Location: Conference Rm 411, New Life Science Building

Morning Research Session (9:30-12:00)
From Chromosomes to the Brain: Genetics, Basic Biology, and Physiology

Hiroshi Akashi/Hongya Gu 9:30 - 9:35
Welcome and introduction

Tetsuji Kakutani, NIG 9:35-10:00
Genetics of DNA methylation in genes and transposons in Arabidopsis

Tatsuo Fukagawa, NIG 10:00-10:25
Molecular basis of faithful chromosome segregation: Architecture of the vertebrate centromere

Kiyoshi Naruse, NIBB 10:25-10:50
National BioResource Project Medaka: Comprehensive Resources for Biology and Biomedical Science

coffee break 10:50-11:10

Minoru Tanaka, NIBB 11:10-11:35
Cellular interactions in vertebrate sex differentiation

Tadashi Isa, NIPS 11:35-12:00
Brain rehabilitation: Cortical compensatory mechanism after spinal-cord injury

Afternoon Research Session (1:30-2:45pm)
Mechanisms of Genome Evolution

Hiroshi Akashi, NIG 1:30 - 1:55
Metabolic economics and proteome evolution

Hideki Innan, Sokendai-Hayama 1:55 - 2:20
Population genetic approaches to genome evolution

Yoko Satta, Sokendai-Hayama 2:20 - 2:45
Molecular Evolutionary Physiology: Biological significance of pseudogenes in primate evolution

Afternoon Recruiting Session (3:00-3:45pm)
Undergraduate and Graduate Research Opportunities at Sokendai

Hiroshi Akashi

refreshments 3:45-4:30

Sokendai Life Sciences Symposium at Peking University
Wednesday March 10, 2010

Sokendai, The Graduate University for Advanced Studies, includes:
National Institute of Genetics (NIG), Mishima, Japan http://www.nig.ac.jp/index-e.html
National Institute for Physiological Sciences (NIPS), Okazaki, Japan http://www.nips.ac.jp/eng/
The Graduate University for Advanced Studies at Hayama, Japan http://www.soken.ac.jp/en/
Genetics of DNA methylation in genes and transposons in Arabidopsis

Tetsuji Kakutani

DNA methylation is an enigmatic modification of genomic DNA, conserved among vertebrates, some fungi, and plants. In the plant genome, most of the methylation is found in repeats and transposons, and the methylation level is much lower in active genes.

To understand control and function of DNA methylation, we are taking genetic approaches using mutants of Arabidopsis (a flowering plant useful for genetics). An Arabidopsis chromatin remodeling protein DDM1 (decrease in DNA methylation) is necessary for methylating repeats and transposons. On the other hand, jmjC-domain-containing protein IBM1 (increase in BONSAI methylation) is necessary for not methylating genes. In mutants of genes encoding these proteins, several types of developmental abnormalities were induced. I am going to talk about our genetic and genomic approaches to understand the impact of these mutations.
Molecular basis of faithful chromosome segregation:  
Architecture of the vertebrate centromere  
Tatsuo Fukagawa

Faithful chromosome segregation during mitosis is essential for the accurate transmission of genetic material. To facilitate this, each replicated sister chromatid assembles a kinetochore on centromeric DNA which forms a dynamic interface with microtubules from the mitotic spindle. To promote the alignment and proper segregation of mitotic chromosomes, kinetochores must attach to microtubules and regulate cell cycle progression. This process requires the integrated activities of multiple kinetochore proteins. This process requires the integrated activities of multiple kinetochore proteins. To fully understand kinetochore structure and the mechanisms that underlie chromosome segregation, it is essential to define the composition, organization, and activities of these numerous kinetochore proteins.

In recent years, multiple kinetochore proteins have been identified in vertebrate cells using a combination of approaches. These studies have revealed that a Constitutive Centromere Associated Network (CCAN) of proteins associates with centromeres throughout the cell cycle and provides a platform for the formation of a functional kinetochore during mitosis. Other kinetochore proteins, including the KNL1/Mis12 complex/Ndc80 complex (KMN) network, are targeted to kinetochores by CCAN-containing pre-kinetochores during G2 and mitosis to establish a fully assembled kinetochore capable of interacting with spindle microtubules and facilitating faithful chromosome segregation.

Here, we focus on CCAN and will present recent topics about CCAN proteins.
Cellular interactions in vertebrate sex differentiation
Minoru Tanaka

Recent studies demonstrate that vertebrates acquire various sex determination genes during evolution but the common mechanism to establish the sex dimorphism is largely unknown. We have been analyzing mutant medaka showing the defect in the germ cells and have found that germ cells deeply commit the proper sex differentiation and maintenance of sex. In this context the balancing of some signal between somatic cells and germ cells is important. Successful positional cloning of medaka mutant called hotei reveals that the gene belonging to TGFβ superfamily gene is involved in the modulation of the cellular interaction between somatic cells and germ cells. This mutant exhibits male to female sex reversal and hypertrophic germ cells. I will talk about the role of germ cells during sex differentiation and discuss biological relevance in other vertebrates. I will also introduce the tubular structure with germline stem cells in the ovary, which may be histologically important for sex reversal in other vertebrates.
Kiyoshi Naruse
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Academic Career
1982 B. S., University of Nagoya (Dept. of Biology, Faculty of Science)
1988 Ph.D., University of Tokyo (Zoological Institute (Department of Biological Sciences), Graduate School of Science)
1988-2003 Assistant Professor (University of Tokyo)
2003-2007 Lecturer (University of Tokyo)
2007-present Associate Professor (National Institute of Natural Science, National Institute for Basic Biology)

Research Interests
Genetics and genomics of vertebrates mainly focused on the ray-finned fish evolution (sex determination, QTL analysis of common phenotypic variation). Development of the research resources for medaka and relatives (Large scale full length cDNA sequencing project and SNP analysis of the regional population of medaka).

Representative Publications

Editorial Board/Memberships
Division Editor (Genetics and Reproductive Biology) Zoological Science
Zoological Society of Japan, Genetics Society of American, Genetics Society of Japan, Society of Evolutionary Studies
Brain rehabilitation:
Cortical compensatory mechanism after spinal-cord injury
Tadashi Isa

To exploit the effective neuro-rehabilitational therapy, experimental studies using non-human primate model of partial brain or spinal-cord injury are useful. Recently we found that transection of the direct cortico-motoneuronal pathway at the mid-cervical segment of the spinal cord in the macaque monkey results in a transient impairment of finger movements but their dexterous finger movements recover within a week to a few months (Sasaki et al. J. Neurophysiol., 2004). We use this model to study the cortical and subcortical neuronal mechanism underlying the functional recovery.

Combination of brain imaging with positron emission tomography (PET) and reversible pharmacological inactivation of motor cortical regions suggest that the recovery involves the bilateral primary motor cortex during the early recovery stage and more extensive regions of the contralesional primary motor cortex and bilateral premotor cortex during the late recovery stage. These changes in the activation pattern represent an adaptive strategy for functional compensation after spinal-cord injury (Nishimura et al. Science, 2007). Moreover, we have found that gene expression change at the cortical level during the functional recovery. We analyzed the expression of GAP-43 mRNA. GAP-43 is a protein related to neurite extension. In-situ hybridization study has shown that the expression of GAP-43 mRNA was enhanced in layers II/III of the M1, PM and the primary sensory cortex (S1) on bilateral side and large cells, presumably corticofugal neurons, in bilateral M1 (Higo et al. J. Comp Neurol, 2009). These results suggested the plastic change occurred on the association networks among PM, M1 and S1 and descending pathways from M1, which well matched the results of the PET study.
Metabolic economics and proteome evolution
Hiroshi Akashi

Natural selection is thought to act upon protein structures to optimize biochemical properties related to their specific functions. Selection pressures related to efficient synthesis of proteins may act globally on the amino acid composition of the proteome, but are less firmly established.

A substantial fraction of bacterial energy budgets are devoted to biosynthesis of amino acids, the building blocks of proteins. The fueling reactions of central metabolism provide precursor metabolites for synthesis of amino acids. Thus, synthesis of an amino acid entails a dual cost; energy is lost by diverting chemical intermediates from fueling reactions and additional energy is required to convert precursor metabolites to amino acids. Selection to reduce energetic costs predicts increases in the abundance of less energetically costly amino acids in highly expressed proteins. Amino acid composition in the proteomes of Escherichia coli and Bacillus subtilis appears to reflect the action of natural selection to enhance metabolic efficiency.

The primary structures of proteins may also reflect natural selection to enhance the rate and accuracy of their synthesis. Differences in cellular concentrations of tRNAs could lead to translation selection both within and among synonymous families. In yeast, usage of several amino acids show striking associations with gene expression. These changes in amino acid composition result in stronger correlations between amino acid usage and tRNA abundances in highly expressed genes than in less expressed loci. Translation selection appears to contribute to surprisingly strong relationships between gene expression and rates of protein evolution in yeast.
Population genetic approaches to genome evolution
Hideki Innan

I would like to introduce several topics that our lab is particularly interested in. One is genome evolution by gene duplication. We developed models of population genetics and molecular evolution of duplicated genes and applied to genomic sequence data to understand how natural selection works on gene duplicates. Of our special interest is gene conversion, a mutational mechanism to cause co-evolution of duplicated copies. Other topics include population genetic theories on the pattern of SNPs (single nucleotide polymorphisms) and bacterial genome evolution by horizontal gene transfer and homologous recombination. With the advent of sequencing technologies, genome-wide SNP data are available for many species, and we are trying to develop population genetic models and theories to analyze them. This would facilitate our understanding of the evolutionary roles of natural selection and historical events that the species experienced. The project about bacteria concerns exchanges of DNA between different cells (individuals), which can be achieved by at least three mechanisms, conjugation, transduction and transformation. With such DNA exchanges, bacteria undergo extremely flexible genome evolution, and we aim to develop a general theoretical framework incorporating those mechanisms and apply to genome sequence data of various bacteria species.
Molecular evolutionary physiology: Biological significance of pseudogenes in primate evolution

Yoko Satta

A pseudogene is defined to be a gene that has lost its function. Especially it lacks the ability of coding a protein. From the viewpoint of mechanisms to generate pseudogenes, they are classified into two categories. The first category is a “processed pseudogene”, which is generated via retrotransposition. The second one is an “authentic pseudogene”, which is caused mainly by gain of premature stop codons due to a point mutation or frame shift mutations. Regarding a processed pseudogene, it had been considered unlikely that a processed gene gains promoter activity at a randomly inserted site. However, functional “processed pseudogenes” have been recently reported in mice: they are at least transcribed and might regulate the transcription of genes. We searched the presence of such probable functional pseudogenes in primate genomes and examined the extent of constraint of these pseudogenes. Regarding an authentic pseudogene, the acceptance of premature stop codons in a gene depends on a functional constraint or importance of the gene. In general, premature stop codons are accepted only when functional compensation is working. However, pseudogenization of single copy genes (single-copy pseudogenes), without possible functional compensation, has been found in humans and non-human primates. Furthermore, in some cases, deterioration of a gene has taken place independently in different primate lineages. For example, UOX (urate oxidase) gene, of which product converts purine to allantoin in a purine catabolic pathway, was deteriorated independently in great apes/humans and gibbons. Further, the search of human specific pseudogenes reveals 14 cases of independent pseudogenization of single-copy genes in human and non-human primate genomes. These are examples of convergent pseudogenization and there might be some biological significance in them. In this presentation, I review several examples of pseudogenes in primate genomes and argue their biological significance.
The Graduate University for Advanced Studies, founded in 1988, is the first university to exclusively offer doctoral programs in Japan. Sokendai is a university affiliated with research institutes and museums administered by the Ministry of Education, Culture, Sports, Science and Technology (called Inter-University Research Institutes, or IURIs). The IURIs support the best researchers and the finest facilities in the nation. Sokendai aims to provide privileged environments for education. “Internationalization” is a priority at Sokendai and we have initiatives for both undergraduate and graduate students from outside of Japan.

Our departments make up the School of Life Science, Sokendai. Please see the links below for information about our undergraduate and graduate education programs.

Sokendai

Hayama Campus of Sokendai

National Institute of Basic Biology

National Institute of Physiological Sciences
http://www.nips.ac.jp/eng/graduate/

Please see the next page for information about NIG
Undergraduate Summer Research
NIG Intern 2010
National Institute of Genetics (NIG), Mishima Japan

The National Institute of Genetics (Department of Genetics, Sokendai) offers a 10 week undergraduate research internship program. NIG consists of about 36 research groups, each headed by a professor or an associate professor who leads an innovative research program in a highly interactive atmosphere. The quality of NIG research is evident from the frequent citations of papers published from the institute and the high funding rates for our grant proposals. NIG houses tremendous resources for basic research in life sciences, such as the well-established DNA database (DDBJ), an extensive collection of mutant strains of various model organisms, and state of the art research equipment. United under the term "Genetics", the graduate students at NIG continue to expand the frontiers of life sciences, in molecular and cell biology, development, neurosciences, evolution, structural biology and bioinformatics. Faculty research summaries can be found at http://www.nig.ac.jp/section/research-e.html. All NIG faculty are committed to providing a friendly and stimulating environment in which students can have in-depth discussions with researchers in their own and in other fields. This approach encourages students to broaden their views and helps them find breakthroughs when research is not going smoothly.

NIG offers a laboratory rotation system for first year students in the international graduate program (IGP). During their first six months in the program, IGP students experience independent research in three laboratories of their choice. This gives students an opportunity to explore several research areas before choosing a thesis advisor.

Students admitted to the International Graduate Program receive competitive financial support. Details of eligibility can be found in the application guidelines (see link below).

Students with a bachelors degree or equivalent are eligible to apply to our 5-year PhD program. Applications for the NIG International Graduate Program are due in December each year. Please see the the following link for updated information http://www.nig.ac.jp/jimu/soken/IGP/.

Students interested in applying should prepare:
• A letter of motivation of about 500 words.
• Resume and school record.
• Two letters of recommendation.

Please see the following URL for application instructions:
NIG Faculty research: http://www.nig.ac.jp/section/research-e.html

Application deadline: January 15, 2010*
Notification of selection: February 26, 2010
Intern period: May to July, 2010

Please e-mail inquiries to info-soken@lab.nig.ac.jp

*Please note that the application deadline for NIGINTERN 2010 has passed. We will seek applications again in 2011 around the same time.