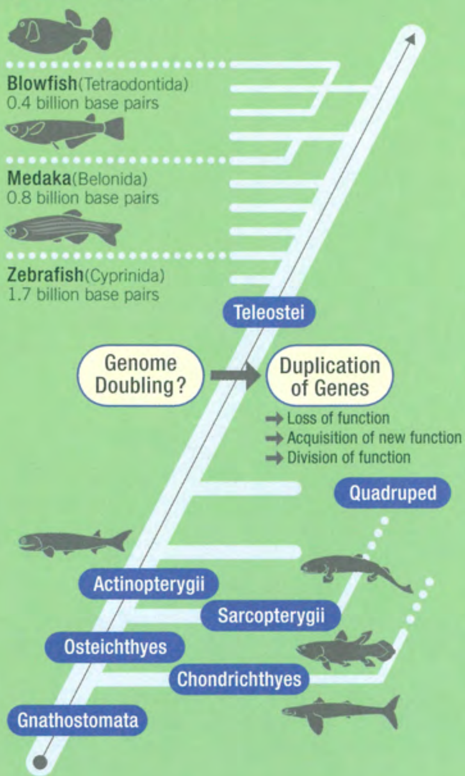
The northern medaka and the southern medaka



Photograph:Dr. Atsuko Shimada

The fish phylogenetic tree and genome size

Teleostei, which account for the majority of extant fish, seem to have given rise to genome duplication during the early stages of evolution. Later, the duplicated genes were lost and deversified.



To understanding of the mechanisms of development, biologists look for the cause of the aberration in the shape of medaka mutants. The mutant *toguro* (toguro means coiled snake in Japanese) has a different shape with no bones in the body. Interestingly, this phenotype was not observed in individuals hatched at low temperatures. This phenomenon is observed only for the medaka, which has a wide temperature range (4-40℃) for its growth.

Another mutant is *Da*, commonly known as the hikari (light in Japanese) medaka. (The silver color of its underbody extends to its back.) Its flat back, which is suited for swimming near the surface, has changed to resemble the tuna (the teardrop shape for swimming at medium depth in the ocean). It can be speculated that the medaka's ancestors were of the tuna type.

There is a great variation in the body types of fish depending on their living environment, even if they are a closely related species. This is likely the key to understanding the evolution of their body type.

Medaka have been kept as pets, and they flourished in wet rice paddies until the days of my childhood. The medaka swimming in water tanks in the laboratory and those in wet rice paddies close to extinction are superimposed within me. I want to apply my thoughts to history and the environment as a Japanese to compile stories about the medaka and conduct research.

Hiroyuki Takeda Ph.D.
Born in 1958, Takeda is currently a professor at the University of Tokyo. He specializes in developmental genetics and experimental embryology.

Coil-shaped medaka

The upper photo shows a normal medaka fingerling, and the lower photo shows the *toguro* mutant.
The *toguro* has no bones at all in the back. This mutant indicates a susceptibility to temperature. Changes in temperature during its growth control the period in which the aberrations occur.

Teardrop-shaped medaka

A normal individual

A mutant (Hikari Medaka)

The trunk of a normal medaka has a flat, orange back with a dorsal fin and a green underbody with an anal fin (above). With the change of a single gene, the back of the medaka assumes the structure of the underbelly, and it becomes shaped like a tuna (below).

RESEARCH

The potential of the science of the wild

Inuit knowledge and modern science

Keiichi Omura The Faculty of Language and Culture, Osaka University

I study the Traditional Ecological Knowledge (TEK) of the Canadian Inuit. Since 1992, I have visited Kugaaruk, Nunavut, Canada, interviewing Inuit elders and skilful hunters, as well as making participant-observation of their subsistence activities. The Inuit are often referred to as "the scientists of the Arctic" for their keen powers of observation and wealth of knowledge developed through their subsistence activities. Nowadays, this knowledge attracts considerable public attention, because there is a recognition that their knowledge provides precise insights into natural phenomena and therefore has the potential to contribute to the sustainable use of the environment. Inuit TEK is based on a monistic worldview in which humans are viewed as part of nature, as opposed to the dualistic worldview of modern science. Thus, Inuit TEK is different from modern science in representational style and basic paradigm but is not at all inferior to modern science. TEK is, rather, regarded as a science comparable to modern science, and complementary to it.

Photograph: Stewart Henry (Professor, The University of the Air)

Tactics and Strategy

Inuit TEK is based on the principle of "tactics" as opposed to "strategies," on which modern science is based. "Tactics" are a mode of practice in which an individual who is embedded in the environment and unable to objectify it, takes advantage of opportunities according to circumstances without planning strategies. In Inuit society, these "tactics" are appreciated as appropriate for adults with "ihuma" (reason), but modern science is disregarded as a childish way without "ihuma". Based on this "tactics", Inuit TEK tries to flexibly utilize the potential of environment as occasion may demand in order to cope with it, in contrast to the modern science. As a result, Inuit TEK regards human ability as something which should be developed, as opposed to modern science. From the perspective of Inuit TEK, the environment is something like a good rival. Inuit TEK as a science of the wild should be a complement to modern science.

Keiichi Omura Ph.D.
Born in 1966, Omura received a Ph.D. from the Graduate School of Letters, Arts, and Sciences of Waseda University. He was named an assistant professor Osaka University in 2000. He conducts research into changes in the Inuit language, art, personality, society, and culture based on fieldwork.

Inuit knowledge	Modern science
qualitative	quantitative
intuitive	rational
holistic (context bounded)	reductionistic (analytical)
mind and matter are considered together	separation of mind and matter
spiritual explanation	mechanistic explanation
moral	supposedly value-free
based on trial-and-error	based on experimentation
based on diachronic data	based on synchronic data
does not aim to control nature	aims to control nature
form of anecdotes or stories	form of principles and laws
not primarily concerned with principles of theory	concerned with principles of theory

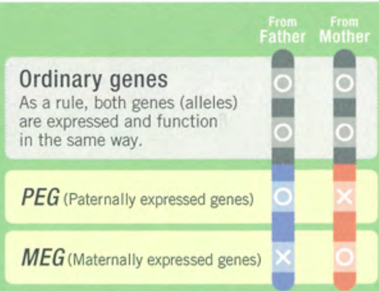
RESEARCH

Genome imprinting

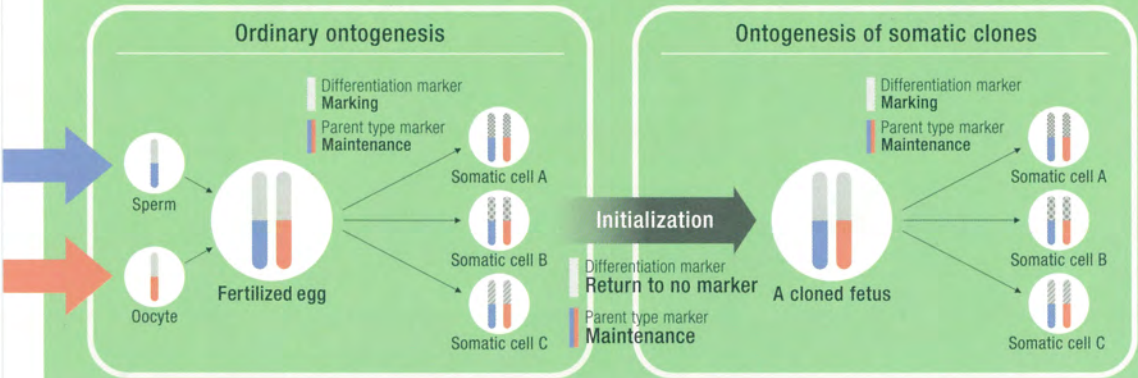
Fumitoshi Ishino Department of Epigenetics. Medical Research Institute, Tokyo Medical and Dental University

Mammals can't usually grow up without fertilization. Exceptions are cloned animals produced from somatic cells. Interestingly, when the somatic nucleus is introduced in an unfertilized egg, its memory for somatic cell is erased and initialized, that is, several differentiation markers in the somatic cell nucleus are eliminated. However, parental memories in the somatic cell, so called genomic imprinting memories from both father and mother, are stable for this initialization. It should be noted that this is an essential point for the normal development of the somatic cell clones.

Because of genomic imprinting, paternal and maternal genomes have different functions by regulating expression of two kinds of imprinted genes, such as paternally expressed genes (*PEG*) and maternally expressed genes (*MEG*). Therefore, both paternal and maternal genomic imprinting memories are essential in mammalian development and growth.



Somatic cells have two sets of genes (genomes), one from father and the other from mother. Usually, genes are expressed from both genomes and function equally during development and growth. Imprinted genes are unique because only paternally or maternally derived genes are expressed, so called *Peg* and *Meg*. Parental memories (paternal or maternal memories) are imprinted in sperm or oocyte genomes during germ cell formation/maturaton and regulate their expressions.

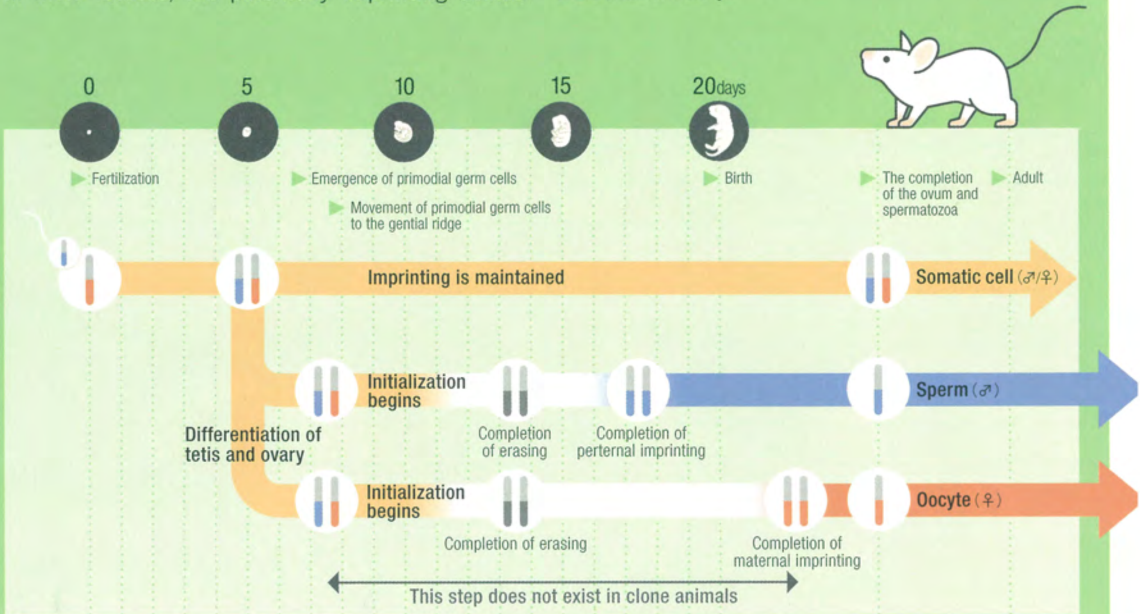


The repetition of genome imprinting by generations

Genome imprinting memories are maintained in the somatic cells, such as those in organs and tissues, over the entire life (somatic cell lines), while they are reprogrammed in the germ cells when they are inherited to the next generation. All the parental memories are erased in the fetal period, and re-imprinted according to the sex of each individual. Such reprogramming process has been elucidated by analysis of cloned embryos produced from germ cells (germ cell clones). Both paternal and maternal memories exist in the germ cells until embryonic day 9.5 and gradually disappear over 10.5 to 13.5 days. In male fetuses, the paternally imprinting occurs after 15.5 days and is almost completed around birth. Prof. Kono's group at the Tokyo University of Agriculture also has shown that the maternal imprinting is completed during oocyte maturation process several days to three weeks after birth.

Our mouse experiment indicates that the same reprogramming process likely occurs in all mammals including human being.

Fumitoshi Ishino Ph.D.
Ishino received Ph.D. from Tokyo University and is currently a professor at the Medical Research Institute of the Tokyo Medical and Dental University.



SCIENTIST LIBRARY

Biohistory through people

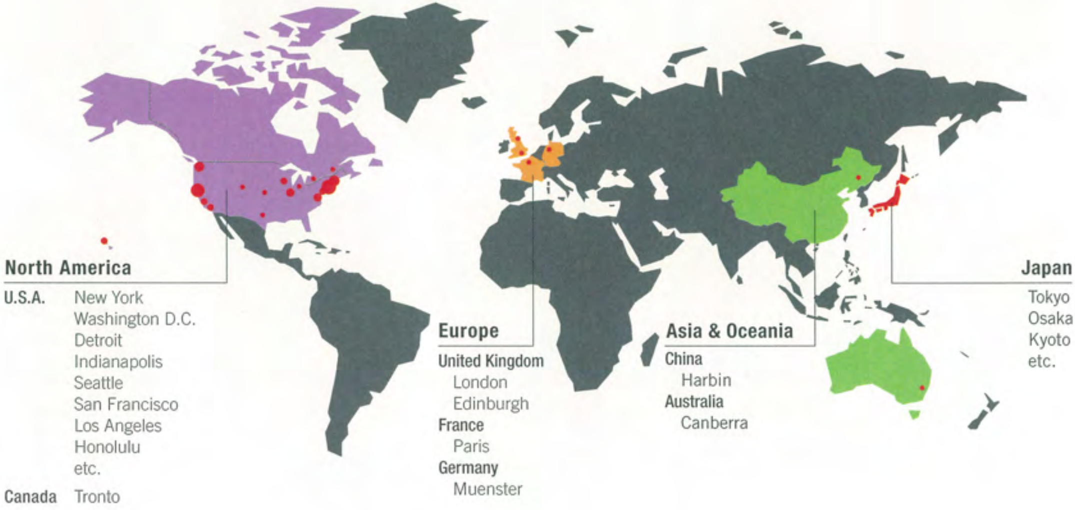
A part of the article can be seen in our website.
www.brh.co.jp/en/

The biology researches of 43 Japanese researchers have been expressed in the quarterly journal Biohistory (Japanese version) from 1993. We believe that science is not only the discovery of facts but also the expression of the personality of the scientist, just as in art. Because the scientists have original viewpoints that reflect their individuality, they can conduct unique research.

Two Japanese researchers are taken up this time among 43 researchers. Please enjoy the passion for biology research through their life and character.

The scientist library world map

In not only Japan but worldwide, the researchers of the scientist library have been active. This is clear when their research location is recorded on the world map. The red circle indicates a place where they researched.



1993

Shozo Osawa
The discovery of change of genetic code

Motoo Kimura
The survival of the luckiest —The neutral theory of evolution

1994

Junnoske Nakai
The success of formation of neuromuscular junction in *vitro*

Yoshiro Shimura
"Intuitional Imagination" —The discovery of RNA modification

Koichi Hiwatashi
Paramecium's sex and my life

Setsuro Ebashi
The importance of calcium in living creatures

Hiroshi Onozato
To learn from the crucian

Takashi Shirouzu
The days of love for the butterfly—The classification of butterflies

1997

Kiyoshi Hama
To observe the structure and function of cells under a microscope

Masukichi Okada
Developmental biology and genetics connected by the *Drosophilla*

1999

Kazuo Moriwaki
Mice taught me about Genetics

Kumao Toyoshima
The discovery of the oncogene

Kosaku Maruyama
Forty year struggle with muscle contraction

Yoshio Masui
The mechanism of multiplication of the cell

2000

Kenichi Matsubara
Continue thinking about humans and life through the genome

1995

Saburo Nishimura
Wandering and searching for the evolution of the living creatures in the sea

Hironori Ishizaki
The study of metamorphic hormones in insects

Setsuya Fujita
From the sea squirt to me —The evolution of the brain and the mind

Kunio Iwatsuki
To make taxonomy into science

1996

Haruo Ozeki
Enjoy the romantic age of molecular genetics

Yoshio Okada
The success of cell fusion

1998

Kazutomo Imahori
Proteins and my reseach history

Koki Horikoshi
Serendipity—The discovery of alkaliphilic bacteria

Haruo Chino
The mechanism of long distance flight of the insects

Tsutomu Sugiyama
The new aspects of hydra with molecular biology

Masao Ito
Demonstration of the importance of the cerebellum

Osamu Hayaishi
The research of oxygenase and a sleep substance

2001

Shoichi Kawano
What is a species? —The challenge for new taxonomy

Tokindo S. Okada
Developmental biology of the newt

Yukimaru Sugiyama
In monkey's forest —Find out of Nature's secret

2002

Tsuneko Okazaki
The discovery of Okazaki fragment

Takashi Sugimura
The apoptosis of cancer cells by substance from butterfly larvae

Hidesaburo Hanafusa
From research of virus to discovery of the oncogene

Kimishige Ishizaka
The mechanism of immunity and allergy

2003

Ryuzo Yanagimachi
The mechanism of reproduction in mammals

Tasuku Honjo
Fascinated by the mechanism of immunity

Tsuneyoshi Kuroiwa
Observing with the heart —The division of cell and organella

Motoya Katsuki
The creation of developmental biotechnology

2004

Takashi Miyata
A physicist attracted by evolution

Jun-ichi Aoki
Nature learned from classification of ticks

Yoshiki Hotta
Genetics of behavior —Search for the new theory

Tairo Oshima
All about thermophiles

2005

Arthur Kornberg
Fell in love with enzymes

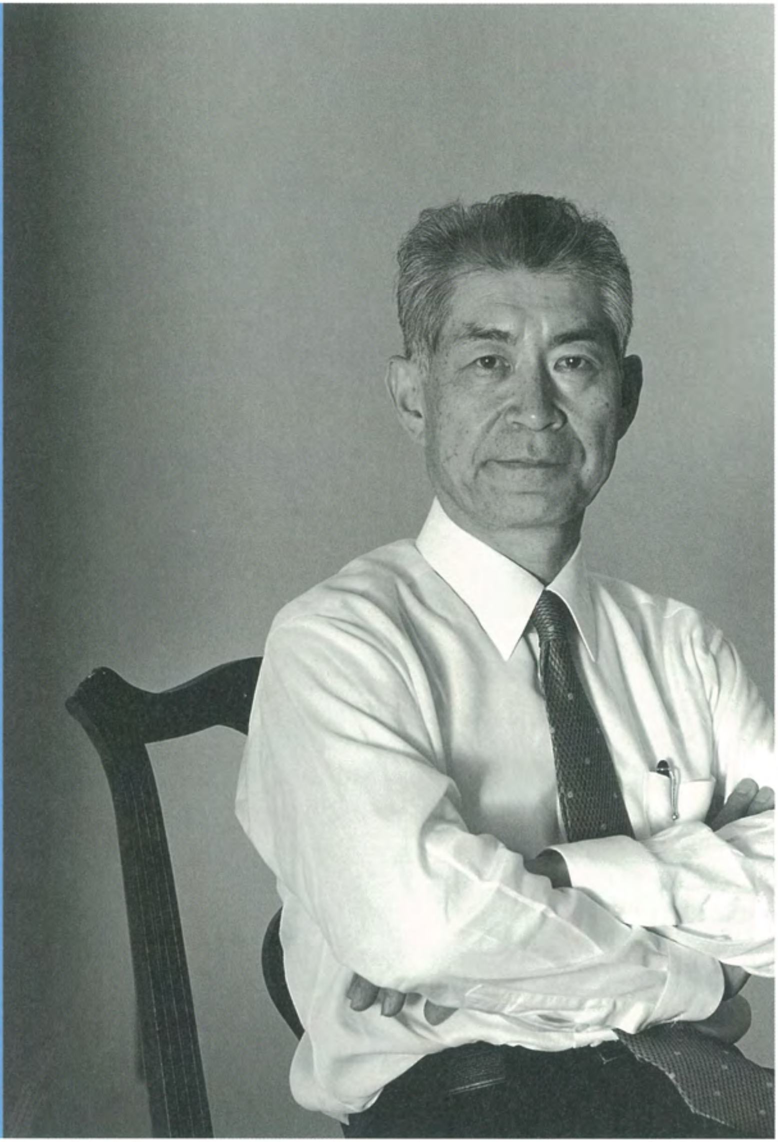
Photograph: Naruaki Onishi
Born in 1952 in Nara. He participated in an exhibition "Ganjin and photographer in the world" with the photographer of seven countries in the world. He takes charge of the photograph of Scientist Library from starting of the quarterly Journal Biohistory (Japanese version).

Fascinated by the mechanism of immunity

Tasuku Honjo
Professor,
Faculty of Medicine, Kyoto University

The youth who was moved with his encounter with molecular biology as a first-year university student later began to study the mechanism of the immune system for the production of diversity in antibodies.
Through the mechanism of immunity, he was enthralled by the flexibility of the genome.
He has the calm intellect to observe the essence, and the heart for the passionate quest into the unknown.

photograph by Naruaki Onishi



My encounter with molecular biology

While it was good to be filled with curiosity during my primary school days, I also could be a little devil. I never paid attention in class, but spent all my time thinking about playing. I finally buckled down to my studies in junior high school. When it came time to enter university, I thought I was unsuited to being used by others, and I couldn't make up my mind whether I wanted to be a doctor, lawyer, or diplomat. I thought I might be able to help a lot of people as a doctor, so I enrolled in the Faculty of Medicine at Kyoto University.

During my first year at university, I encountered molecular biology through the book, *The Revolution in Biology* by Dr. Atsuhiro Shibatani. That was the dawn of the period when the DNA codon was being unraveled using bacteria. The book stated, "The day will soon come when DNA abnormalities can be corrected with a pair of tweezers as in surgery." Right away, I went to visit Dr. Shibatani, and he gave me a thick thesis to read. I didn't understand a word of it.

During my second year at university I was in and out of the lab of Dr. Osamu Hayaishi (Kyoto University professor emeritus). During my third year, I decided to make basic research my career. After starting the Ph.D. program, I began my career in research under the instruction of Dr. Yasutomi Nishizuka (former president of Kobe University).

My encounter with immunology

I wanted to study the molecular biology of eukaryotic organisms, so I got the idea to study in the United States. My new teacher was Dr. Donald Brown

1. Primary school days
2. As a high school student, with a friend participating in a costume procession during a sports festival.
   I sought many new challenges during my university days.
3. The English Club. I am at the far right at front row.
4. Class Regatta

5. In the United States
6. In a discussion with Dr. Brown
7. With family at home
8. With a lab member while presenting a model
   From left: Dr. Naoki Takahashi (Now at Nara Institute of Science and Technology), Dr. Toshiaki Kawakami (Now at La Jolla Institute), Dr. Akira Shimizu (Now at Kyoto University), and Tasuku Honjo. Dr. Toru Kataoka, also a member of the group, is unfortunately not shown because he probably took the photo.

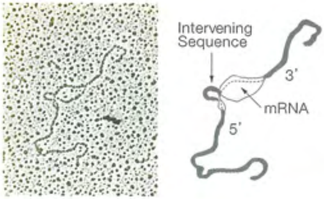
9. Motto: Think of what the other persons want to know and tell them.
10. At an academic society party with Dr. Nishizuka (center). On the right is Dr. Kumao Toyoshima.
11. I also play tennis, but like golf the best.

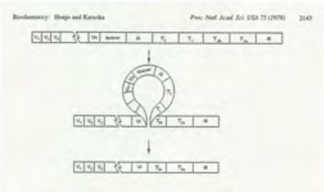
1


2


3


4



Above: An electron microscope photo showing the combination of H-chain mRNA and cloned DNA, which shows the existence of intron
Below: The model diagram for the composition of H-chain constant genes and the missing gene, from a thesis published to the *Proceeding of National Academy of Sciences* (*PNAS*) in 1978.

(Carnegie Institute), who was conducting research into the ribosome genes of frogs.

During a seminar by Dr. Brown, I was inspired by the discussion of a theory regarding the diversity production mechanism of antibodies based on an analogy with the structure of ribosome genes. I began to study under Dr. Philip Leader, conducting research into the antibody genes of mice at NIH. I plunged headfirst into one of about 10 groups around the world at that time engaged in fierce competition to discover the molecular mechanism that created antibody diversity. Placing myself in intense competition when I was young also had an effect on my later research.

The discovery of the class switch model

I returned to Japan with the desire to do world-class research in Japan. The B lymphocytes first make antibodies in the IgM class to very efficiently eliminate diverse antigens. They later produce antibodies of the IgE and IgA classes in response to the locations penetrated by antigens, such as blood and mucous membranes (intestines, trachea). Antibody classes define effector functions after antibodies bind to antigens. I wanted to elucidate molecular mechanisms controlling the generation of different antibody classes. To this end, I purified mRNA encoding antibodies, generated their cDNA, and measured the number of antibody genes in the genome.

During the days at the University of Tokyo, I used to organize my experimental data while commuting on a train for one hour and a half. One day, I noticed that types of deletion in antibody genes correlate with the antibody classes generated by B cells, and came up with the models where B cells may switch antibody classes by deleting genes encoding the constant

5

6

7

8


regions of antibodies from the genome. If so, I could propose an order of heavy chain constant-region genes, which conformed closely to my hypothetical model. I hurried home and tried to review all my lab notes to reassure myself that there was no contradictory data. Still, I could not see any contradiction in my discovery.

I talked to everyone at the lab the next day, and right away we began to devise an experiment that would verify the model. That became the class switch model. I published this model in the *PNAS* in 1978. This received international acclaim, and it also was covered in the News & Views section of *Nature*. My joy was doubled. In the 20 years since then, I have determined the genetic structure, elucidated the details of the mechanism, and discovered the enzyme causing the class switch.

I persisted in following up a question that had arisen within me, and became aware of closely examining the essence of the problem to be analyzed. I think that was the key to my success. Various biological principles are concentrated in immunity. I expect that we will learn as yet undiscovered biological principles, primarily in immunology. This will undoubtedly grow more interesting. Now, I am involved in applying my findings to treatment, and I have finally returned to my original point of departure during my youth of wanting to help people.

(Text: SICP sector)

Tasuku Honjo ⑨

1942	Born in Kyoto
1971	Completed the School of Medicine and Faculty of Medicine at Kyoto University
1971	Investigator at Carnegie Institution in the United States
1973	Researcher at the National Institute of Health (NIH) in the United States
1974	Assistant at the University of Tokyo School of Medicine
1979	Professor, Osaka University Faculty of Medicine
1984	Professor, Kyoto University Faculty of Medicine
1988	Director, Kyoto University Center of Molecular Biology and Genetics
1996-2000	Director, School of Medicine and Faculty of Medicine, Kyoto University; Dean, Faculty of Medicine

Honorary member, American Association of Immunology

Overseas member, National Academy of Science (United States)

Awards

The Japanese Biochemical Society Award for Young Scientist, The Noguchi Hideo Memorial Award for Medicine, Asahi Award, Osaka Science Award, Kihara Award, Beltz Award, The Takeda Prize for Medical Science, Fogarty Scholar in Residence (NIH), Behring-Kitasato Award, Uehara Award, Imperial Prize - Japan Academy Prize, Person of Cultural Merit

A bottle of 1962 Vega-Sicilia, the highest-quality Spanish wine. I received a bottle when I discovered AID (Activation induced Cytidine Deaminase), the enzyme causing the class switch. Everyone signed and dated the label on the bottle, and it is on display in the teachers' room.

⑩

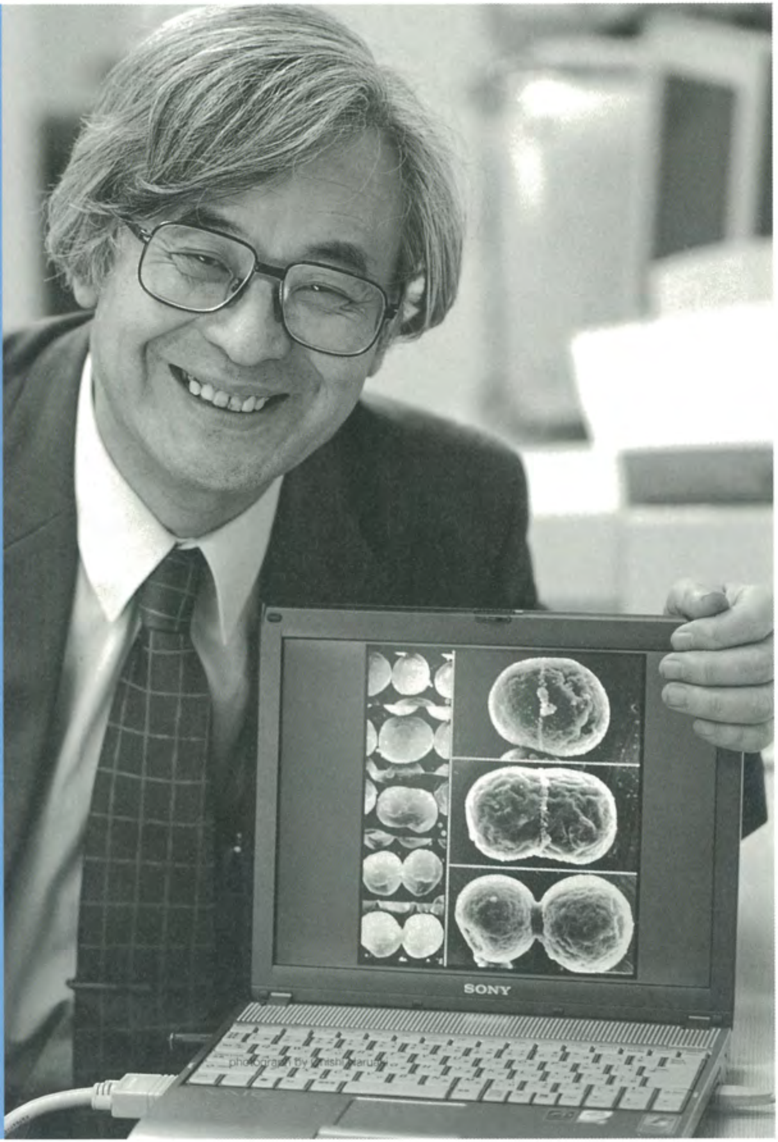
⑪

Observing with the heart

The division of cell and organella

Tsuneyoshi Kuroiwa
Professor, Department of Science, Rikkyo University;
Professor Emeritus, The University of Tokyo

Dr. Kuroiwa has discovered the mitotic apparatus of chloroplast and mitochondria (organelles), and depicted the mechanism of heredity.
Laughing heartily, he says, "After following through on activities I thought were really interesting with my unique inspiration and persistency, I wonder if my research has finally approached an art."



photograph by Naruaki Onishi

My encounter with observation

To take a photograph that anyone can understand at a glance requires hours and days of searching while envisioning a three-dimensional body from an ultra-thin section of a cell or organelle. One looks through the microscope with one's heart. Once you've found it, anyone can look for it. To find a new phenomenon, I look through the microscope.

I was great at fighting and judo, but was a terrible student in primary school. I was saved by my dexterity and sharp eyes. When I saw mold growing in miso(bean paste) using a microscope, I discovered a micro-world where ticks wriggled. I was surprised and moved.

Until high school, judo was my primary ambition, but I had to give it up when I contracted tuberculosis. I thought about becoming an artist, and attended an art preparatory school. But I realized I had no talent. My final choice was to become a biologist and use a microscope. Since then, I've been going at it full tilt.

The discovery of the mitochondria nucleus

I think that the essence of life is multiplication. I entered the Tokyo Metropolitan University to study with developmental biologist Dr. Katsuma Dan. He stressed that the requirements for original research were the choice of materials and the development of a method. On a sketch done during a sea side practice, I wrote "What is this?", indicating the constriction of the blastomere of a sea urchin during cleavage. That was my starting point.

At graduate school, I elucidated the correlation between the changes in the chromosome structure and function. I wanted to do basic research, so I

① Entered primary school in 1948.
② Third grade in primary school, at a festival, which I loved. Last row, to the left and below the lantern.
③ In 1959, with other judo club members on the roof of a hospital. I am on the end at right.
④ Fishing at a mountain stream with the members of the university fishing club. I am on the end at right.

⑤ In 1977, in front of the Okazaki National Institute for Basic Biology under construction. I am on the end at left. The fourth person from the left is Dr. Kamiya.
⑥ Caught a black porgy at Lake Hamana. Stayed until I was alone with a sea gull.
⑦ 1992, to the University of Naples in search of schyzon. At the Botanical Garden with Prof. Marco.

⑧ 1993, discovered the mitotic apparatus of mitochondria using an electron microscope.
⑨ At the faculty room on the main campus at the University of Tokyo. The desk was used by Prof. Dan at Misaki.

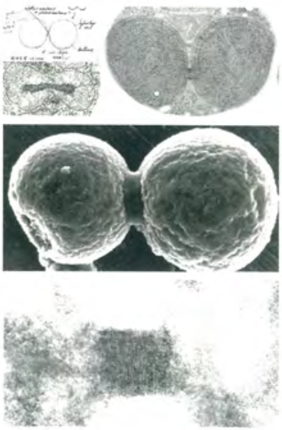
①

②

③

④


The form of division that I pursued
The development of the form of division as seen through electron microscopes, starting with a sketch of a sea urchin egg (upper left) and moving to nuclear division in the mitochondria of slime mold (lower left), a simple model red algae cell cyanidium (upper right) and the schyzon chloroplast (center, right). The power of division comes from a four nano diameter PD/MD ring, the "lifeline of humankind and the spool of dreams".



went to Okayama University in 1973. I discovered that when the genes began to move vigorously, some of the chromosomes immediately became flaccid. Therefore, I tried to isolate this substance. I had the idea that the nucleus of the *Physarum polycephalum* plasmodium might divide in synchronization. When I used it, I unexpectedly discovered that the DNA of mitochondria had a nuclear structure. This ran counter to the conventional wisdom that the DNA of an organelle or bacteria was free. I was excited. The organelle was a descendant of bacteria that coexisted inside a cell two billion years ago, so this division and multiplication was extremely interesting as a research model for cellular division. I eagerly changed the subject of my research to organelles.

Discovery of the organelle division ring

In 1977, at the invitation of Prof. Noburo Kamiya, I moved to the Okazaki National Institute for Basic Biology. I developed a high-resolution fluorescence microscope that could distinguish a single gene, discovered that the organelle DNA of most creatures had a nuclear structure, and proposed the "Theory of Tri-Nuclear Cells". There are many organelles in a cell, and I had difficulty because they broke up and dispersed. So, I began to observe *Cyanidum caldarium* which has single set of each organelle. I searched for the equator during an organelle's division.

In 1986, I discovered the mitotic apparatus of the chloroplast (PD ring). I noticed that the PD ring was universal among plants. So, I went to Italy in search of the smallest eucaryote. In addition to the huge PD ring, I also discovered the mitotic apparatus of the mitochondria (MD ring), in the red algae cell (schyzon) separated from hot spring algae. I had continuously

⑤

⑥

⑦

Tsuneyoshi Kuroiwa ⑨

1941	Born in Ushigome, Tokyo
1966	Graduated from the Tokyo Metropolitan University Science Department with a degree in Biology
1971	Completed the Ph.D. course in Botany at the University of Tokyo
1971	Researcher, Tokyo Metropolitan Isotope Research Institute
1973	Lecturer in Biology in the Graduate School of Science, Okayama University
1974	Named Associate Professor
1977	Named Associate Professor at Okazaki National Research Institutes' National Institute for Basic Biology
1983	Named Professor
1987	Named Professor, Department of Biological Sciences, School of Science, the University of Tokyo
1991-1993	Director, Botanical Garden, affiliated with the University of Tokyo Graduate School of Science (Koishikawa, Nikko)
1993	Named Professor, Department of Biological Sciences, Graduate School of Science, the University of Tokyo
1997-1998	Served as University of Tokyo trustee
2003	Named Professor, college of Science, Rikkyo University

been looking for the form to answer the question "What is this?" from the constriction of the sea urchin. I was persistent, if I do say so myself.

Elucidating the organelle's division mechanism

To elucidate the entire aspect of the organelle's division mechanism, I determined the entire DNA sequence of the three genomes of the schyzon chloroplast, mitochondria, and cell nucleus. I found that in both the mitochondria and the chloroplast, the dynamin formed a ring only in the final part of division, and it divided the daughter organelle. In the case of the chloroplast division, there were the FtsZ ring, involved in determining the fission plane, three PD rings, involved in the contractile force, and finally the dynamin ring dividing the daughter chloroplast. Roughly the same mechanism functions in the mitochondria division.

The genes of the dynamin and the PD ring have not yet been found in the genome of the prokaryotic organism. When the eucaryotic cell was created, these rings may have played the crucial role as the host that controlled the division of the mitochondria and chloroplast ancestor bacteria.

The essence of the organelle division mechanism is both simple and beautiful. If this can be controlled, it might be utilized to deal with the urgent problems, including global warming, desertification, and starvation. When I see the mitochondria and chloroplast under the microscope, I can only believe they are performing a grand drama of past, present, and future.
(Text: SICP)

⑧

My partner, Dr. Haruko Kuroiwa, and I have always been together since we worked jointly on our graduation research. She has maintained a consistent interest in the mechanism of double fertilization in the higher plants. I realized once again that when I had this wonderful partner for life that I was able to devote myself to one thing.