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

Sokendai
The Graduate University for Advanced Studies

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, The Graduate University for Advanced Studies, includes:

National Institute for Basic Biology (**NIBB**), Okazaki, Japan http://www.nibb.ac.jp/en/index.php

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.

Tetsuji Kakutani

Department of Integrated Genetics,
National Institute of Genetics (NIG), Mishima, 411-8540 JAPAN
E-mail: tkakutan@lab.nig.ac.jp
http://www.nig.ac.jp/section/kakutani/kakutani-e.html

Academic Career

2006-present Professor; University of Tokyo
2005-present Professor; National Institute of Genetics
2000-2005 Associate Professor; National Institute of Genetics
1992-2000 Senior Researcher; National Institute of Agrobiological Resources
1987-1992 Research Scientist; National Institute of Agrobiological Resources
1982-1987 Ph.D. in Botany; Kyoto University
1978-1982 BS in Biology; Kyoto University

Research Field

Epigenetic control of genes and transposons in Arabidopsis.

Research Interests

Chromatin structure; Evolution of repeated sequences; Genetic mechanisms in general.

Representative Publications

Tsukahara S, Kobayashi A, Kawabe A, Mathieu O, Miura A, and Kakutani T (2009) Bursts of retrotransposition reproduced in Arabidopsis. ***Nature*** 303, 423-426

Miura A, Nakmura M, Inagaki S, Kobayashi A, Saze H, and Kakutani T (2009) An Arabidopsis jmjC domain protein protects transcribed genes from DNA methylation at CHG sites. ***EMBO J.*** 28, 1078-1086

Saze H, Shiraishi A, Miura A, and Kakutani T (2008) Control of Genic DNA methylation by a jmjC domain-containing protein in Arabidopsis thaliana. ***Science*** 319, 462-465

Fujimoto R, Kinoshita Y, Kawabe A, Kinoshita T, Takashima K, Nordborg M, Nasrallah M, Shimizu K, Kudoh H, Kakutani T (2008) Evolution and control of imprinted FWA genes in the genus Arabidopsis. ***PLoS Genet.*** 4, e1000048

Saze H, and Kakutani T (2007) Heritable epigenetic mutation of a transposon-flanked gene due to lack of the chromatin-remodeling factor DDM1. ***EMBO J.*** 26, 3641-3652

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.

Tatsuo Fukagawa

Department of Molecular Genetics,
National Institute of Genetics (NIG), Mishima, 411-8540, JAPAN
E-mail: tfukagaw@lab.nig.ac.jp
http://www.nig.ac.jp/labs/MolGene/index.html

Academic Career

1991, 3: B.Sc., Food Science and Technology, Hokkaido University, JAPAN
1993, 3: M.Sc., Microbiology, Hokkaido University, JAPAN
1995, 9: Ph.D., Genetics, The Graduate University for Advanced Studies, Mishima, JAPAN
1995, 12 -1999, 2: Postdoctoral Research Fellow, Dept of Biochemistry, University of Oxford
1999, 3 - 2002, 3: Assistant Professor, National Institute of Genetics
2001, 12 – 2005, 3: Researcher (Adjunct), PRESTO of the Japan Science and Technology Corporation.
2002, 4 – 2003, 6: Associate Professor, The Graduate University for Advanced Studies
2003, 7 – 2008, 11: Associate Professor, National Institute of Genetics
2008, 12 - : Professor, National Institute of Genetics

Research Interests

Fundamental to all life processes is the ability of cells to divide faithfully. Division can result in equal partitioning of the replicated genetic material of the mother cell to two daughter cells (mitosis) or accurate reduction of chromosomes to the haploid number (meiosis). The centromere plays a fundamental role in accurate chromosome segregation during mitosis and meiosis in eukaryotes. We use cell lines to study centromere functions including sister chromatid adhesion and separation, microtubule attachment, chromosome movement, and mitotic checkpoint control. We employ conditional knockouts to analyze the functions of centromere proteins and combine biochemical and genetic approaches to identify and characterize new centromere components. We have identified and characterized dozens of centromere proteins with a long-term goal of understanding how centromeres function in chromosome segregation.

Representative Publications

M Amano, A Suzuki, T Hori, C Backer, K Okawa, IM Cheeseman, and **T Fukagawa** "The CENP-S complex is essential for the stable assembly of outer kinetochore structure." **Journal of Cell Biology** Vol. 186, 173-182 (2009).

T Hori, M Amano, A Suzuki, C Backer, J P Welburn, Y Dong, B F McEwen, W-H Shang, E Suzuki, K Okawa, IM Cheeseman, and **T Fukagawa** "CCAN makes multiple contacts with centromeric DNA and provides distinct pathways to the outer kinetochore" **Cell** Vol. 135, 1039-1052 (2008)

M Okada, IM Cheeseman, T Hori, K Okawa, IX McLeod, JR Yates III, A Desai, and **T Fukagawa**" The CENP-H-I complex is required for the efficient incorporation of newly synthesized CENP-A into centromeres. " **Nature Cell Biology** Vol. 8, 446-457 (2006).

T Fukagawa, M Nogami, M Yoshikawa, M Ikeno, T Okazaki, Y Takami, T Nakayama, and M Oshimura "Dicer is essential for formation of the heterochromatin structure in vertebrate cells." **Nature Cell Biology** Vol. 6, 784-791 & Cover (2004).

A Nishihashi, T Haraguchi, Y Hiraoka, T Ikemura, V Regnier, H Dodson, WC Earnshaw, and **T Fukagawa** "CENP-I is essential for centromere function in vertebrate cells." **Developmental Cell** Vol. 2, 463-476 (2002).

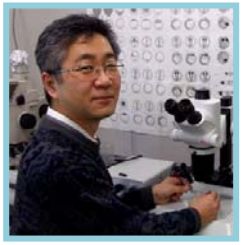
Fellowships/Awards

1993, 4 -1996, 3: JSPS Junior Research Fellowship
1996, 4 -1998, 3: JSPS Fellowship for Research Abroad
1998, 3-1999, 3: BBSRC Research Fellowship
2002: The Award of Genetics Society of Japan for young investigators
2005: The Award for Young Scientists from MEXT

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 contex 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.



Minoru Tanaka

Associate Professor,
Laboratory of Molecular Genetics for Reproduction,
National Institute for Basic Biology (NIBB), Okazaki, 444-8585, JAPAN
E-mail: mtanaka@nibb.ac.jp
http://www.nibb.ac.jp/en/sections/tanaka.html

Academic Career

Associate Prof in Hokkaido University
Visiting Researcher in Northwestern University, Chicago, USA
Graduated from Nagoya University, Faculty of Science, PhD.

Current Research

(Key Words; sex differentiation, reproduction, stem cells)
The aim of our lab is to reveal the molecular mechanisms of sex differentiation and sex reversal of the gonads. Many vertebrates exhibit their own ways of sexual dimorphic processes and we try to understand the fundmantal mechanism behind the variety. Recently, using transgenic and mutant medaka, our lab has revealed the critical roles of germ cells on sex differentiation and has, for the first time in vertebrates, identified the unique histological structure harboring germline stem cells in ovary. The regulation of germline stem cells is also our current research.

Representative Publications

Saito et al., (2009) Sex. Dev. 3, 99-107 (Invited Review).
Kurokawa et al., (2007) Germ cells are essential for sexual dimorphism in the medaka gonad. PNAS 104, 16958-16963.
Morinaga et al., (2007) The *hotei* mutation of medaka in the anti-Mullerian hormone receptor causes the dysregulation of germ cell and sexual development. PNAS 104, 9691-9696.
Nakamura et al., (2006) Identification and lineage tracing of two populations of somatic gonadal precursors in medaka embryos. Dev. Biol. 295, 678-688.
Tanaka et al., (2001) Establishment of medaka (*Oryzias latipes*) transgenic lines with the expression of green fluorescent protein fluorescence exclusively in germ cells: A useful model to monitor germ cells in a live vertebrate. PNAS 98, 2544-2549.

National BioResource Project Medaka:
Comprehensive Resources for Biology and Biomedical Science

Kiyoshi Naruse

Medaka was developed as a model organism of vertebrates and has been widely used in various fields of biology and biomedical science such as development, genetics, evolution, toxicology and basic medicine. Recent completion of medaka genome sequencing project (http://medaka.utgenome.org and http://www.ensembl.org/ Oryzias_latipes/index.html) has promoted the use of medaka as the comparative and complemented material for research in other vertebrates such as zebrafish, stickleback, mouse and human. Japanese government has supported the medaka bioresources since 2002 and the second period of this project started in 2007. National Institute for Basic Biology and Niigata University have been selected as core facilities of this project. Now we have provided 667 strains (555 spontaneous and induced mutants, 7 inbred lines, 21 transgenic lines, 18 medaka related species, 66 regional strains from natural populations) to the scientific community. In addition to these live fish, we also provide 15,000 non-redundant cDNA/EST clones, BAC and fosmid clones covering 90% of medaka genome. In 2007, we have started the full-length cDNA sequencing project and sequenced both ends of 206220 clones from cDNA libraries of three different developmental stages of embryos and adult liver, ovary, testis and brain. After the mass alignment of 3' sequences, we identify 18640 non-redundant clones. These sequence information and clones are now available through NBRP Medaka website (http://www.shigen.nig.ac.jp/medaka/est/est.jsp). In addition to these resources, we also provide the atlas of brain and blood vessel, phylogenetic trees of regional populations and medaka related species, medaka genome browser with ensembl interface and protocols for sperm cryopreservation/artificial insemination and method for identification of BAC/Fosmid clones harboring your genes of interest. I will summarize the current status medaka bioresources and explain how to access these informations.

Kiyoshi Naruse

Associate Professor,
Laboratory of BioResource,
National Institute for Basic Biology (NIBB), Okazaki, 444-8585, JAPAN
E-mail: naruse@nibb.ac.jp
http://www.nibb.ac.jp/en/sections/naruse.html

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

Tani S, Kusakabe R, Naruse K, Sakamoto H, Inoue K. Genomic organization and embryonic expression of miR-430 in medaka (Oryzias latipes): insights into the post-transcriptional gene regulation in early development. **Gene**, in press, 2009.

Kasahara M., Naruse K. Sasaki S, Nakatani Y, Qu W. et. al.,(2 番目/38 人). The medaka draft genome and insights into vertebrate genome evolution. **Nature,** 446, 714-719, 2007.

Naruse K, Tanaka, M Mita K, Shima A, Postlethwait J, Mitani H. A Medaka Gene Map: The Trace of Ancestral Vertebrate Proto-chromosomes Revealed by Comparative Gene Mapping. **Genome Res** 14, 820-828, 2004.

Naruse K, Fukamachi S, Mitani H, Kondo M, Matsuoka T, Kondo S, Hanamura N, Morita Y, Hasegawa K, Nishigaki R, Shimada A, Wada H, Kusakabe T, Suzuki N, Kinoshita M, Kanamori A, Terado T, Kimura H, Nonaka M, Shima A. A detailed linkage map of medaka, Oryzias latipes. Comparative genomics and genome evolution. **Genetics** 154:1773-1784, 2000.

Kinoshita, M., Murata, K., Naruse, K.,Tanaka, M. Medaka: Biology, Management, and Experimental Protocols. Wiley-Blackwell, Iowa, USA, 2009.

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 recovers 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.

Tadashi Isa

M.D. & Ph.D.
Professor, National Institute for Physiological Sciences (NIPS),
Myodaiji, Okazaki 444-8585, JAPAN,
E-mail: tisa@nips.ac.jp
http://www.nips.ac.jp/hbfp/English/index.html

Academic Career

1985	Graduated from Faculty of Medicine, Univ of Tokyo,
1989	PhD degree at Institute for Brain Research, Univ of Tokyo
1988	Research fellow at University of Göteborg, Sweden
1989	Assistant professor, Institute for Brain Research, Univ of Tokyo
1993	Lecturer and associate professor, Gunma University,
1996-Present	Professor, National Institute for Physiological Sciences

Research Interests

We aim at clarifying the neural mechanism for the control of saccadic eye movements and dexterous hand movements, and functional restoration of these motor systems after brain injury, especially of the spinal cord and primary visual cortex (blindsight). Toward this goal, we combine various methods, including local circuit analysis in rodent brain slices, especially of the superior colliculus, behavioral analysis, electrophysiology and brain imaging in non-human primate model. Recently, we are also engaged in brain-machine interfaces, optogenetics with viral vectors.

Representative Publications

Nishimura Y, Morichika Y, Isa T (2009) A common subcortical oscillatory network contributes to recovery after spinal cord injury. *Brain*,132: 709-721.

Yoshida M, Takaura K, Kato R, Ikeda T, Isa T (2008) Striate cortical lesions affect deliberate decision and control of saccade: implication for blindsight. *Journal of Neuroscience*, 28: 10517-10530.

Nishimura Y, Onoe T, Morichika Y, Perfiliev S, Tsukada H, Isa T (2007) Time-dependent central compensatory mechanism of finger dexterity after spinal-cord injury. *Science*, 318: 1150-1155.

Lee PH, Sooksawate T, Yanagawa Y, Isa K, Isa T, Hall WC (2007) Identity of a pathway for saccadic suppression. *Proc Natl Acad Sci, USA* 104: 6824-6827.

Isa T, Endo T, Saito Y (1998) The visuo-motor pathway in the local circuit of the rat superior colliculus. *Journal of Neuroscience* 18: 8496-8504.

Activities/Awards

A secretary in general of the Japan Neuroscience Society (since 2008)

A chairperson of the 32nd Annual Meeting of the Japan Neuroscience Society in 2009

Editorial board member of *Journal of Physiological Sciences*, *Neuroscience Research*, *Current Opinion in Neurobiology*

Guest editor in chief of Special Issue of *Neural Networks* 2009

2000	Human Frontier Science Program Research Grant Award
2005	Human Frontier Science Program Research Grant Award
2006	Tsukahara Nakaakira Memorial Award

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.

Hiroshi Akashi

Division of Evolutionary Genetics
National Institute of Genetics (NIG), Mishima, 411-8540, JAPAN
E-mail: hiakashi@lab.nig.ac.jp
http://www.nig.ac.jp/labs/EvoGen/

Academic Career

2009 -	Professor, National Institute of Genetics
2006 - 2008	Associate Professor, Department of Biology, Penn State University
2000 - 2006	Assistant Professor, Department of Biology, Penn State University
1998 - 2000	Assistant Professor, Department of Ecology and Evolutionary Biology, University of Kansas
1996 – 1998	Post-Doctoral Fellow, Center for Population Biology, University of California, Davis
1990 - 1996	Department of Ecology and Evolution, University of Chicago, Ph.D.
1985 - 1990	Harvard College, B.A.

Research Interests

My research combines theoretical and laboratory studies to identify the causes of genome evolution. I'm particularly interested in testing whether subtle forms of natural selection, those related to optimizing the overall physiology of organisms, are a pervasive evolutionay force. Current interests include testing global models of proteome evolution and identifying the causes of strong lineage- and region-specific base composition evolution in Drosophila.

Representative Publications

Akashi, H., W. Y. Ko, S. Piao, A. John, P. Goel, C. F. Lin, and A. Vitins, 2006 Molecular evolution in the *Drosophila melanogaster* species subgroup: Frequent parameter fluctuations on the time-scale of molecular divergence. *Genetics* 172: 1711.

Akashi, H., 2003 Translational selection and yeast proteome evolution. *Genetics* 164: 1291.

Akashi, H, and T. Gojobori, 2002 Metabolic efficiency and amino acid composition in the proteomes of *Escherichia coli* and *Bacillus subtilis*. *Proceedings of the National Academy of Sciences, USA*. 99: 3695.

Akashi, H., 2001 Gene expression and molecular evolution. *Current Opinions in Genetics and Development* 11: 660.

Akashi, H., 1999 Detecting the "footprint" of natural selection in within and between species DNA sequence data. *Gene* 238: 39.

Activities/Awards

2004 -	Contributing Faculty Member, Faculty of 1000 Biology
2003	National Science Foundation, Population Biology Grant Review Panel
1999 -	*Genetical Research*, Editorial Board
2007 – 2008	*Gene*, Associate Editor
1999 – 2001	*Journal of Molcular Evolution*, Associate Editor
1998	American Society of Naturalists' Young Investigator Award
1998	Alfred P. Sloan Foundation Young Investigator Award in Molecular Evolution

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.

Hideki Innan

The Graduate University for Advanced Studies (SOKENDAI),
Hayama, Kanagawa, 240-0193, JAPAN
Tel: +81-46-858-1600 E-mail: innan_hideki@soken.ac.jp
http://www.sendou.soken.ac.jp/esb/innan/InnanLab/

Academic Career

1996–1999	Doctor of Science (PhD), University of Tokyo, Japan
1999–2000	Postdoctoral Fellow, University of Rochester, NY
2001–2002	Postdoctoral Fellow, University of Southern California, CA
2002–2006	Assistant Professor, University of Texas at Houston
2006-Present	Associate Professor, Graduate University for Advanced Studies

Research Interests

-Genome evolution and gene duplication
-Understanding genome-wide DNA polymorphism data
-Coalescent and diffusion theory in population genetics
-Application of population genetics to agriculture and ecology

Representative Publications

Innan, H., 2003. A two-locus gene conversion model with selection and its application to the human RHCE and RHD genes. Proc. Natl . Acad. Sci . USA. 100: 8793-8798.

Innan, H., and Y. Kim, 2004. Pattern of polymorphism after strong artificial selection in a domestication event. Proc. Natl . Acad. Sci . USA. 101: 10667-10672.

Gao, L. Z., and H. Innan, 2004. Very low gene duplication rate in the yeast genome. Science 306: 1367-1370.

Takuno, S., and H. Innan, 2008. Evolution of complexity in miRNA mediated gene regulation systems. Trends in Genet. 24: 57-59.

Innan, H., and F. Kondrashov, 2010. The evolution of gene duplications: classifying and distinguishing between models. Nat. Rev. Genet. (in press)

Activities/Awards

Feb 2004 NIH Genetics Study Section, ad hoc member
May 2005 – BMC Genetics, Editorial Board
May 2007 – J. Mol. Evol., Associate Editor
Mar 2008 – Mol. Biol. Evol., Associate Editor
Jan 2009 – Evolution, Associate Editor
Feb 2006 Alfred P. Sloan Research Fellowship (USA)
Apr 2008 Commendation for Science and Technology by the Minister of
Education, Culture, Sports, Science and Technology, Young Scientists' Prize (Japan)

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 flame 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 grate 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.

Yoko Satta

Department of Evolutionary Studies of Biosystems,
Department of Biosystems Science, Hayama Center for Advanced Studies,
The Graduate University for Advanced Studies (SOKENDAI),
Hayama, Kanagawa, 240-0193, JAPAN
Tel/Fax: +81-46-858-1574/1544 E-mail: satta@soken.ac.jp
http://www.sendou.soken.ac.jp/esb/satta/index.html

Education

Ochanomizu University (B.S., 1984) Biology.
Ochanomizu University (M.S., 1986) Genetics.
Kyushu University (D.S., 1990) Molecular Evolutionary Genetics.

Academic Career

1990-1992	JSPS (the Japan Society for the Promotion of Science) Fellowships for Japanese Junior Scientist, Department of Population Genetics, National Institute of Genetics, Mishima, Japan.
1992-1995	Max–Planck Gesellschaft Fellowships, Abteilung Immungenetik, Max–Planck Institute für Biologie, Tübingen, Germany.
1995-1996	Research Fellowships, Coordination Center for Research and Education, The Graduate University for Advanced Studies.
1996-1999	Associate Professor, Coordination Center for Research and Education, The Graduate University for Advanced Studies.
1999-2006	Associate Professor, Department of Biosystems Science, The Graduate University for Advanced Studies.
2006-present	Professor, Department of Biosystems Science, Department of Evolutionary Studies of Biosystems, The Graduate University for Advanced Studies.

Research Interests

I am interested in the evolution of human beings, especially, in evolution of physiological traits specific to humans. One of my research aims is to know the genetic basis supporting such physiological traits and know the process how the traits evolve after the divergence from chimpanzees. Therefore, not only the nucleotide sequences of genes, but also genomic structures, gene expression in a particular tissue are compared between humans and nonhuman primates. Recently, we examined gene expression profiles in skins between humans and chimpanzees, and identified several genes showing large differences in their expression amounts between the two species. Furthermore, to know the effect on physiological traits by habitat and dietary properties of humans and nonhuman primates, we examined genes in immune response and detoxification systems, especially from viewpoints of birth and death process of genes and in expression patterns.

Representative Publications

SAWAI, H., Y. GO, and Y. SATTA, 2008 Biological implication for loss of function at Major Histocompatibility Complex loci. Immunogenetics **60**:295-302.

KANEKO, S., I, AKI, K. TSUDA, K. MEKADA, K. MORIWAKI, N. TAKAHATA and Y. SATTA, 2006 Origin and evolution of processed pseudogenes that stabilize functional *Makorin1* mRNAs in mice, primates and other mammals. Genetics **172**:2421-2429.

Go, Y., Y. Satta, O.Takenaka, N. Takahata, 2005 Lineage-specific loss of function of bitter taste receptor genes in humans and non-human primates. Genetics **170**:313-326.

SATTA, Y., M. Hickerson, H. Watanabe, C. O’HUIGIN, and J. KLEIN, 2004 Ancestral population size and species divergence times in the primate lineage on the basis of intron and BAC end sequences. J Mol Evol **59**: 478-487.

Satta, Y., and N. TAKAHATA, 2004 The distribution of the ancestral haplotype in finite stepping-stone models with population expansion. Mol Ecol **13**: 877-886.

The Graduate University for Advanced Studies, Sokendai, School of Life Science

HAYAMA Campus

NIBB

NIPS

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
http://www.soken.ac.jp/en/admissions/guidebook.html

Hayama Campus of Sokendai
http://www.soken.ac.jp/en/academics/evolutBiosystems.html

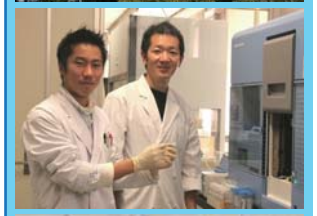
National Institute of Basic Biology
http://www.nibb.ac.jp/en/univ/univ.php

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

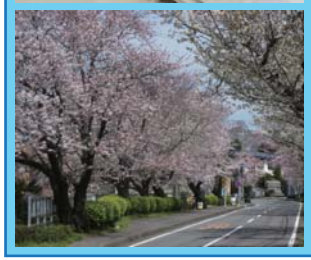
Please see the next page for information about NIG

Sokendai
The Graduate University for Advanced Studies

Graduate studies for International Students
National Institute of Genetics





The National Institute of Genetics (NIG) welcomes international graduate students. Our 5-year PhD program provides an interdisciplinary education with frequent seminars, journal clubs, and workshops on scientific writing and presentation. Education and research at NIG is conducted in English and knowledge of Japanese is not required for PhD studies.

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/.





Department of Genetics, SOKENDAI

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 group studying a breadth of subjects including molecular and cell biology, developmental biology, neuroscience, evolutionary genetics, genome biology and bioinformatics. Each intern will conduct research in a world-class research group and will participate in departmental activities including lecture courses, journal clubs, and seminars by outstanding researchers from within and outside of NIG. Research/education activities are conducted in English but Japanese lessons are available. Travel, on-campus housing, living expenses and insurance will be provided.

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 Intern: http://www.nig.ac.jp/jimu/soken/intern/2010/2010index.html
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.