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Research Organization of Information and Systems
NATIONAL INSTITUTE OF GENETICS

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Introduction

The National Institute of Genetics (NIG) was established in 1949 as the central institute to study various aspects of genetics. It was reorganized in 1984 as an inter-university research institute to promote collaborations with researchers at universities. Since 1988, NIG has been participating in graduate education as the Department of Genetics of the Graduate University for Advanced Studies (SOKENDAI). NIG also serves as a center for various genetic resources such as mutant strains, clones and vectors, and houses DDBJ, the DNA Data Bank of Japan, and a DNA sequencing center.

The history of NIG overlaps the period of a revolution in the field of life science. Genetics is no longer a discipline to study the rules and mechanisms of heredity, but has become the basis for all fields of life science. Molecular techniques now allow us not only to decipher the entire genome sequence of organisms including humans, but also to understand the details of higher biological phenomena: cell differentiation, morphogenesis, brain function, and evolution --- the history of life itself. Currently, 36 research groups are actively performing pioneering and cutting-edge researches in these fields at NIG.

Recent generation of massive information on biological systems and their environment calls for new directions in life sciences, such as bioinformatics, system-level analysis, and theoretical approaches to extract knowledge from databases. To this end NIG and three other national institutes, the National Institute of Informatics, The Institute of Statistical Mathematics and the National Institute of Polar Research have formed a new organization, the Research Organization of Information and Systems (ROIS) since April 2004, as a part of the reform of national universities and research institutes in Japan. Inter-institutional collaborations within the new organization are in progress.

We welcome your comments and suggestions on our research activities and endeavors.

Yuji Kohara, Director-General

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Laboratory for DNA Data Analysis
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SUZUKI, Yoshiyuki, M. D., Ph. D., Assistant Professor
Laboratory for Gene-Product Informatics
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Laboratory for Gene Function Research
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Laboratory for the Research and Development of Biological Databases
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YATA, Katsunori, Assistant Chief of the Section

15. Department of Administration

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ENDO, Tsuyoshi, Chief of the Financial Affairs Section

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SHINOZAKI, Kazuo; Director, Plant Science Center, RIKEN
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TAKAGI, Toshihisa; Professor, Graduate School of Frontier Sciences, The University of Tokyo
TSUJI, Shoji; Professor, Graduate School of Medicine, The University of Tokyo

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ARAKI, Hiroyuki; Professor, Department of Cell Genetics
GOJOBORI, Takashi; Professor, Center for Information Biology and DNA Data Bank of Japan
HIROMI, Yasushi; Professor, Department of Developmental Genetics
KATSURA, Isao; Professor, Structural Biology Center
KURATA, Nori; Professor, Genetic Strains Research Center
SAITOU, Naruya; Professor, Department of Population Genetics
SASAKI, Hiroyuki; Professor, Department of Integrated Genetics
SHIMAMOTO, Nobuo; Professor, Structural Biology Center
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YAMAO, Fumiaki; Professor, Department of Molecular Genetics

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TAKEICHI, Masatoshi; Director, Center for Developmental Biology, RIKEN

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Research Outline

Code	Division/Laboratory	Group name
A-a	Division of Molecular Genetics	Tatsuo Fukagawa
A-b	Division of Mutagenesis	Fumiaki Yamao
A-c	Molecular Mechanism Laboratory	Hiroaki Seino
B-a	Division of Cytogenetics	Takehiko Kobayashi
B-b	Division of Microbial Genetics	Hiroyuki Araki
C-a	Division of Developmental Genetics	Yasushi Hiromi
C-a	Division of Developmental Genetics	Hiroshi Shimizu
C-b	Division of Neurogenetics	Takuji Iwasato
C-b	Division of Gene Expression	Susumu Hirose
C-c	Division of Molecular and Developmental Biology	Koichi Kawakami
D-a	Division of Population Genetics	Naruya Saitou
D-a	Division of Population Genetics	Toshiyuki Takano
D-b	Evolutionary Genetics	Hiroshi Akashi
E-a	Division of Human Genetics	Hiroyuki Sasaki
E-b	Division of Agricultural Genetics	Tetsuji Kakutani
E-b	Division of Agricultural Genetics	Keiichi Shibahara
E-c	Division of Brain Function	Tatsumi Hirata
E-e	Division of Human Genetics	Itsuro Inoue
F-a	Mammalian Genetics Laboratory	Toshihiko Shiroishi
F-b	Mammalian Development Laboratory	Yumiko Saga
F-c	Mouse Genomics Resource Laboratory	Tsuyoshi Koide
F-d	Model Fish Genomics Resource	Noriyoshi Sakai
F-e	Plant Genetics Laboratory	Nori Kurata
F-f	Microbial Genetics Laboratory	Hironori Niki
F-g	Invertebrate Genetics Laboratory	Ryu Ueda
G-a	Genetic Informatics Laboratory	Yukiko Yamazaki
G-b	Genome biology Laboratory	Yuji Kohara
G-c	Comparative Genomics Laboratory	Asao Fujiyama
H-a	Biological Macromolecules	Kazuhiro Maeshima
H-a	Biological Macromolecules Laboratory	Makio Tokunaga
H-b	Molecular Biomechanism Laboratory	Nobuo Shimamoto
H-c	Multicellular Organization Laboratory	Isao Katsura
H-d	Biomolecular Structure Laboratory	Yasuo Shirakihara
H-e	Gene Network Laboratory	Emiko Suzuki
H-f	Multicellular Organization Laboratory	Hitoshi Sawa
I-a	Laboratory for DNA Data Analysis	Takashi Gojobori

I-b	Laboratory for Gene-Product Informatics	Yasukazu Nakamura
I-b	Laboratory for Gene-Product Informatics	Ken Nishikawa
I-c	Laboratory for Gene Function Research	Yoshio Tateno
I-d	Laboratory for Research and Development of Biological Databases	Toshihisa Takagi
I-d	Laboratory for Research and Development of Biological Databases	Hideaki Sugawara
I-e	Laboratory for Gene-Expression Analysis	Kousaku Okubo
J-a	Laboratory for Cell Lineage	Takako Isshiki
J-b	Neural Morphogenesis Laboratory	Emoto Kazuo
J-c	Cell Architecture Laboratory	Kimura Akatsuki
K	RADIOISOTOPE CENTER	RADIOISOTOPE CENTER
L	EXPERIMENTAL FARM	EXPERIMENTAL FARM
M	Publicity and Intellectual Property Unit	Munehiro Tomikawa
M	Intellectual Property Unit	Intellectual Property Unit
N	Technical Section	Technical Section

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A. DEPARTMENT OF MOLECULAR GENETICS
A-a. Division of Molecular Genetics

Tatsuo Fukagawa

RESEARCH ACTIVITIES

Identification and characterization of the CENP-H-I complex proteins in higher vertebrate cells.

Masahiro Okada, Tetsuya Hori, Mi-Sun Kwon, Aussie Suzuki, Mayumi Takahashi, and Tatsuo Fukagawa

The centromere plays a fundamental role in accurate chromosome segregation during mitosis and meiosis in eukaryotes. Its functions include sister chromatid adhesion and separation, microtubule attachment, chromosome movement and mitotic checkpoint control. Although chromosome segregation errors cause genetic diseases including some cancers, the mechanism by which centromeres interact with microtubules of the spindle apparatus during cell division is not fully understood.
To understand the function of the centromere, we were led to develop a genetic method that utilizes the hyper-recombinogenic chicken B lymphocyte cell line DT40. The high level of homologous recombination in DT40 cells permit efficient targeted disruption of genes of interest. We have improved this system and have created several cell lines with conditional knockouts of several centromere proteins to investigate the molecular mechanism of centromere assembly and function. We have proposed a model for kinetochore assembly in vertebrate cells (Fukagawa et al., EMBO J., 2001; Nishihashi et al., Dev. Cell, 2002; Fukagawa, Exp. Cell Res., 2004; Regnier et al., Mol. Cell. Biol., 2005; Mikami et al., Mol. Cell. Biol., 2005). In this model we explained that many unidentified proteins could be involved in kinetochore assembly. Therefore, we tried to identify new centromere proteins that associate with CENP-H or CENP-I using the proteomics approach. We prepared DT40 cell lines in which expression of CENP-H was replaced by expression of CENP-H-Flag or CENP-H-GFP (Mikami et al., Mol. Cell. Biol., 2005). We also prepared DT40 cell lines in which expression of CENP-I was replaced by expression of CENP-I-Flag or CENP-I-GFP. We extracted chromosome fraction from these cell lines and performed immunoprecipitation with anti-Flag or anti-GFP antibodies. Proteins co-precipitated with antibodies were analyzed by mass spectrometry, and we identified several polypeptides and cloned the corresponding cDNAs. As we confirmed that these proteins constitutively localize to centromeres in DT40 cells, we named them CENPs. We also performed immunoprecipitation experiments with human cells and identified similar proteins. In total, our purifications in chicken and human cells identified 11 interacting proteins (CENP-K, CENP-L, CENP-M, CENP-N, CENP-O, CENP-P, CENP-Q, CENP-R, CENP-50 (U), CENP-H and CENP-I) that localize constitutively to centromeres as components of the CENP-H-I associated complex. Our analysis of these proteins using chicken DT40 knockouts and RNAi analysis in human cells demonstrates that the CENP-H-I complex can

be divided into three functional sub-complexes, each of which is required for chromosome alignment and faithful chromosome segregation. Interestingly, newly expressed CENP-A is not efficiently incorporated into centromeres in knockout mutants of a subclass of CENP-H-I complex proteins, indicating that the CENP-H-I complex may function in part as a mark directing CENP-A deposition to centromeres.

Functional analysis of CENP-O-class proteins that are required for recovery from spindle damage.

Tetsuya Hori, Masahiro Okada, Tomoko Motohashi, Kazuko Suzuki, and Tatsuo Fukagawa

We previously identified a multi-subunit complex (CENP-H/I complex) at kinetochores from human and chicken cells. We showed that the CENP-H/I complex can be divided into three functional classes. Among them, we investigated CENP-O class-proteins, which include CENP-O, -P, -Q, -R, and -50 (U). We created chicken DT40 cell knockouts of each of these proteins and found that all knockout lines were viable but showed slow proliferation and mitotic defects. Phenotype analysis showed that all proteins except for CENP-R were required for recovery from spindle damage. Kinetochore localization of CENP-O, -P, -Q, and -50 was interdependent, but kinetochore localization of these proteins was observed in CENP-R-deficient cells, and CENP-R localization was abolished in CENP-O, -P, -Q, or -50 knockouts. A coexpression assay in bacteria showed that CENP-O, -P, -Q, and -50 proteins form a stable complex, which can associate with CENP-R. These results indicate that CENP-O-class proteins are tightly associated, and this complex contributes to kinetochore function.
Although the CENP-50 knockout was not lethal at cellular level, it is interesting to investigate function of CENP-50 at individual level. Therefore, we are making and characterizing knockout mice of CENP-50. We also discovered that expression of a brain specific gene was reduced in CENP-50-deficient cells.

Functional analysis of the CENP-C complex, which associates with the Mis12 complex.

Mi-Sun Kwon, Masahiro Okada, Tetsuya Hori, and Tatsuo Fukagawa

CENP-C is a conserved inner kinetochore component. To understand the precise roles of CENP-C in the kinetochore, we created a cell line with a conditional knockout of CENP-C with the tetracycline-inducible system, in which the target protein is inactivated at the level of transcription. We found that CENP-C inactivation causes mitotic delay. However, observations of living cells showed that CENP-C-knockout cells progressed to the next cell cycle without normal cell division following mitotic delay. Interphase cells with two nuclei before subsequent cell death were sometimes observed. We also found that ~60% of CENP-C-deficient cells had no Mad2 signals even after treatment with nocodazole, suggesting that lack of CENP-C impairs the Mad2 spindle checkpoint pathway. We also observed significant reductions in the signal intensities of Mis12 complex proteins at centromeres in CENP-C-deficient cells. CENP-C signals were also weak in interphase nuclei but not in mitotic chromosomes of cells with a knockout of CENP-K, a member of CENP-H complex proteins. These results suggest that centromere localization of CENP-C in interphase nuclei occurs upstream of localization of the Mis12 complex and downstream of localization of the CENP-H complex (Kwon et al., Mol. Bio. Cell in press).

Functional roles of Ago family proteins in verterbrate centromeres

Tomoko Motohashi, and Tatsuo Fukagawa

RNAi-mediated silencing of gene expression occurs when double-stranded RNAs (dsRNAs) are cleaved by Dicer into 21- to 23-nt small interfering RNAs (siRNAs). These siRNAs guide a multicomponent nuclease, RNA-induced silencing complex (RISC), to

degrade specific mRNAs. Although the Dicer-mediated gene-silencing is evolutionarily conserved system, the biological functions of the RNAi machinery are not fully understood. Genetic strategies have been used to examine the biological functions of the RNAi machinery in C. elegans, Arabidopsis, Drosophila and fungi. There are also many reports that the RNAi machinery via RNA-induced initiation of transcriptional silencing (RITS) complex is related to heterochromation formation and chromosome segregation in fission yeast. However, it was unclear whether the RNAi machinery is associated with chromosome segregation in vertebrate cells. To examine the biological function of the RNAi-related pathway in vertebrate cells, we generated and characterized a conditional loss-of-function mutant of Dicer in a chicken-human hybrid DT40 cell line that contains human chromosome 21 (Fukagawa et al, Nature Cell Biol., 2004). Loss of Dicer leads to cell death with accumulation of abnormal mitotic cells that show premature sister chromatid separation. Aberrant accumulation of transcripts from α-satellite sequences, which consist of human centromeric repeat DNAs, was detected in Dicer-deficient cells. We then started to examine expression profile of non-coding region using high-density DNA-microarray, when expression of Dicer was lost. We identified several non-coding RNAs from this method. We are characterizing biological function these RNAs. We also created conditional knockout cells for other components involved in RNAi machinery such as Ago-family proteins. Phenotype analyses of Ago-deficient cells were started. We found several genes whose expression are increased or decreased upon Ago knockouts. We are characterizing these genes how these are related to functions of Ago family proteins.

PUBLICATIONS

Papers

1．Okada, M., Hori, T., and Fukagawa T（2006）The DT40 system as a tool for analyzing kinetochore assembly.，**Subcell Biochem.**，40，91 - 106

2．Kline, S., Cheeseman, M. I., Hori, T., Fukagawa, T., and Desai, A.（2006）The Human Mis12 Complex is Required for Kinetochore Assembly and Proper Chromosome Segregation.，**J. Cell Biol.**，173，9 - 17

3．堀哲也、深川竜郎（2006）セントロメアクロマチン上に集合するキネトコア蛋白質のダイナミクス，蛋白質核酸酵素，51，326 - 334

4．Okada, M., and Fukagawa, T.（2006）Purification of a protein complex that associates with chromatin.，**Nature Protocols**，，0 - 0

5．Kimura, H., Takizawa, N., Allemand, E., Hori, T., Iborra, J. F., Nozaki, N., Muraki, M., Hagiwara, M., Krainer, R. A., Fukagawa, T., and Okawa K.（2006）A novel histone-exchange factor, protein phosphatase 2Cγ, mediates the exchange and dephosphorylation of H2A/H2B.，**J. Cell Biol.**，175，389 - 400

6．Okada, M., Cheeseman, I. M., Hori, T., Okawa, K., McLeod, I. X., Yates III, J. R., Desai, A., and Fukagawa, T.（2006）The CENP-H-I complex is required for the efficient incorporation of newly synthesized CENP-A into centromeres.，**Nature Cell Biol.**，8，446 - 457

7．Sanematsu, F., Takami, Y., Barman, H. K., Fukagawa, T., Ono, T., Shibahara, K., and Nakayama, T.（2006）Asf1 is required for viability and chromatin assembly during DNA replication in vertebrate cells.，**J. Biol. Chem.**，281，13817 - 13827

ORAL PRESENTATION

1．Tatsuo Fukagawa　Formation of kinetochore and its function in higher vertebrate cells.　University of California, San Diego　12/15

2．深川竜郎　高等動物における染色体分配のダイナミクス　早稲田大学・教育学部　11/14

3．深川竜郎　高等動物のセントロメア構築　岡山大学・医学部　11/9

POSTER PRESENTATIONS

1．Tatsuo Fukagawa 「Kinetochore assembly in higher vertebrate cells」, 6th Human

Genome Organization (HUGO) Pacific meeting , Taipei , 3/9
2 . Hori, T., Fukagawa, T 「 The CENP-H/I complex is required for the efficient incorporation of newly synthesized CENP-A into centromertes. 」, 第20回国際分子生物学会会議 , 京都市 , 6/23
3 . Okada, M., Fukagawa, T. 「 The CENP-H/I complex is required for the efficient incorporation of newly synthesized CENP-A into centromertes. 」, 第20回国際分子生物学会会議 , 京都 , 6/23
4 . 深川竜郎 「 セントロメアへ集合するキネトコアタンパク質のダイナミクス 」, 特定領域研究「細胞核ダイナミクス」「メンブレントラフィック」合同公開シンポジウム「細胞内のダイナミックネットワーク:前進するオルガネラ研究」, 大阪府豊中市 , 6/2
5 . 深川竜郎 「 染色体安定性を保障するセントロメア複合体の解析 」, 日本がん学会シンポジウム , 横浜市 , 9/29
6 . 深川竜郎 「 高等動物の染色体分配制御 」, 日本遺伝学会シンポジウム , つくば市 , 9/25
7 . Fukagawa, T. 「 The CENP-H/I complex proteins are required for faithful chromosome segregation in vertebrate cultured-cells and are essential for early development in mice. 」, アメリカ細胞生物学会 , サンディエゴ(米国) , 12/12
8 . Kwon Mi-sun, 深川竜郎他 「 CENP-C is involved in chromosome segregation, mitotic checkpoint function and kinetochore assembly. 」, 日本分子生物学会フォーラム , 名古屋市 , 12/9
9 . 堀哲也, 深川竜郎他 「 初期発生進行に必須なCENP-50 キネトコアタンパク質複合体の解析 」, 日本分子生物学会フォーラム , 名古屋市 , 12/9
10 . 岡田聖裕, 深川竜郎他 「 CENP-A のセントロメアへの局在化に関与するセントロメア蛋白質 」, 日本分子生物学会フォーラム , 名古屋市 , 12/9

PATENT

1 . 特願2006-016079 , セントロメア局在タンパク質遺伝子ノックアウト細胞 , 深川竜郎、岡田聖裕、堀　哲也 , 大学共同利用機関法人情報・システム研究機構
2 . 特願2006-016080 , セントロメア局在タンパク質遺伝子コンディショナルノックアウト細胞 , 深川竜郎、岡田聖裕、堀　哲也 , 大学共同利用機関法人情報・システム研究機構

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A. DEPARTMENT OF MOLECULAR GENETICS
A-b. Division of Mutagenesis
Fumiaki Yamao

RESEARCH ACTIVITIES

Replication factor required for centromeric structures and functions in fission yeast.

T. Natsume, Y. Tsutsui, H. Iwasaki and F.Yamao

The chromatin is assembled into a various higher order structures that are essential for its functional regulation and expression. It is maintained via a variety of the post-translational modifications. The preservation of the chromatin structure during duplication of the chromosome is another aspect of the epigenetic inheritance of the structural information. To address this issue, we focused a replication factor, the dysfunction of which caused defect in chromosomal integrity shown in chromosomal segregation and heterochromatin maintenance as well as those in DNA replication and damage repair.
Fission yeast Mcl1, a conserved protein through mammalian cells, strongly interacts with Swi7, a largest subunit of DNA polymerase a, and factors involved in processing of Okazaki fragment, suggesting that Mcl1 is concerned with lagging strand DNA synthesis. Cells mutated in *mcl1* gene show premature separation of sister centromeres, indicating that Mcl1 is required for sister chromatid cohesion (SCC), especially in centromere region. As SCC depends on the heterochromatin structure, the possible involvement of Mcl1 in the integrity of heterochromatin was examined by the alleviation of transcriptional silencing on the spot. The gene silencing in three typical heterochromatin regions in fission yeast, centromere, telomere regions and mating type locus, were all disrupted. However, Swi6 protein, a HP1 homologue in fission yeast, was still associated in the heterochromatin regions. Thus, Mcl1 seems to function in Swi6-independent pathway in maintaining heterochromatin structure. Coincidently, *mcl1* and *swi6* mutations showed synergistic sensitivity to TBZ, an inhibitor of microtubule attachment to kinetochore.
mcl1 as well as *swi7* mutation caused sensitivity to histone deacetylase inhibitor, implicating the involvement of Mcl1 in HDAC-related processes. This was confirmed by the accumulation of acetylated histone H4 at the outer centromere region as well as mat locus and telomere region. Interestingly, in *mcl1* mutant cells, the acetylated histone H4 accumulated in not only outer centromere but also central kinetochore domains. The transcriptional silencing was deficient in the central domain of centromere. Thus, Mcl1 seems to be required for integral maintenance of kinetochore structure and function. Indeed, in *mcl1* mutant cells, unequal chromosomal segregation was frequently observed. A specific structure of at the central domain of centromere was disrupted, and association of central domain- specific SpCENP-A protein to kinetochore was abolished in *mcl1* mutant cells.
Mcl1 seems to play a pivotal role in kinetochore structure and function through histone acetylation on the spot though the precise processes are sill unclear. Most interestingly,

however, these processes are likely linked with DNA replication machinery, providing a novel insight into mechanism of epigenetic inheritance of chromosomal structures.

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ORAL PRESENTATION

1．山尾文明　分子生物学概論　　山口大学農学部獣医学科　12/24-27

POSTER PRESENTATIONS

1．T. Natsume, Y.Tsutsui, T.Morishita, H.Iwasaki, H.Shinagawa, F.Yamao「Fission yeast Mcl1 is involved in the maintenance of heterochromatin」，20th IUBMB（第20回国際生化学・分子生物学会議），Kyoto，6
2．筒井康博、夏目豊彰、森下卓、岩崎博史、品川日出夫、山尾文明「分裂酵母Mcl1のヘテロクロマティンと姉妹染色分体接着における役割」，酵母遺伝学フォーラム，三島，7/
3．夏目豊彰、筒井康博、森下卓、岩崎博史、品川日出夫、山尾文明「分裂酵母Mcl1のキネトコアにおける役割」，酵母遺伝学フォーラム，三島，7/
4．筒井康博、夏目豊彰、岩崎博史、品川日出夫、山尾文明「分裂酵母Mcl1の複製期ヒストンアセチル化への関わり」，組換え・ゲノム再編ワークショップ，淡路島 夢舞台，11
5．夏目 豊彰、筒井 康博、岩崎 博史、品川 日出夫、山尾 文明「分裂酵母Mcl1 はヒストンの脱アセチル化を促進してセントロメア構造の維持に関与する」，　日本遺伝学会第78回大会，つくば，9/25-27

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A. DEPARTMENT OF MOLECULAR GENETICS
A-c. Molecular Mechanism Laboratory

Hiroaki Seino

RESEARCH ACTIVITIES

POSTER PRESENTATIONS

1．清野浩明「 ユビキチン経路によるDNA損傷チェックポイントの制御 」，日本分子生物学会，福岡，12/7-10

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B. DEPARTMENT OF CELL GENETICS
B-a. Division of Cytogenetics
Takehiko Kobayashi

RESEARCH ACTIVITIES

Division of Cytogenetics, Takehiko Kobayashi group (December 1st , 2006~)

RESEARCH ACTIVITIES

One feature of organisms is the ability to adapt to the environment. Thanks to this ability, organisms could survive on the earth in changeable conditions. Such an ability is supported by flexibility of the genome. On the other hand, the genome determines the design of life. Therefore, changing of genomic information, if it occurs randomly, is likely to be toxic for organisms. Indeed, it is known that genomic instability causes cancer and premature senescence. We are studying how cells change the genome safely. One attractive mechanism for this change is gene amplification. Gene amplification makes it possible to create new genes and modify them without destroying the original one.
We have been analyzing amplification of the ribosomal RNA gene repeats (rDNA) as a model system.

(1) Mechanisms to maintain the stability of rDNA
-Analysis of the relationship between replication and gene amplification-

Austen R.D. Ganley, and Takehiko Kobayashi

The ribosomal RNA gene repeats (rDNA) is one of the most characteristic regions in eukaryotic chromosomes. The repeats consist of more than 100 tandem units occupying large regions of the chromosome(s) in most organisms. Cells are known to deal with this “unusual domain” in a unique manner. In particular, repeated genes families such as rDNA are one of the most fragile sites for deletional recombination. Even though the rDNA is susceptible to this kind of instability, each organism is known to maintain a specific repeat copy number of rDNA, thereby indicating the presence of a mechanism for maintenance of copy number. We have been studying this mechanism and found a unique amplification system that uses replication fork blocking activity. The replication fork barrier site (RFB) inhibits the replication fork and causes DNA double strand breaks (DSBs). These DSBs are then repaired by recombination. If the broken end recombines with an unequal sister-chromatid, some copies are replicated twice and the copy number increases. In this way, amplification takes place.
In the above “RFB-dependent rDNA amplification model”, replication initiation is also expected to affect RFB activity and change the amplification rate. In fact, replication origins are often found in mammalian repeated genes such as DHFR and c-myc. These

observations suggest a strong relationship between replication origins and gene amplification, though there is no direct evidence for this.
To address this relationship, we used a yeast strain that has two rDNA copies instead of the usual wild-type 150 copies. In this strain we modified the replication origin sequence to change its efficiency and monitored the amplification rate. We found that reduced replication initiation resulted in reduced amplification.
It is also known that rDNA recombination produces circular DNA molecules called ERC (extrachromosomal rDNA circles). ERC accumulation promotes cellular aging. We looked at the effect of rDNA replication initiation-modification on ERC production and found that these modifications change ERC number. Now we are analyzing the mechanism.

(2) Evolutionary study of repetitive genes

-Analysis of concerted evolution in the ribosomal DNA repeats-

Austen R.D. Ganley and Takehiko Kobayashi

Repeat families within genomes are often maintained with similar sequences. Traditionally this has been explained by concerted evolution, where repeats in an array evolve “in concert” with the same sequence by continual recombination between the repeats. Another form of evolution, birth-and-death evolution, can also explain this pattern, although in this case selection is the critical force. The level of intragenomic variation is the key difference between these two forms of evolution. The huge size and repetitive nature of large repeat arrays have made it difficult to determine the total level of intragenomic variation, so there is little evidence to support concerted evolution over birth-and-death evolution for many large repeat arrays.
We used whole genome shotgun sequence data from five fungal species genome projects to show total levels of sequence variation within the ribosomal RNA gene repeats (rDNA). The level of sequence variation was remarkably low. Furthermore, the polymorphisms that were detected were not functionally-constrained and exist beneath the level of selection. These results suggest the rDNA is evolving via concerted evolution. Comparisons with a repeat array undergoing birth-and-death evolution provide a clear contrast in the level of repeat array variation between these two forms of evolution, confirming that the rDNA does evolve via concerted evolution. These results suggest that concerted evolution is very rapid and efficiently maintains highly-similar repeat arrays.

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Papers

1．小林武彦,オーステン　ガンレイ（2006）noncodingな転写がrDNAのコピー数を調節する，蛋白質核酸酵素，51，2141 - 2143
2．Kobayashi, T（2006）Strategies to maintain the stability of the ribosomal RNA gene repeats-Collaboration of recombination, cohesion, and condensation- ，**Genes Genet. Syst.**，81，155 - 161
3．小林武彦（2006）rDNAの恒常性の維持機構，細胞工学，25，481 - 485
4．小林武彦（2006）酵母の老化制御機構，医学のあゆみ，217，743 - 747
5．小林武彦（2006）ゲノムを変化させる遺伝子増幅，総研大ジャーナル，9，8 - 10

ORAL PRESENTATION

1．Kobayashi, T　How are repeated genes maintained?　Pastuer Institute Seminar Pastuer Institute, Paris, France　5/12
2．Kobayashi, T　Strategies to maintain the stability of the ribosomal RNA gene repeats フランス国立科学研究センター　Montpellier, France　5/10
3．小林武彦　基礎生物学概論「生物の老化を如何に捉えるか」　基礎生物学研究所　6/6

POSTER PRESENTATIONS

1．Kobayashi, T「Replication initiation regulates rDNA amplification」, The Chromosome Cycle，Tokyo，6/26-27
2．Kobayashi, T, Ganley, A.R.「Replication initiation regulates rDNA amplification」, 20th IUBMB International Congress of Biochemistry and Molecular Biology &，Kyoto，6/18-23
3．Serizawa, N., Horiuchi, T., Kobayashi, T.「Transcription-mediated hyper-recombination in *HOT1*」, 20th IUBMB International Congress of Biochemistry and Molecular Biology &，Kyoto，6/18-23
4．Kobayashi, T., Ganley, A.R.「系統発生学的フットプリント法による機能性DNA配列の同定」, 日本遺伝学会第78回大会，つくば市，9/25-27
5．小林武彦、オーステン　ガンレイ「複製開始活性が遺伝子の増幅に与える影響」, 第18回DNA複製・分配ワークショップ，熱海市，10/30
6．井手聖、渡辺圭一、渡辺寛光、白髭克彦、小林武彦、真木寿治「染色体の複製開始制御異常をモニターする機構」, 第18回　DNA複製・分配ワークショップ，熱海市，10/30
7．小林武彦,オーステン　ガンレイ「複製と組み換えの共役による遺伝子増幅機構の解析」, 組換え、染色体再編ワークショップ，兵庫県淡路島，11/27
8．井手聖、渡辺圭一、渡辺寛光、白髭克彦、小林武彦、真木寿治「染色体複製開始異常のモニター機構」, 日本分子生物学会2006フォーラム，名古屋市，12/6-8
9．井手聖、渡辺圭一、渡辺寛光、白髭 克彦、小林武彦、真木寿治「染色体複製開始異常のモニター機構」, 日本遺伝学会第78回大会，つくば市，9/25-27
10．小林武彦,Austen R.D. Ganley「DNA複製開始活性はrDNAの増幅に必要て繧函□る」, 酵母遺伝学フォーラム，三島市，7/15-17

EDUCATION

1．益谷央豪、小林武彦　組換え、修復によって維持されるゲノムの恒常性　日本分子生物学会2006フォーラム　シンポジウム　名古屋　12/6-8

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B. DEPARTMENT OF CELL GENETICS
B-b. Division of Microbial Genetics

Hiroyuki Araki

RESEARCH ACTIVITIES

We have been studying on eukaryotic chromosomal DNA replication and its regulation by the cell cycle. For this purpose, we have employed budding yeast, *Saccharomyces cerevisiae*, as a model system of eukaryotic cells. Using strong genetics of budding yeast, we have identified novel factors involving in chromosomal DNA replication and revealed their functions in chromosomal DNA replication.

(1) CDK targets in the initiation of DNA replication

Seiji Tanaka, Toshiko Umemori, Kazuyuki Hirai, Sachiko Sakamoto and Hiroyuki Araki

Cyclin-dependent kinase (CDK) is essential in the initiation of chromosomal DNA replication in eukaryotes. Although yeast Sld2 is known as an essential target, its phosphomimetic form alone does not confer DNA replication in the absence of CDK activity. We show that a *JET1* mutation of *CDC45* or high copy *DPB11*, in combination with the phosphomimetic form of Sld2, confers CDK-independent DNA replication. Sld3, which associates with Cdc45, is phosphorylated by CDK and then binds to the N-terminal pair of BRCT domains in Dpb11, which has two pairs of tandem BRCT domains. Cdc45 enhances this binding, and the *JET1* mutation as well as high copy *DPB11* bypasses the requirement of Sld3 phosphorylation. Because phosphorylated Sld2 binds to the C-terminal pair of BRCT domains in Dpb11, we argue that when CDK phosphorylates the replication proteins, Sld2 and Sld3, two pairs of BRCT domains in Dpb11 connect them to initiate DNA replication.

(2) The pre-Landing complex of replication proteins formed in a CDK-dependent manner

Sachiko Sakamoto, Kazuyuki Hirai, Yoichiro Kamimura, and Hiroyuki Araki

As described above, we revealed that the interactions between Dpb11 and phosphorylated Sld2 and Sld3, promotes the initiation of DNA replication. However, we do not know how these interactions promotes the initiation step of DNA replication. At replication origins in eukaryotes, the pre-Replicative Complex (pre-RC) forms from late M to G1 phases in the absence of CDK (Cyclin-dependent kinase) activity and other replication proteins including DNA polymerases assemble when CDK activity increases from G1/S boundary. We have found that a complex containing at least four replication factors, Dpb11, Sld2, GINS and Pol ε, is formed in a CDK-dependent dependent manner. To elucidate how this complex is formed, we purified these factors to near homogeneity and examined whether they interact each other in vitro. It is revealed that they bind each other and form a complex *in vitro*. This result suggests that they can form a complex without any other factor. Thus, this complex

formation is one of the key steps to promote the initiation of DNA replication.

(3) Functional analysis of Sld7

Tamon Tanaka and Hiroyuki Araki

sld7 was isolated as a novel *sld* (synthetic lethality with *dpb11*). Although the *SLD7* gene is not essential, cells deleting this gene (*sld7*) showed sensitivity to hydroxyurea (inhibitor of DNA replication) and MMS (DNA-damaging agent). Moreover, *sld7* cells replicate chromosomal DNA slower than wild-type cells. Furthermore, sld7 is synthetic lethal with temperature-sensitive alleles of replication proteins, such as Sld3, Cdc45 and Sld2. These results suggest that Sld7 plays an important role for DNA replication. To know function of Sld7, we tried to isolate factors interacting with Sld7 and found that Sld7 forms a complex with Sld3. These proteins expressed in Escherichia coli actually formed a complex. In *sld7* cells, the protein level of Sld3 decreased and high copy *SLD3* suppressed defect of *sld7* cells. Moreover, high copy *SLD7* suppressed the growth defect of one of temperature allele of *SLD3*. Thus, all the results suggest that Sld7 functions for DNA replication through Sld3.

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1． Tak,Y.-S. ,Tanaka,Y.,Endo,S.,Kamimura,Y., and ,Araki,H. （2006） A CDK-catalysed regulatory phosphorylation for formation of the DNA replication complex Sld2-Dpb11 , **EMBO J.**, 25 , 1987 - 1996

ORAL PRESENTATION

1．田中誠司　CDKによる真核細胞の染色体DNA複製開始の制御機構　セミナー　京都大学大学院生命科学研究科　12/18

POSTER PRESENTATIONS

1． Li,Y., and Araki,H.「 Dynamical assembly of chromosomal replication initiation proteins in budding yeast 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
2． Tanaka,T., and Araki,H. 「 Functional analysis of budding yeast Sld7 in chromosome dynamics 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
3． Yanagisawa,Y., and Araki,H.「 Molecular dissection of yeast replication protein Sld2 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
4． Tak,Y.-S.,Tanaka,Y.,Endo,S.,Kamimura,Y., and Araki,H.「 A novel mechanism of CDK-catalyzed multisite phosphorylation for formation of the DNA replication camplex Sld2-Dpb11 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
5． Tanaka,S., and Araki,H. 「 ISOLATION AND ANALYSIS OF THE MUTANT THAT BYPASSES THE CDK REQUIREMENT IN THE INITIATION OF DNA REPLICATION 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
6． Hirai,K., Sakamoto,S., Kamimura,Y., and Araki,H. 「 Pre-Landing Complex: a protein complex produced during the assembly of chromosomal DNA replication machinery in budding yeast 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
7． Tak,Y.-S., Tanaka,Y., Muramatsu,S., Endo,S., Tanaka,S., Kamimura,Y., and Araki,H. 「 CDK-DEPENDENT INITIATION OF CHROMOSOME DNA REPLICATION IN BUDDING YEAST 」, 第20回国際生化学・分子生物学会議 , 京都 , 6/23
8． Tanaka,S., and Araki,H. 「 Isolation and analysis of the mutant that bypasses the CDK requirment in the initiation of DNA replication 」, FASEB SUMMER RESEARCH CONFERENCES (Yeast Chromosome Structure, Replication & Segregation) , Indian Wells, CA, USA , 6/27
9． Araki,H. 「 CDK-Mediated Regulation of Chromosomal DNA Replication in Budding Yeast 」,「染色体サイクル」第一回国際シンポジウム , 東京 , 6/26
10． 田中誠司, 荒木弘之 「 Isolation and analysis of the mutant that bypasses the CDK requirment in the initiation of DNA replication 」, 酵母遺伝学フォーラム　第39回研究報告会

，三島，7/16
11．田中太門, 荒木弘之「DNA複製と他の細胞周期イベントをつなぐ出芽酵母Sld7タンパク質複合体の役割」, 酵母遺伝学フォーラム　第39回研究報告会，三島，7/16
12．Araki,H.，Tanaka,S.，Tak,Y.-S.，Tanaka,Y.，Muramatsu,S.，Endo,S.，Umemori,T.，Hirai,K., and Kamimura,Y.「CDK-Mediated Regulation of Chromosomal DNA Replication in Budding Yeast」, DNA Replication and Genome Integrity，San Diego, CA, USA，8/10
13．平井和之，坂本佐知子，上村陽一郎，荒木弘之「染色体DNAの複製開始期に形成されるタンパク質複合体，Pre-Landing Complexの解析」，第18回DNA複製・分配ワークショップ，熱海，10/30
14．Li,Y.,Araki,H.「Dynamic Assembly of Chromosomal Replication Initiation Proteins in Budding Yeast」，第18回DNA複製・分配ワークショップ，熱海，10/30
15．梅森稔子，平井和之，田中誠司，上村陽一郎，荒木弘之「出芽酵母複製タンパク質Sld3のCdkによるリン酸化」，第18回DNA複製・分配ワークショップ，熱海，10/30
16．田中誠司，梅森稔子，平井和之，村松佐知子，上村陽一郎，荒木弘之「CDKによる染色体DNA複製開始の制御機構」，第18回DNA複製・分配ワークショップ，熱海，10/31
17．田中太門，荒木弘之「DNA複製と他の細胞周期イベントをつなぐ出芽酵母Sld7タンパク質複合体の役割」，第18回DNA複製・分配ワークショップ，熱海，10/31
18．Hirai,K.，Sakamoto,S.，Kamimura,Y.，and ARAKI, H.「Pre-Landing Complex: a protein complex produced during the assembly of chromosomal DNA replication machinery in budding yeast」，日本分子生物学会2006フォーラム，名古屋，12/7
19．田中誠司，梅森稔子，平井和之，村松佐知子，上村陽一郎，荒木弘之「CDKによる染色体DNA複製開始の制御機構」，日本分子生物学会2006フォーラム，名古屋，12/8

EDUCATION

1．荒木弘之　酵母遺伝学フォーラム　三島　7/15-17

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1．Walter, J. C., and Araki, H（2006）Activation of pre-replication complexes. In DNA Replication and Human Disease **Cold Spring Harbor Laboratory Press** 89 - 104

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C. DEPARTMENT OF DEVELOPMENTAL GENETICS
C-a. Division of Developmental Genetics
Hiroshi Shimizu

RESEARCH ACTIVITIES

PUBLICATIONS
Papers

1． Yoshida, K., Fujisawa, T., Hwang, J.S., Ikeo, K., Gojobori, T. （2006） Degeneration after sexual differentiation in hydra and its relevance to the evolution of aging， **Gene**， 385 ， 64 - 70

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1． Fujisawa, T. Peptidomic approach to identify novel neuropeptides in *Hydra* University Heidelberg 9/5
2． Fujisawa, T. Compartmentalization of nervous system in *Hydra* University Heidelberg 9/6

POSTER PRESENTATIONS

1． Noro, Y., Fujisawa, T.「 Generation of stable transgenic *Hydra* 」，日本発生生物学会第39回大会，広島，5/31-6/3
2．藤澤敏孝「ヒドラの再生 」，日本動物学会第77回大会，松江，9/21-24
3．高橋俊雄、早川英介、西宮一藤澤千笑、藤澤敏孝 「 ペプチドーム解析によるヒドラ新規神経ペプチドの同定とその機能解析 」，日本動物学会第77回大会，松江，9/21-24
4． Fujisawa,T., Hirose, M., Fujisawa, C., Hayakawa, E., Takahashi, T. 「 Cholinergic system in *Hydra* and its evolutionary implication 」， *Second International Symposiumn on* Non-neuronal Acetylcholine， Mainz, Germany， 8/31-9/2
5． Fujisawa, T. 「 Compartmentalization of *Hydra*nervous system and its functional significance 」， International Symposium on Cellular Signaling during Development， Pune, India， 11/23-25

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C. DEPARTMENT OF DEVELOPMENTAL GENETICS
C-a. Division of Developmental Genetics

C. DEPARTMENT OF DEVELOPMENTAL GENETICS
C-a. Division of Developmental Genetics
Yasushi Hiromi

RESEARCH ACTIVITIES

PUBLICATIONS
Papers

1．Hiramoto, M. and Hiromi, Y. （2006） ROBO directs axon crossing of segmental boundaries by suppressing responsiveness to relocalized Netrin , **Nature Neuroscience** , 9 , 58 - 66
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2．Yasushi Hiromi Intra-axonal patterning: its mechanism and implications MRC National Institute for Medical Research 2006.5.10.
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4．Tony De Falco The amazing neuron:神経細胞に魅せられて 磐田南高校 2006.11.13

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1． 浅岡美穂 「 ショウジョウバエ生殖幹細胞とニッチの形成に関わる新規遺伝子の探索 」, 「幹細胞の可塑性と未分化性維持機構」公開班会議 , 東京 , 5/19
2．梅村 徹, 勝木健雄, 広海健「 Identification of a sub-axonally localized antigen. 」, 第9回国際膜研究フォーラム , 京都 , 2006.3.
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OTHERS

1．広海　健，1，日本分子生物学会　男女共同参画委員会委員 Dr. Hiromi served as a member of the Gender Equality Committee of The Molecular Biology Society of Japan.
2．，1，Dr. Hiromi co-chaired the Gender Equality Symposium "Career development of female researchers in the life sciences" at the 20th IUBMB Congress. Kyoto,
3．，1，Dr. Y. Hiromi served as an editor for Development, Growth & Differentiation.
4．，1，Dr. Y. Hiromi served as a member of the council of The Genetics Society of Japan.

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C. DEPARTMENT OF DEVELOPMENTAL GENETICS
C-b. Division of Gene Expression
Susumu Hirose

RESEARCH ACTIVITIES

RESEARCH ACTIVITIES

(1) Role of histone modifications and chromatin remodeling in epigenetic gene expression

Takahiro Nakayama, Kenichi Nishioka, Yi-Xin Dong, Tsukasa Shimojima, Kazuma Hanai, Takashi Yamamoto[1], Koji Akasaka[2] and Susumu Hirose ([1]Graduate Department of Gene Science, Hiroshima University, Higashi-Hiroshima, Japan; [2]Department of Biological Science, University of Tokyo, Tokyo, Japan)

Epigenetic maintenance of the expression state of the genome appears to be crucial for development. *Drosophila Trithorax-like* (*Trl*) gene is a member of *trithorax* group and encodes the GAGA factor that binds to a GAGAG sequence on DNA. The GAGA factor directs chromatin remodeling to its binding sites. We have shown that *Drosophila* FACT, a heterodimer of dSSRP1 and dSPT16, associates with the GAGA factor, binds to a nucleosome, and facilitates GAGA factor-directed chromatin remodeling. Physical and functional interactions between the GAGA factor and FACT implicated the GAGA factor-FACT complex in the modulation of chromatin structure for the maintenance of gene expression (Nakayama *et al*. 2006).
Previous study from this laboratory has shown that the GAGA factor recruits the SWI/SNF-type chromatin remodeling factor PBAP complex to the regulatory regions of *Hox*. Consisitent with this finding, we observed genetic interactions between *Trl* and *polybromo* encoding a unique subunit of the PBAP complex.
Previously we found that the GAGA factor directs chromatin remodeling and replacement of histone H3 by its variant H3.3, and maintains *white* expression against the heterochromatin spreading. In good agreement with this finding, we demonstrated that the GAGA factor recruits HIRA, a specific chaperone for histone H3.3, to the *white* locus, and also found that a *hira* mutation enhances PEV (Nakayama *et al*. 2007).
RSF is a chromatin remodeting factor consisting of a regulatory subunit RSF1 and a catalytic subunit ISWI. We found that RSF1 contributes to *Polycomb*-dependent silencing in addition to PEV.

(2) Chromatin transcription

Mikage Nakajima, Toshiharu Komori[1], Kenichi Nishioka, Tadashi Wada[1], Hiroshi Handa[1], Brock, H. W[2]., Mazo, A[3]., and Susumu Hirose ([1]Faculty of Bioscience and Biotechnology, Tokyo Institute of Technology, Nagatsuda, Yokohama, Japan; [2]Department of Zoology,

University of British Columbia, Vancouver, Canada,; [3]Department of Biochemistry, Thomas Jefferson University, Philadelphia, USA)

Biochemical studies have shown that Spt6 is a transcriptional elongation factor. To understand *in vivo* role of Spt6 in metazoans, we isolated mutants of *Drosophila spt6* through imprecise excision of a P-element inserted in the coding region of *spt6*, and started genetic studies on the factor.
Drosophila Ash1 encoding a SET domain protein is a member of *trithorax* group, but its function remains unknown. We are trying to isolate a *Drosophila* Ash1 complex from a transgenic fly line expressing epitope-tagged Ash1.
Much of the genome is transcribed into long noncoding RNAs (ncRNAs). Previous data suggested that *bithoraxoid* (*bxd*) ncRNAs of the *Drosophila* bithorax complex (BX-C) prevent silencing of *Ultrabithorax* (*Ubx*) and recruit activating proteins of the trithorax group (trxG) to their maintenance elements (MEs). We found that, surprisingly, *Ubx* and several *bxd* ncRNAs are expressed in nonoverlapping patterns in both embryos and imaginal discs, suggesting that transcription of these ncRNAs is associated with repression, not activation, of *Ubx*. Our data rule out siRNA or miRNA-based mechanisms for repression by *bxd* ncRNAs. Rather, ncRNA transcription itself, acting in *cis*, represses *Ubx*. The Trithorax complex TAC1 binds the *Ubx* coding region in nuclei expressing *Ubx*, and the *bxd* region in nuclei not expressing *Ubx*. We propose that TAC1 promotes the mosaic pattern of *Ubx* expression by facilitating transcriptional elongation of *bxd* ncRNAs, which represses *Ubx* transcription (Petruck *et al*., 2006).

(3) Role of DNA topology in the formation of active chromatin

Hirofumi Furuhashi, Kuniharu Matsumoto, Mikage Nakajima, Youhei Ogasawara and Susumu Hirose

Supercoiling factor (SCF) forms a complex with DNA topoisomerase II and generates negative supercoils into DNA. Previous studies from this laboratory have indicated that approximately twice activation of the male X chromosome in *Drosophila* is achieved through a balance between SCF forming an open and active chromatin and ISWI working toward a compact and silent chromatin (Furuhashi *et al*., 2006). To elucidate the mechanism underlying dosage compensation of the X chromosome, we started ChIP on chip analyses to examine distribution of SCF along the male X chromosome.
Based on the preferential binding of psoralen to negatively supercoiled DNA, we have succeeded in visualization of negatively supercoiled DNA domains within a cell. Using the method, strong signals have been detected on heat shock puffs of *Drosophila* salivary gland polytene chromosomes. The *scs* and *scs'* sequences are required for detection of the strong signals on the *hsp70* genes upon heat shock. Consistent with this finding, genetic studies revealed requirement of BEAF32 and ZW-5 proteins, that bind to *scs* and *scs'*, to detect the strong signals on *hsp70*.

(4) Functional cooperation between FACT and the MCM helicase complex facilitates initiation of chromatin DNA replication

Bertrand Chin-Ming Tan[1], Cheng-Ting Chien[2], Susumu Hirose and Sheng-Chung Lee[1,3] ([1]Institute of Molecular Medecine, National Taiwan University, Taipei, Taiwawn; [2]Institute of Molecular Biology, and [3]Institute of Biological Chemistry, Academia Sinica, Taipei, Taiwan)

Chromatin is suppressive in nature to cellular enzymes that metabolize DNA, mainly due to the inherent inaccessibility of the DNA template. Despite extensive understanding of the involvement of chromatin-modifying factors in transcription, roles of related activities in DNA replication remain largely elusive. Here we show that the heterodimeric transcriptional elongation factor FACT is functionally linked to DNA synthesis. Its involvement in DNA replication is partly mediated by the stable association with the replicative helicase

complex, MCM, and further by the coexistence with MCM on replication origin. Furthemore, relying on its nucleosome-reorganizing activity, FACT can facilitate chromatin unwinding by the MCM complex, which is otherwise inert on the nucleosomal template. As a consequence, the physical and functional interaction between FACT and MCM is an important determinant in the normal initiation of DNA replication and conserved component of the endogenous replication machinery, and support a model in which the concerted action of helicase and chromatin-modifying activities promotes chromosome replication (Tan *et al*., 2006).

(5) The heterotrimeric G protein signaling organizes cell movements during *Drosophila* gastrulation

Naoyuki Fuse, Takuma Kanesaki and Susumu Hirose

Gastrulation is a common developmental process and creates germ layers by dynamic morphogenetic movements. In gastrulation of a *Drosophila* embryo, the ventral cells acquire the mesodermal cell fate and undergo sequential cell movements. It has been shown that the *concertina* (*cta*) gene, encoding a Ga subunit of the heterotrimeric G proteins (G proteins), is required for an initial event of the cell movements. However, mechanisms underlying other cell movements and the G protein signaling *in vivo* are largely unknown. To address these issues, we characterize the G protein signaling in the gastrulation process.
Since Cta and other Ga subunits are expressed ubiquitously at the gastrulation stage, we examined mutants for these Ga subunits. Among them, the *Gai* mutant embryos showed gastrulation defects, which are distinct from the phenotypes of the cta mutant, suggesting that two Ga subunits regulate different cell movements.
Ric-8 has been thought to be an activator for the G protein signaling, however the role of Ric-8 *in vivo* is still controversial. We identified a missense mutant for Ric-8, *abortex*, which has been isolated as a female sterile mutant before. In the *abortex* mutant gastrulae, cell movements were perturbed and the Cta signaling was compromised. These results suggest that Ric-8 is involved in the turning of the G protein signaling to organize cell movements during gastrulation.

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7．広瀬　進「細胞記憶を支えるクロマチンダイナミクス」，第11回分生研シンポジウム，東京，5/17
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9．広瀬　進「ポリコームとトリソラックス群による転写制御」，大阪大学蛋白質研究所セミナー，大阪，10/2-3
10．中山貴博「GAGA因子によるヘテロクロマチンの侵攻を防ぐ分子機構」，国立遺伝学研究所研究会，三島，10/6-7
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C-c. Division of Molecular and Developmental Biology
Koichi Kawakami

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ORAL PRESENTATION

1 . Kawakami, K. Transposon-mediated gene trapping and enhancer trapping in zebrafish Washington University Medical School 3/3
2 . Kawakami, K. Development of a transposon-mediated Gal4 enhancer trap method in zebrafish and its application to inhibition of the neuronal function Harvard University 6/19

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2．川上浩一「トランスポゾンを用いたエンハンサートラップ法によるゼブラフィッシュ器官形成研究」,第3回骨と関節の代謝調節を考える基礎の会，木更津市かずさ，9/30-10/1
3．Urasaki, A., Morvan, G., Ueda, R., Kawakami, K.「Tol2の転移の研究：最小必須cis領域の解析とDrosophila中での転移」,2006年度組換え・ゲノム再編ワークショップ，淡路夢舞台国際会議場，11/27-29
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13．水澤寛太、浅川和秀、浦崎明宏、小谷友也、永吉さおり、岸本康之、日比正彦、近藤滋、川上浩一「トランスポゾンを用いた遺伝子トラップ法による、ゼブラフィッシュ成魚において部位特異的に発現する遺伝子の同定」,第12回 小型魚類研究会，三島，9/16-17
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23 . 小谷友也,川上浩一「 Misty somites, a maternally expressed gene essential for somite boundary formation identified by the transposon-mediated gene trap method in zebrafish 」, 日本発生生物学会第39回大会 , 広島 , 5/31-6/3
24 . 岸本康之,越田澄人,古谷-清木誠,川上厚志,Joechen Reiss,小原雄治,近藤寿人,川上浩一 「 The zebrafish bobtail mutation identifies the MOCS1 (the molybdenum cofactor synthesis step-1) gene that is required for the posterior body formation as an essential element of the Fgf/ERK signaling 」, 日本発生生物学会第39回大会 , 広島 , 5/31-6/3
25 . Takahashi, Y., Sato, Y., Kasai, T., Kawakami, K., Tanabe, K., Nakagawa, S. 「 Transposon-mediated gene transfer enables an exogenously introduced transgene to be stably retained and expressed in chicken embryos 」, 日本発生生物学会第39回大会 , 広島 , 5/31-6/3
26 . Sato, Y., Hayashi, E., Kawakami, K., Takeda, H., Horikawa, K. 「 Live-imaging of migrating lateral line primordium in zebrafish 」, 日本発生生物学会第39回大会 , 広島 , 5/31-6/3
27 . Kawakami, K. 「 The Tol2 transposable element: minimum cis-requirements and remobilization 」, ASM conferences: Mobile DNA , Banff, Alberta, Canada , 2/24-3/1

EDUCATION

1 . Kawakami, K. Technology workshop (Chair) 7th International Conference on Zebrafish Development & Genetics Madison, Wisconsin 6/14-18
2 . 川上浩一、酒井則行、新屋みのり、岸本康之 第12回 小型魚類研究会 三島 9/16-17

PATENT

1 . US7034115B1 , Transposase and method of gene modification , 川上浩一 , 科学技術振興機構(JST)

OTHERS

1 . Kotani, T.,Kawakami, K. , 2 , Poster prize at 7th International Conference on Zebrafish Development & Genetics

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D. DEPARTMENT OF POPULATION GENETICS
D-a. Division of Population Genetics

Naruya Saitou

RESEARCH ACTIVITIES

Division of Population Genetics
Saitou Naruya Group

Ape Genome Project Silver

Saitou Naruya, Sumiyama Kenta

In search of genetic changes responsible for human uniqueness, we are determining genomic sequences of chimpanzee and gorilla that are phylogenetically close to human, and do molecular evolutionary analyses. In 2006, we have two publications on this subject.
(i) We compared nucleotide sequences of chimpanzee and human Y chromosomes and described their evolutionary uniquness (Kuroki et al., 2006).
(ii) We examined human Endogenous Retrovirus (HERV)-R family in primates, and described their hromosomal location, gene expression, and evolution (Kim et.al., 2006).

Molecular evolution of developmental regulation

Sumiyama Kenta, Kim Hyung-Cheol, Ishibashi Minaka, Saitou Naruya

We are studying cis-control elements of the developmental genes by sequence analysis and gene transfer experiments of large scale genomic clones, in order to elucidate relationship between evolution of cis-elements and body plan.

Human population genetics

Saitou Naruya, Ishibashi Minaka

We are mainly interested in evolutionary relationship of various human populations. In 2006, we hade two publications on this subject.
(i) ABCC12 was discovered to be earwax (cerumen) gene (Yoshiura et al., 2006).
(ii) We discussed relationship between genetic and linguistic differentiation of people in Eurasia, in particular Japanese Archipelago (Saitou, 2006).

Evolution of blood group genes

Saitou Naruya

Blood group antigens are expressed on cell surface, and have a higher chance of being affected by bacteria or virus. Therefore, their genes may have undergone positive selection. We are studying evolution of ABO and Rh blood group genes for humans and non-human primates with collaboration of Dr. Kitano Takashi of Yamagata University School of Medicine and Professor Antoine Blancher of Paul Sabatier University at Toulouse, France.

Genome scale evolutionary analysis

Saitou Naruya, Kawai Yosuke, Kim Hyung-Cheol, Masuyama Waka, Suzuki Rumiko,

Takahashi Mahoo
We do genome-wide comparison of many protein coding and non-protein coding nucleotide sequences among various organisms to elucidate evolutionary patterns. In 2006, we conducted systematic analysis of SNP data (mainly done by Kawai), ultra-conserved elements (mainly done by Kim and Takahashi), protein domains (mainly done by Masuyama), and synonymous susbstitution (mainly done by Suzuki).

PUBLICATIONS

Papers

1．Masuya, H., Sezutsu, H., Sakuraba, Y., Sagai, T., Hosoya, M., Kaneda, H., Miura, I., Kobayashi, K., Sumiyama, K., Shimizu, A., Nagano, J., Yokoyama, H., Kaneko, S., Sakurai, N., Okagaki, Y., Noda, T., Wakana, S., Gondo, Y., and Shiroishi, T.（2006） A series of ENU-induced single base substitutions in a long-range cis-element altering Sonic hedgehog expression in the developing mouse limb bud.，**Genomics**，89，207 - 214

2．Kuroki, Y., Toyoda, A., Noguchi, H., Taylor, D. T., Itoh, T., Kim, D. 窶鉄., Kim, D.-W., Choi, S.-H., Kim, I.-C., Choi, H. H., Kim, Y. S., Satta, Y., Saitou, N., Yamada, T., Morishita, S., Hattori, M., Sakaki, Y., Park, H.-S., and Fujiyama, A.（2006） Comparative analysis of chimpanzee and human Y chromosomes unveils complex evolutionary pathway，**Nature Genetics**，38，158 - 167

3．Yoshiura K, Kinoshita A, Ishida T, Ninokata A, Ishikawa T, Kaname T, Bannai M, Tokunaga K, Sonoda S, Komaki R, Ihara M, Saenko VA, Alipov GK, Sekine I, Komatsu K, Takahashi H, Nakashima M, Sosonkina N, Mapendano CK, Ghadami M, Nomura M, Liang DS, Miwa N, Kim DK, Garidkhuu A, Natsume N, Ohta T, Tomita H, Kaneko A, Kikuchi M, Russomando G, Hirayama K, Ishibashi M, Takahashi A, Saitou N, Murray JC, Saito S, Nakamura Y, Niikawa N.（2006） A SNP in the ABCC11 gene is the determinant of human earwax type，**Nature Genetics**，38，324 - 330

4．Li, S.L., Yamamoto, T., Yoshimoto, T., Uchihi, R., Mizutani, M., Kurimoto, Y., Tokunaga, K., Jin, F., Katsumata, Y., and Saitou, N.（2006） Phylogenetic relationship of the populations within and around Japan using 105 short tandem repeat polymorphic loci.，**Human Genetics**，118，695 - 707

5．Kim, H.S., Yi, J.M., Hirai, H., Huh, J. W., Jeong, S. B., Jang, S. B., Kim, C. G., Saitou, N., Hyun, B. H., and Lee, W. H.（2006） Human Endogenous Retrovirus (HERV)-R family in primates: Chromosomal location, gene expression, and evolution.，**Gene**，370，34 - 42

6．Ezawa, K., OOta, S., and Saitou, N.（2006） Genomewide search of gene conversions in duplicated genes of mouse and rat.，**Molecular Biology and Evolution**，23，927 - 940

7．Aruga, J., Kamiya, A., Takahashi, H., Fujimi, T., Shimizu, Y., Ohkawa, K., Yazawa, S., Umesono, Y., Noguchi, H., Shimizu, T., Saitou N., Mikoshiba, K., Sasaki, Y., Agata, K., and Toyoda, A.（2006） A wide-range phylogenetic analysis of Zic proteins: Implications for correlations between protein structure conservation and body plan complexity.，**Genomics**，87，783 - 792

8．Kitano, T., Tian, W., Umetsu, K., Yuasa, I., Yamazaki, K., Saitou, N., and Osawa, M.（2006） Origin and evolution of gene for prolaction-induced protein.，**Gene**，Jul 28，0 - 0

9．Yuasa, I., Umetsu, K., Harihara, S., Kido, A., Miyoshi, A., Saitou, N., Dashnyam, B., Jin, F., Lucotte, G., Chattopadhyay, P. K., Henke, L., and Henke, J.（2006） Distribution of the F374 allele of the SLC45A2 (MATP) gene and fouder-haplotype analysis.，**Annals of Human Genetics**，69，1 - 10

10．斎藤成也（2006）ポストゲノム時代の進化解析，数理科学，44，73 - 80

11．斎藤成也（2006）神経系の基礎反応に関与する遺伝子群の進化，数理科学，44，64 - 68

12．斎藤成也（2006）神経中枢としての脳の進化，数理科学，44，72 - 76

13．斎藤成也（2006）進化の産物としての意識の階層構造，数理科学，44，72 - 77

14．斎藤成也（2006）地球世紀の幕開けに臨んで日本学術会議に望むこと，学術の動向，2月号，34 - 37

15．斎藤成也（2006）研究者とは，日本学術会議中部地区会議ニュース，，4 - 5

16．斎藤成也（2006）書評:「種の起源」の現代版入門書，科学，76，330 - 331
17．石橋みなか，斎藤成也（2006）東アジアにおける人類集団の遺伝的近縁関係，**DNA**多型，14，174 - 176
18．斎藤成也（2006）大陸からの道，大陸への夢，学士会会報，858，121 - 126
19．斎藤成也（2006）ゲノムの塩基配列と人間の意識をつなぐには，**WEDGE**，7月号，58 - 59
20．斎藤成也（2006）分科会に希望を託して，科学，76，834 - 0

ORAL PRESENTATION

1．斎藤成也　遺伝子の系統樹と系統ネットワーク　講義　東京大学大学院新領域創成研究科　6/29
2．斎藤成也　分子進化学　講義　東京大学理学部　6/7,14,28,7/5
3．斎藤成也　比較ゲノム学　講義　東京大学理学部　4/8
4．斎藤成也　進化の系統樹と系統ネットワーク　講義　北海道大学・理学部　7/7
5．斎藤成也　分子進化学　講義　埼玉大学・理学部　12/20-22
6．斎藤成也　DNAからみた人類進化　講義　福井工業大学　10/26
7．隅山健太　Dlx遺伝子間領域の進化ゲノム解析と遺伝子導入マウスによる発現解析　セミナー　筑波大学　1/24
8．隅山健太　分子進化解析入門 (ClustalW)　第15回 DDBJing 講習会 in 三島　国立遺伝学研究所・生命情報・DDBJ研究センター　6/15
9．隅山健太　形態進化のバックグラウンドとしてのゲノム転写制御領域進化　セミナー　科学博物館新宿分館　2/20

POSTER PRESENTATIONS

1．隅山健太「ほ乳類Dlx3-7遺伝子クラスター発現調節領域に起きた過去の急速な進化」，第8回進化学会大会，東京，8/29-31
2．Saitou, N.「Comparative genomic analyses of mammalian species including human.」，RIKEN Brain Science Center，Wako, Japan，7/5
3．Saitou N.「Role of DDBJ for constructing Asian Network on Bioinformatics-related Researches.」，Sokendai International Symposium on Networks on Science and Culture Exchanges among Asian Countries.，Hayama Japan，1/21
4．Saitou N.「Relic of ancient recombinations in gibbon ABO blood group genes suggests transsprcific polymorphism.」，GlycoT2006，Tsukuba,Japan，6/28
5．Saitou N.「Utility of chimpanzee and other non-human primate genomes for understanding evolution of modern human.」，International Symposium "Human Genome, Evolution, and Disease".，Tokyo，12/16
6．Saitou Naruya「Fundamentals of Molecular Evolution.」，5th Japan-korea-China Bioinformatics Training Course.，Mishima Japan，3/15
7．斎藤成也「生物学的基盤から創発する人種差別のメカニズム」，大14回東京大学大学院総合文化研究科シンポジウム「人種と人種主義を問う繧悦n域文化研究の視点から繧恂v」，東京，11/25
8．斎藤成也「自意識創出を促した自己言及を可能にする神経回路の進化とは」，国立遺伝学研究所研究会「遺伝子と意識をつなぐ」，東京，6/24
9．Saitou, N.「Phylogenetic analyses to genetic and linguistic data.」，MPI-CAS Partner Institute of Computational Biology.，Shanghai, China，4/27
10．Saitou, N.「Power and limit of evolutionary genome sequence analysis.」，Shanghai Center for Bioinformation Technology，Shanghai, China，4/29
11．Saitou, N.「Phylogenetic trees and networks.」，Nankai University Center for Combinatorial Mathematics，Tenjin, China，5/2
12．斎藤成也「霊長類ゲノムにひそむ網状の系統関係」，特定領域研究「ゲノム」4領域一般公開講演会，東京，1/29
13．斎藤成也「ゲノムが創り出した人間界と非人間界の断絶」，東京慈恵会医科大学DNA医学研究所10周年記念科学と人間公開フォーラム，東京，3/4
14．斎藤成也「日本人はどこから来て，どこへ行くのか」，カフェDEサイエンスin福井，福井市，4/21

15．斎藤成也「 あなたはどこから来たのか-日本人のDNA- 」，カフェDEサイエンスin福井，福井市，4/22
16．斎藤成也「 ゲノムの塩基配列と人間の意識をつなぐには 」，フォーラム地球学の世紀「ゲノム学が生み出す新しい世界像」，東京，5/15
17．斎藤成也「 遺伝子の系統樹と系統ネットワーク 」，第37回数学者のための分子生物学入門-新しい数学を造ろう-，東京，7/1
18．斎藤成也「 進化の系統樹と系統ネットワーク 」，北海道大学理学部セミナー，札幌市，7/7
19．斎藤成也「 諸民族の遺伝学的関係推定のためのDNA分析研究の現状 」，骨から探るオホーツク人の生活とルーツ，札幌市，7/8
20．斎藤成也「 遺伝子は35億年の夢を見る 」，大和成和病院心臓病センター設立10周年記念講演会，相模大野市，9/2
21．斎藤成也「 人類進化における中立進化 」，第78回日本遺伝学会大会，つくば市，9/26
22．斎藤成也「 遺伝子データから長谷部・鈴木の「変形説」を考える 」，鈴木尚記念シンポジウム，東京，10/15
23．斎藤成也「 遺伝子と苗字の地域差 」，第60回日本人類学会大会，高知市，11/3
24．斎藤成也「 こころ，高次脳機能，疾病と遺伝子 」，大阪大学蛋白質研究所セミナー「ヒトゲノムの進化的階層構造」，大阪市，11/16

EDUCATION

1．斎藤成也　国立遺伝学研究所研究会「遺伝子と意識をつなぐ」 東京　6/24

BOOK

1．斎藤成也（2006）遺伝子からの証拠　シリーズ進化学　第５巻　65 - 108
2．斎藤成也（2006）序章：人類進化の研究が世界観に与えてきた影響　シリーズ進化学　第５巻　1 - 12
3．Saitou, N.（2006）Relationship between genetic and linguistic differentiation of people in Eurasia.　**Proceedings of the Pre-symposium of RIHN and 7th ESCA Harvard-Kyoto Roundtable**　220 - 222
4．植田信太郎，斎藤成也（2006）古代DNA　シリーズ進化学　第２巻　219 - 238
5．斎藤成也（2006）遺伝子進化のメカニズム　シリーズ進化学　第２巻　15 - 66
6．斎藤成也（2006）序章：遺伝子を軸とする進化研究の発展　シリーズ進化学　第２巻　1 - 14

OTHERS

1．隅山健太，1，進化学会2006年大会・実行委員会・庶務

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D. DEPARTMENT OF POPULATION GENETICS
D-a. Division of Population Genetics
Toshiyuki Takano

RESEARCH ACTIVITIES

PUBLICATIONS
Papers

1．Yoshiura, K., Kinoshita, A., Ishida, T., Ninokata, A., Ishikawa, T., Kaname, T., Bannai, M., Tokunaga, K., Sonoda, S., Komaki, R., Ihara, M., Saenko, V. A., Alipov, G. K., Sekine, I., Komatsu, K., Takahashi, H., Nakashima, M., Sosonkina, N., Mapendano, C. K., Ghadami, M., Nomura, M., Liang, D.-S., Miwa, N., Kim, D.-K., Garidkhuu, A., Natsume, N., Ohta, T., Tomita, H., Kaneko, A., Kikuchi, M., Russomando, G., Hirayama, K., Ishibashi, M., Takahashi, A., Saitou, N., Murray, J. C., Saito, S., Nakamura, Y., and Niikawa, N.（2006）A SNP in the ABCC11 gene is the determinant of human earwax type.，**Nature Genetics**，38，324 - 330
2．Tatsuta, T., and Takano-Shimizu, T.（2006）Genetic architecture of variation in sex-comb tooth number in *Drosophila simulans*.，**Genetical Research, Cambridge**，87，93 - 107
3．Takeuchi T., Watanabe Y., Takano-Shimizu T., and Kondo S.（2006）Roles of jumonji and jumonji family genes in chromatin regulation and development.，**Dev. Dyn.**，235，2449 - 2459

POSTER PRESENTATIONS

1．Watanabe, Y., Takahashi, A., Itoh, M., and Takano-Shimizu, T.「Spontaneous mutation spectrum in *Drosophila melanogaster*.」，SMBE 2006 Conference，Tempe, Arizona，5/24-5/28
2．Takano-Shimizu,T.,Inomata, N.,Itoh, M.,and Kondo, R.「Detecting single-generation selection acting on inversion polymorphism in Drosophila」，47th Annual Drosophila Research Conference，Houston, Texas，3/29-4/2
3．岡本はるか,伊藤雅信,高橋文,高野敏行,山岡亮平,尾崎まみ「TaiwanG23に特徴的に見られる絶食時間に依る甘味及び苦味感受性の上昇」，日本味と匂学会 第40回記念大会，福岡，7/11-7/13
4．高橋文,高野敏行「分化した集団間の表現型変異及びDNA多型情報を用いたショウジョウバエの適応と種分化の解析」，日本進化学会 2006年大会，東京，8/29-8/31
5．高橋文,高野敏行「キイロショウジョウバエにおける胸部三叉の色素沈着パターンの集団内多型に関する分子基盤」，日本遺伝学会 第78回大会，つくば市，9/25-9/27
6．渡邊豊,高橋文,伊藤雅信,高野敏行「キイロショウジョウバエの自然突然変異スペクトラムの雌雄差」，日本遺伝学会 第78回大会，つくば市，9/25-9/27
7．高橋一男,田中健太郎,伊藤雅信,高野敏行「キイロショウジョウバエのX染色体に働く自然淘汰の検出」，日本遺伝学会 第78回大会，つくば市，9/25-9/27
8．近藤るみ,大島未来,吉藤裕佳子,猪股伸幸,伊藤雅信,高野敏行「ショウジョウバエ嗅覚・味

覚受容体遺伝子の変異に働く自然淘汰の調査 」, 日本遺伝学会　第78回大会 , つくば市 , 9/25-9/27
9 . 高橋亮,高野敏行 「 冗長なシステムにおける機能喪失型変異の進化動態:機能喪失型変異の固定は突然変異率が高いほど遅くなることがある 」, 日本遺伝学会　第78回大会 , つくば市 , 9/25-9/27
10 . 伊藤雅信,難波紀子,長谷川雅子,猪股伸幸,近藤るみ,高野敏行 「 遺伝子の機能ネットワーク推定の試み:ショウジョウバエを用いた集団遺伝学的アプローチ 」, 平成18年度日本蚕糸学会九州支部・関西支部　昆虫機能・利用学術講演会 , 福岡市 , 11/9-11/10

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E. DEPARTMENT OF INTEGRATED GENETICS
E-a. Division of Human Genetics

E. DEPARTMENT OF INTEGRATED GENETICS
E-a. Division of Human Genetics
Hiroyuki Sasaki

RESEARCH ACTIVITIES

PUBLICATIONS
Papers

1．鈴木智広，佐々木裕之（2006）ゲノムDNAメチル化解析法，細胞工学別冊 実験プロトコールシリーズ マウス表現型解析プロトコール，，160 - 166
2．金田正弘，佐々木裕之（2006）生殖細胞とゲノムインプリンティング，実験医学 (増刊号) エピジェネティクス医科学，20，1166 - 1171
3．Hata, K., Kusumi, M., Yokomine, T., Li, E., and Sasaki, H.（2006）Meiotic and epigenetic aberrations in Dnmt3L-deficient male germ cells.，**Mol. Reprod. Dev.**，73，116 - 122
4．Arnaud, P., Hata, K., Kaneda, M., Li, E., Sasaki, H., Feil, R., and Kelsey, G.（2006）Stochastic imprinting in the progeny of Dnmt3L-/- females.，**Hum. Mol. Genet.**，15，589 - 598
5．Yokomine, T., Hata, K., Tsudzuki, M., and Sasaki, H.（2006）Evolution of the vertebrate DNMT3 gene family: a possible link between existence of DNMT3L and genomic imprinting.，**Cytogenet. Genome Res.**，113，75 - 80
6．Kobayashi, H., Suda, C., Abe, T., Kohara, Y., Ikemura, T., and Sasaki, H.（2006）Bisulfite sequencing and dinucleotide content analysis of 15 imprinted mouse differentially methylated regions (DMRs): paternally methylated DMRs contain less CpGs than maternally methylated DMRs.，**Cytogenet. Genome Res.**，113，130 - 137
7．Ohhata, T., Hoki, Y., Sasaki, H., and Sado, T.（2006）Tsix-deficent X chromosome does not undergo inactivation in the embryonic lineage in males: implications for Tsix-independent silencing of Xist.，**Cytogenet. Genome Res.**，113，345 - 349
8．Fukasawa, M., Kimura, M., Morita, S., Matsubara, K., Yamanaka, S., Endo, C., Sakurada, A., Sato, M., Kondo, T., Horii, A., Sasaki, H., and Hatada, I.（2006）Microarray analysis of promoter methylation in lung cancers.，**J. Hum. Genet.**，51，368 - 374
9．Xie, Z.-H., Huang, Y.-N., Chen, Z.-X., Riggs, A.D., Ding, J.-P., Gowher, H., Jeltsch, A., Sasaki, H., Hata K., and Xu, G.-L.（2006）Mutations in DNA methyltransferase DNMT3B in ICF syndrome affect its regulation by DNMT3L..，**Hum. Mol. Genet.**，15，1375 - 1385
10．Hatada, I., Fukasawa, M., Kimura, M., Morita, S., Yamada, K., Yoshikawa, T., Yamanaka, S., Endo, C., Sakurada, A., Sato, M., Kondo, T., Horii, A., Ushijima, T., and Sasaki, H.（2006）Genome-wide profiling of promoter methylation in human.，**Oncogene**，25，3059 - 3064
11．Arima, T., Hata, K., Tanaka, S., Kusumi, M., Li, E., Kato, K., Sasaki, H., and Wake, N.（2006）Loss of the maternal imprint in Dnmt3Lmat-/- mice leads to a differentiation defect in the extraembryonic tissue.，**Dev. Biol.**，297，361 - 373
12．Watanabe, T., Takeda, A., Tsukiyama, T., Mise, K., Okuno, T., Sasaki, H., Minami, N.,

and Imai, H.（2006）Identification and characterization of two novel classes of small RNAs in the mouse germline: retrotransposon-derived siRNAs in oocytes and germline small RNAs in testes.，**Genes Dev.**，20，1732 - 1743
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14．佐々木裕之（2006）進化を促進するエピジェネティクス，現代思想，34，112 - 118
15．Sado, T., Hoki, Y., and Sasaki, H.（2006）Tsix defective in splicing is competent to establish Xist silencing.，**Development**，133，4925 - 4931

ORAL PRESENTATION

1．佐渡敬　東京大学医科学研究所大学院セミナー　東京大学医科学研究所　6/5
2．佐々木裕之　連合大学院特別講義　鹿児島大学　2/22
3．佐々木裕之　セミナー「発生・生殖とエピジェネティクス」　東京大学　2/3
4．佐々木裕之　山梨大学医学部講義　山梨大学医学部　6/29
5．佐々木裕之　九州大学歯学部講義「障害児歯科学」　九州大学歯学部　7/4
6．佐渡敬　東京工業大学大学院生命理工学研究科生命情報と区別講義第二　東京工業大学生命理工学研究科　7/12
7．佐々木裕之　COE特別講義　東京大学大学院理学系研究科　12/21-12/22

POSTER PRESENTATIONS

1．Hirasawa, R., Kaneda, M., Okano, M., Li, E., Sasaki, H.「Role of DNA methyltransferases (Dnmts) in the maintenance of genomic imprinting in mouse pre-implantation embryos.」，20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress.，Kyoto，6/18-6/23
2．Ohhata, T., Hoki, Y., Sasaki, H., and Sado, T.「Implications for Tsix-independent silencing of Xist in the embryonic lineage」，International Genomic Imprinting Workshop 2006，Tokyo，11/30-12/1
3．Watanabe, T., Tsukiyama, T., Sasaki, H., Minami, N., and Imai, H.「Identification and characterization of two novel classes of small RNAs in the mouse germline」，Cold Spring Harbor Meeting on Mouse Molecular Genetics，New York，8/30-9/3
4．佐々木裕之「ここまで分かったゲノムインプリンティング」，第20回モロシヌス研究会，熱海，6/15-6/16
5．Ohhata, T., Hoki, Y., Sasaki, H., Sado, T.「Significance of the antisense transcription across the Xist promoter in the transcriptional control of Xist.」，CNRS The Jacques Monod Conference, Epigenetics in development and disease: perspectives from multiple organisms，Aussois, France，1/5-1/7
6．Sado, T.「Mechanisms of Xist silencing by Tsix.」，International Symposium on X chromosome inactivation and epigenetic regulation.，Tsukuba，2/27
7．Sado, T.「Towards the understanding of antisense regulation at the Xist locus.」，CNRS, The Jacques Monod Conference, Epigenetics in development and disease: perspectives from multiple organisms,，Aussois, France，1/5-1/7
8．鈴木智広, 古海弘康, 幸田尚, 岩舩浩孝, 京野志保, 金田秀貴, 若菜茂晴, 佐々木裕之, 石野史敏, 城石俊彦「ENU Mutagenesisによる生殖細胞ゲノムインプリンティング確立異常変異体の探索」，第53回日本実験動物学会，神戸，5/11-5/13
9．佐々木裕之「ゲノムインプリンティングの機構と個体発生」，千里ライフサイエンスセミナー「クロマチン・ダイナミックスと高次生命現象」，豊中，3/15
10．佐々木裕之「哺乳類のゲノムインプリンティングの機構を探る」，第3回日本癌学会カンファレンス「動物モデルによる新時代のがん研究」，茅野，3/9-3/11
11．大畑樹也, 保木裕子, 佐々木裕之, 佐渡敬「TsixによるXistプロモーター領域のアンチセンス転写の意義」，第8回RNA学会年会，淡路，7/18-7/20
12．Kato, Y., Hata, K., Hisano, M., Okano, M., Li, E., Nozaki, M., Sasaki, H.「Establishment of paternal methylation imprints in normal and Dnmt-deficient male germ cells.」，20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress.，Kyoto，6/18-6/23

13．渡部聡朗, 竹田篤史, 簗山智之, 三瀬和之, 奥野哲郎, 佐々木裕之, 南直治郎, 今井裕「マウス生殖細胞から同定した新種のsmall RNA」, 第8回RNA学会年会, 淡路, 7/18-720
14．佐々木裕之「ゲノムインプリンティングの機構とポリコーム群」, 大阪大学蛋白質研究所セミナー「ポリコーム超分子複合体を介した細胞記憶の制御メカニズム」, 吹田, 10/2-10/3
15．佐々木裕之, 平澤竜太郎, 岡野正樹, リー エン「着床前胚におけるゲノム刷り込み維持機構」, 日本人類遺伝学会第51回大会, 米子, 10/17-10/20
16．秦健一郎, 有馬隆博, 久須美真紀, 田中智, 塩田邦郎, Li E, 佐々木裕之「DNAメチル化による生殖システム制御機構」, 日本人類遺伝学会第51回大会, 米子, 10/17-10/20
17．佐渡敬「哺乳類X染色体のエピジェネティクス」, 染色体学会2006年度（第57回）年会シンポジウム, 千葉, 11/24
18．佐渡敬「X染色体不活性化を担うXist遺伝子のアンチセンス制御」, 第78回日本遺伝学会シンポジウム「発生分化のgeneticsとepigenetics」, つくば, 9/24-9/27
19．Kato, Y., Hata, K., Hisano, M., Okano, M., Li, E., Nozaki, M., Sasaki, H.「Role of DNA methyltransferase genes in methylation of imprinted and repetitive sequences in mouse male germ cells.」, Cold Spring Harbor Laboratory Meeting on Germ Cells, New York, 10/11-10/15
20．Furuumi, H., Iwafune, H., Suzuki, T., Kohda, T., Kyono, S., Kaneda, H., Wakana, S., Shiroishi, T., Ishino, F., Sasaki, H.「Recent results of a screening system for mutants affected in genomic imprinting in the RIKEN ENU-Mutagenesis project」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
21．Hirasawa, R., Chiba, H., Kaneda, M., Okano, M., Jaenisch, R., Li, E., and Sasaki,H.「Role of DNA methyltransferases(Dnmts) in maintenance of genomic methylation imprints during mouse pre-implantation development」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
22．Kato, Y., Kaneda, M., Hata, K., Kumaki, K., Hisano, M., Kohara, Y., Okano, M., Li, E., Nozaki, M., and Sasaki,H.「Role of the Dnmt3 family in de novo methylation of imprinted and repetitive sequences during male germ cell development in the mouse」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
23．Watanabe, T., Takeda, A., Tsukiyama, T., Sasaki, H., Minami, N., Imai, H.「Two novel classes of small RNAs from mouse germline」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
24．渡部聡朗「マウス卵母細胞におけるレトロトランスポゾン由来small RNA」, 日本分子生物学会2006フォーラム, 名古屋, 12/6-12/8
25．Hata, K., Arima, T., Tanaka, S., Li, E., Shiota, K., Wake, N., and Sasaki, H.「Placental defects in mice lacking maternal methylation imprints」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
26．Sado, T.「Tsix-mediated Xist silencing requires antisense transcription across the Xist promoter.」, 2nd Conference on X-inactivation, Paris, 9/17-9/22
27．Sasaki, H.「DNA methyltransferases in genomic imprinting and transposon silencing in the mouse germ cells」, International Genomic Imprinting Workshop 2006, Tokyo, 11/30-12/1
28．Hisano, M., Kaneda, M., Okano, M., Sato, S., Shiota, K., Tsujimoto, N., Li, E., Sasaki, H. and Nozaki, M.「DNA methylation occures in a part of the genome associated with histones in sperm nuclei」, 日本分子生物学会2006フォーラム, 名古屋, 12/6-12/8
29．Hata, K.「Placental defects in mice lacking maternal methylation imprints.」, The 12th International Federation of Placenta Associations Meeting(IFPA), Kobe, 9/6-9/9
30．佐々木裕之「アレルギー疾患とエピジェネティクス（特別講演2）」, 第56回日本アレルギー学会秋季学術大会, 東京, 11/2-11/4
31．佐々木裕之「マウス生殖細胞におけるゲノム刷り込み機構」, 大阪大学蛋白質研究セミナー「生殖細胞形成と減数分裂」, 吹田, 11/21-11/22
32．佐々木裕之「生殖細胞におけるゲノムインプリンティングと反復配列のサイレンシング」, 第4回 クロマチン・フロンティアーズ・ジャパン, 名古屋, 12/5
33．加藤譲「生殖細胞におけるゲノムインプリンティングと反復配列のサイレンシング」, 第4回 クロマチン・フロンティアーズ・ジャパン, 名古屋, 12/5
34．Hata, K.「Epigenetic regulation during gametogenesis and embryogenesis.」, ASPIRE (The Asia Pacific Initiative on Reproductive Endocrinology) Symposium on Clinical and Laboratory Aspects of ART, Changsha, China, 3/31-4/2

EDUCATION

1．Sasaki, H., Ishino, F., and Kaneko-Ishino, T. International Genomic Imprinting Workshop 2006 Tokyo 11/30-12/1
2．Sasaki, H., Wynshaw-Boris, T., Guillemot, F., and Rossant, J. Cold Spring Harbor Meeting on Mouse Molecular Genetics New York 8/30-9/3
3．佐渡敬・阿部訓也 発生分化のgeneticsとepigenetics 日本遺伝学会第78回大会シンポジウム つくば 9/25-9/27

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1．Sasaki, H. and Ishino, F. (eds.)（2006）. **Genomic Imprinting (Special Issue of Cytogenet. Genome Res.)** 0 - 0
2．佐々木裕之 (分担執筆)（2006）. 分子細胞生物学事典（第２版） 0 - 0
3．佐渡敬（2006）エピジェネティクス ベーシックマスター 分子生物学 0 - 0
4．平澤竜太郎, 佐々木裕之（2006）DNAメチル化 再生医療教科書シリーズ, 第**3**巻再生医療のための分子生物学 80 - 96
5．久須美真紀, 佐々木裕之（2006）生殖・発生とエピジェネティクス 図説**ART**マニュアル**(**改訂第**2**版 492 - 496

PATENT

1．2006-294829，恒常不活性化X染色体を有するモデル非ヒト哺乳類動物およびその製造方法，佐渡敬，佐渡敬

OTHERS

1．佐々木裕之 ，1，日本人類遺伝学会評議員
2．佐々木裕之 ，1，(財)遺伝学普及会評議員
3．佐々木裕之 ，3，静岡県立静岡がんセンター研究所遺伝子組換え実験安全委員会委員
4．佐々木裕之 ，3，浜松医科大学遺伝子組換え実験安全委員会委員
5．佐々木裕之 ，3，三島社会保険病院倫理委員会委員
6．佐々木裕之 ，1，日本生殖医療エンジニアリング研究会世話人
7．佐々木裕之 ，３，バイオインフォマティックス-すぐに役立つ実践講座・講師（ぬまづ産業振興プラザ）
8．佐渡敬 ，2，日本遺伝学会奨励賞

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E. DEPARTMENT OF INTEGRATED GENETICS
E-b. Division of Agricultural Genetics

Keiichi Shibahara

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1． Sanematsu, F., Takami, Y., Barman, H.K., Fukagawa, T.,Ono, T., Shibahara, K-I., and Nakayama, T （０） Asf1 is required for viability and chromatin assembly during DNA replication in vertebrate cells.， **J. Biol. Chem.**， 281， 13817 - 13827
2． Iiizumi, S., Nomura, Y., So, S., Uegaki, K., Aoki, K., Shibahara, K-i., Adachi, N., and Koyama, H. （０） Simple, one-week method to construct gene-targeting vectors: application to production of human knockout cell lines.， **Bio Techniques**， 41， 311 - 316
3． Berman, HK, Takami, Y., Ono, T., Nishijima, H., Sanematsu, F., Shibahara, K-i. and Nakayama, T. （０） Histone acetyltransferase 1 is dispensable for replication-coupled chromatin assembly but contributes to recover DNA damages creasted following replication blackage in verterate cells.， **Biochem. Biophys. Res. Commun.**， 345， 1547 - 1557
4． Endo, M., Ishikawa, Y., Kaya, H., Araki, T., Shibahara, K-i., Ito, Y., Osakabe, K., Abe, K., Ichikawa, H., Valentine, L., Hohn, B. and Toki, S. （０） Enhanced homologous recombination and T-DNA integration in chromatin assembly factor-1 mutants in /Arabidopsis thaliana/.， **EMBO J.**， 25， 5579 - 5590
5． 柴原慶一（０）DNA複製に伴うヌクレオソーム構築機構， 上原記念生命科学財団研究報告集， 20， 211 - 215
6． Nishijima, H., Nakayama, J. Yoshioka, T.,Kusano, A., Nishitani, H., Shibahara, K-I. and Nishimoto, T.（０） Nuclear RanGAP is required for the heterochromatin assembly and is reciprocally regulated by histone H3 and Clr4 histone methyltransferase in /Schizosaccharomyces pombe/.， **Mol. Biol. Cell**， 17， 2524 - 2536
7． Ono, T., Kaya, H., Takeda, S., Abe, M., Ogawa, Y., Kato, M., Kakutani, T., Scheid, O.M., Araki, T. and K-i. Shibahara （０） Chromatin assembly factor 1 ensures the stable maintenance of silent chromatin states in /Arabidopsis/， **Genes to Cells**， 11， 153 - 162

ORAL PRESENTATION

1． 柴原慶一　ヒト培養細胞における遺伝子発現誘導型のコンディショナルジーンターゲティング法の確立とヒトDDM1の機能解析　第16回染色体コロキウムーゲノム科学と染色体ー　千葉大学けやき会館　11/24-25

POSTER PRESENTATIONS

1． 小野達也、西嶋仁、飯泉晋、足立典隆、小山秀機、柴原慶一 「ヒトDDM1がヘテロクロマチン形成維持に果たす役割」，日本分子生物学会2006フォーラム，名古屋市，12/7
2． Shibahara, K-i., Ono, T., and Nishijima, H.「 Chromatin assembly factor 1 ensures the

stable maintenance of chromatin states」, 20th IUBMB Congress , Kyoto , June 18-23
3 . Takami, Y., Sanematsu, F., Ono, T., Shibahara, K-i. and Nakayama, T.「 Roles of CAF-1 and ASF1 in a nucleosome assembly coupled with DNA replication and cell prolifieration in vertebrate cells. 」, 20th IUBMB Congress , Kyoto , June18-23
4 . Barman, H., Takami, Y., Nishijima, H., Ono, T.,Shibahara, K-i., and Nakayama, T.「 The impact of HAT1 in forming stable H4-containing complex in the cytoplasm of chicken DT40 cells. 」, 20th IUBMB Congress , Kyoto , June 18-23
5 . 西嶋仁、小川裕也、小野達也、 若田裕香、柴原慶一 「 ヒストンバリアントmacroH2Aヌクレオソームに特異的に集積するスプライソソーム構成因子群 」, 第8回RNAミーティング（第8回日本RNA学会年会）, 淡路市 , 7/18-20
6 . 柴原慶一、小野達也、西嶋仁 「 DDM1によるヘテロクロマチン形成にRNA分子が関与する可能性 」, 特定領域研究「RNA情報発現系の時空間ネットワーク」第4回合同班会議 , 宮崎市 , 1/11

PATENT

1 . 2006-288020 , テトラサイクリン誘導型の遺伝子発現系に使用する目的遺伝子導入ベクター、トランスアクチベーター発現用ベクターおよびその用途 , 柴原慶一、 小野達也 , 大学共同利用機関法人情報・システム研究機構

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E. DEPARTMENT OF INTEGRATED GENETICS
E-b. Division of Agricultural Genetics

E. DEPARTMENT OF INTEGRATED GENETICS
E-b. Division of Agricultural Genetics
Tetsuji Kakutani

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1． Ono, T., Kaya, H., Takeda, S., Abe, M., Ogawa, Y., Kato, M., Kakutani, T., Mittelsten Scheid, O., Araki, T., Shibahara, K. （2006） Chromatin assembly factor 1 insures the stable maintenance of silent chromatin states in Arabidopsis , **Genes to Cells** , 11 , 153 - 162
2． 佐瀬英俊,角谷徹仁 （2006） DNAメチル化と遺伝子制御とトランスポゾン , 実験医学 , 24 , 1220 - 1224
3． Jullien, P., Kinoshita, T., Ohad, N., Berger, F.（2006） Maintenance of DNA methylation during the Arabidopsis life cycle is essential for parental imprinting. , **The Plant Cell** , 18 , 1360 - 1372

ORAL PRESENTATION

1．角谷徹仁 集中講義 北海道大学農学部 4/13-4/14
2．角谷徹仁 集中講義 大阪大学理学部 6/7-6/9
3．角谷徹仁 集中講義 埼玉大学理学部 9/5-9/7
4．角谷徹仁 集中講義 静岡大学理学部 9/28-9/29
5．角谷徹仁 集中講義 東京大学理学部 10/26-10/27
6．角谷徹仁 集中講義 東京大学農学部 10/13

POSTER PRESENTATIONS

1． Miura A, Nakamura M, Kato M, Kakutani T 「 Basis for CACTA Transposon Immobilization by DNA Methylation 」, 17th International Conference on Arabidopsis research , , 6/28-7/2
2．三浦明日香,角谷徹仁「 トランスポゾンCACTAの転移と脱メチル化 」, 遺伝学会 , つくば , 9/27
3． 佐瀬英俊,角谷徹仁 「 シロイヌナズナにおける機能喪失型bonsaiエピジェネティック変異 」, 遺伝学会ワークショップ「染色体動態とエピジェネティクス」, つくば , 9/25
4． Saze H, Kinoshita T, Miura A, Kato M, Kinoshita Y, Takashima K, Kakutani T 「 Epigenetic inheritance of developmental variation, transposon activity, and DNA methylation in Arabidopsis 」, The 52th NIBB Conference, Reproductive Strategy , 岡崎 ,
5． Saze H,Kakutani T 「 Loss-of-function epigenetic mutation induced in the ddm1 (decrease in DNA methylation) background. 」, The 17th International Conference on Arabidopsis Research , Madison, WI, USA ,

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E. DEPARTMENT OF INTEGRATED GENETICS
E-c. Division of Brain Function

E. DEPARTMENT OF INTEGRATED GENETICS
E-c. Division of Brain Function
Tatsumi Hirata

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1． Gil, V., Nicolas, O., Mingorance, A., Urena, J.M., Tang, B.L., Hirata, T., Saez-Valero, J., Ferrer, I., Soriano, E., del Rio, J.A. （0） Nogo-A and Nogo receptor expression in the human hippocampus in neuronal aging and Alzhheimer's disease， **J Neuropathol Exp Neurol**，65，433 - 444
2． Kawasaki, T., Ito, K. and Hirata, T. （0） Netrin 1 regulates ventral tangential migration of guidepost neurons in the lateral olfactory tract.， **Development**，133，845 - 853

POSTER PRESENTATIONS

1． Kawasaki, T.,Hirata, T.「Distinctive guidance of main and accessory olfactory bulb axons in the lateral olfactory tract.」, CSHL meeting "Axon Guidance, Synaptogenesis & Neural Plastisity"，CSHL New York，9/13-17
2． 川崎能彦,平田たつみ「主嗅球と副嗅球の神経軸索ガイダンス機構」，第29回日本神経科学学会大会，京都，7/20
3． 伊藤圭祐,川崎能彦,平田たつみ「Protein kinase 阻害剤・K252aの移動性ニューロンに対する効果」，第29回日本神経科学学会大会，京都，7/21
4． 川崎能彦,平田たつみ「嗅覚2次神経回路形成機構」，日本発生生物学会第39回大会，広島，6/3
5． Yamatani, H.,Hirata, T.「Identification of temporally different proteins expressed during the collateral branching of the lateral olfactory tract」，20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress，京都，7/20

EDUCATION

1． 平田たつみ　小田洋一　男女共同参画シンポジウム　神経科学における男女共同参画はどうあるべきか？　第29回日本神経科学学会大会　京都　7/20

OTHERS

1．平田たつみ，1，日本神経科学学会　男女共同参画推進委員

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F. GENETIC STRAINS RESEARCH CENTER
F-a. Mammalian Genetics Laboratory
Toshihiko Shiroishi

RESEARCH ACTIVITIES

(1) A novel long-range enhancer to specify the Sonic hedgehog (Shh) expression in the oral cavity morphogenesis

Tomoko Sagai, Takanori Amano, Yoichi Mizushina, Hiromi Yamamoto, Noriko Sakurai-Yamatani, Ayaka Okagaki, Masaru Tamura and Toshihiko Shiroishi

Shh is a secreted glycoprotein that is essential for the fundamental morphogenesis in vertebrate embryogenesis. In developing embryos, Shh expresses in various organogenesis processes including head, lung, heart and limbs formation. Mutant mice in which normal Shh expression is affected in the organogenesis exhibit severe defects in the relevant organs. The Shh expression in a particular organogenesis is controlled by specific cis-acting regulatory elements. Recently, such several long-range enhancers have been identified by cross species comparison of genome sequences and exploration of conserved sequences among evolutionary remote species. A noncoding sequence, MFCS1, localized in the 1Mb upstream of the Shh coding sequence is one of such cis-acting elements, which includes limb bud-specific Shh enhancer (Sagai et al., 2005).
Here we report another novel long-range enhancer involving in morphogenesis of mouse oral cavity. MFCS4 is a phylogenetically conserved noncoding sequence residing in the 800kb upstream region of the Shh coding. In order to test whether the sequence acts as cis-acting regulatory element, first we carried out transgenic assay with a LacZ-reporter gene flanked by the MFCS4 fragment. In the transgenic mice, we found that MFCS4 induces expression of the reporter gene specifically in the oral epithelium of palate, epiglottis and arytenoid. Next, we conducted ES targeting to generate MFCS4 knockout (KO) mice. The mice heterozygous for the MFCS4 KO did not show any defect. By contrast, the KO homozygotes caused hypoplastic defects in the palate and epiglottis surrounding the naso-pharyngeal opening. Because of this defect, airway of the homozygotes was disturbed, and eventually it resulted in neonatal lethality.
In the oral cavity of wild-type embryos, endogenous Shh expression was detected in palatal and tongue epithelium and partially overlapped the expression domain of the reporter gene in the transgenic mice. Then, we examined the Shh expression in the MFCS4 KO homozygotes. Section in situ hybridization with a Shh riboprobe showed that in the MFCS4 KO homozygotes, Shh did not express in the oral epithelium where the signal of transgenic reporter gene was detected. Finally, in order to confirm that MFCS4 is a cis-acting element, we carried out a test cross of the Shh-coding KO and the MFCS4 KO mice. From the above cross, we generated compound heterozygotes of the both KO alleles. We observed that all compound heterozygotes exhibited the phenotype almost identical to that of the single MFCS4 KO homozygotes. Thus, all data demonstrated that MFCS4 is a cis-acting element including glossopharyngeal specific long-range enhancer of Shh.

(2) Chromatin dynamism of a long-range cis-regulator for limb bud-specific Shh expression

Takanori Amano, Tomoko Sagai, Hideyuki Tanabe1 and Toshihiko Shiroishi
(1The Graduate University for Advanced Studies)

MFCS1 (mammal-fish conserved sequence) is located at the intron 5 of Lmbr1 locus, which is 1 Mb apart from the Shh coding sequence. We have reported that elimination of MFCS1 causes a defect of Shh expression and distal truncation of skeletal elements of mouse limb. It is suggested that MFCS1 is a limb bud-specific cis-acting regulatory element of Shh (Sagai et al., 2005). This fact raises a question of how MFCS1 controls a transcription of Shh beyond such a long distance. To address this question, we paid attention on higher-order chromosomal structure surrounding the Shh locus.
To examine topological relationship of the Shh coding region and MFCS1, we performed 3D-FISH analysis using fluorescent-labeled probes that hybridize with these two genomic regions. We dissected anterior, intermediate and posterior portions of developing limb buds at E10.5 embryos. The posterior portion of limb bud is referred to as zone of polarizing activity (ZPA) and it expresses Shh exclusively in wild-type mice. We immediately prepared single cell suspension from the each dissected specimen, and used for the FISH analysis. After capturing 3D images of the two fluorescent signals, physical distance between the Shh coding region and MFCS1 was computationally calculated. This result clearly indicated that the mean distance in the posterior limb bud cells was significantly shorter than that in the intermediate limb bud cells, suggesting that MFCS1 tends to approach the Shh locus in the Shh-expressing cells. Notably, the mean Shh-MFCS1 distance in the anterior limb bud cells was somewhat smaller than that in the posterior limb bud cells, but the value was close to that in the posterior limb bud cells. It is known that many mouse mutants exhibit ectopic Shh expression at the anterior margin of limb buds, and it lead to preaxial polydactyly. It is, therefore, conceivable that the anterior limb bud cell potentially has a competence to express Shh. Thus, adjoining of physically distant two regions, MFCS1 and the Shh coding, implies that the cells have a competence for expressing Shh.
To further investigate the chromatin dynamism surrounding the Shh coding and MFCS1 regions, we adopted a method of chromosome conformation capture (3C). Limb buds from E10.5 embryos, which express Shh at very high level, were used for the analysis. We used limb buds from E12.5 embryo, in which Shh expression already ceased, as a control. As a result, we captured an expected positive signal only in the limb buds from E10.5 embryos, suggesting that MFCS1 physically interacts with the Shh coding region in Shh-expressing cells.

(3) Molecular mechanisms of epithelium formation of skin and gastrointestinal tract in mice

Masaru Tamura, Shigekazu Tanaka, Tomoaki Fujii, Hiromitsu Komiyama1 and Toshihiko Shiroishi
(1Graduate School of Medicine, Juntendo University)

Epithelial cells are tightly connected to one another in sheets and tubes, and form epidermis and mucosal epithelium of gastrointestinal tracts. Homeostasis of the epithelial linings is controlled by the balance between proliferation of the stem cells and apoptosis following terminal differentiation. Disruption of this balance may cause abnormal cell proliferation and several diseases like as cancers. However, our knowledge on the molecular basis underlying the epidermis development and homeostasis is still limited. We have overcome this problem using the forward and reverse genetics approaches. We performed three fundamental studies: (i) Screening and phenotype analysis of mutant mice, which exhibit abnormal epidermal development; (ii) identification of causative gene of these mutant mice; (iii) analysis of these gene functions using the transgenic and gene knockout technique. We identify five novel genes during the analysis of just one mutant mouse. Four of five these genes are clustering in the mouse chromosome 15, and these genes have several

conserved sequences and novel functional motifs. Each of these genes is expressed in the epidermis and gastrointestinal tract (GI) in a tissue specific manner, and expression patterns and levels were depended heavily on proximal-distal axis in the GI tract. We are now examining the function of these genes using the reverse genetics approach.

(4) Transgenesis with a modified-BAC DNA harboring the Rim3-type GsdmA3 mutation recaptures the mutant skin phenotype

Shigekazu Tanaka, Masaru Tamura, Aya Aoki1, Tomoaki Fujii, Hiromitu Komiyama2, Toshihiko Shiroishi
(1Department of Neurosurgery, Tokyo Metropolitan Hiroo Hospital 2Graduate School of Medicine, Juntendo University)

In our previous study, we showed that a spontaneous dominant skin mutant, Rim3, has a point mutation in Gasdermin A3 (GsdmA3). The Rim3 mutation has a single base substitution, 1124 G to A, which results in a missense change, alanine 348 threonine. To confirm that the genetic alteration found in the GsdmA3 gene causes the mutant phenotype, in this study we carried out transgenesis using a modified-BAC DNA containing the Rim3-type GsdmA3 mutation (alanine 348 threonine). A BAC clone RP23-438D7 contains 160 kb genomic region that includes GsdmA cluster except for GsdmA1 and most likely contains the promoter and the cis-regulatory elements of GsdmA3 gene within its 115 kb upstream fragment of GsdmA3. We introduced the Rim3-type mutation into the exon 9 of GsdmA3 in the RP23-438D7 clone by means of BAC modification technology. The modified BAC construct was transferred into genome of wild-type (DBA/2J x C57BL/6J)F1 mice. We selected transgenic mice by genotyping for the vector sequence, and established three transgenic founder lines carrying the Rim3-type GsdmA3 mutation. We found that these all three lines exhibit skin phenotype similar to that of Rim3. Histological analysis revealed that the transgenic mice have degenerated hair follicles at 10 months of age as was observed in Rim3 mutant mice. In contrast, transgenic mice that express wild-type GsdmA3 did not exhibited any phenotype in the skin. The result clearly demonstrated that GsdmA3 is the causative gene for Rim3.

(5) Disruption of genetic interaction between two autosomal regions and the X chromosome causes hybrid breakdown in a mouse intersubspecific cross

Ayako Oka, Toshihiro Aoto1, Yoshikazu Totsuka1, Riichi Takahashi1, Masatsugu Ueda1, Akihiko Mita, Noriko Sakurai-Yamatani, Hiromi Yamamoto Nobuo Takagi2, Kazuo Moriwaki3 and Toshihiko Shiroishi
(1The YS Institute, Inc., 2Hokusei Gakuen University, 3RIKEN BioResource Center)

Reproductive isolation that initiates speciation is likely caused by incompatibility between multiple loci in organisms belonging to genetically diverging populations. Laboratory C57BL/6J mice, which predominantly originated from Mus musculus domesticus, and a MSM/Ms strain derived from Japanese wild mice (M. m. molossinus) are reproductively isolated. These two strains exhibit hybrid breakdown: F1 hybrids are fertile, but succeeding intercrosses result in male sterility. A consomic strain, C57BL/6J-ChrXMSM, which carries the X chromosome of MSM/Ms in the C57BL/6J background, shows male sterility, suggesting genetic incompatibility of the MSM/Ms X chromosome and other C57BL/6J chromosome(s). In this study, genome-wide linkage analysis and subsequent QTL mapping successfully detected significant QTLs on chromosomes 1 and 11 that interact with the X chromosome and are responsible for the hybrid breakdown. This was confirmed by the observation that introduction of the MSM/Ms chromosomes 1 and 11 into the C57BL/6J-ChrXMSM background partially restored fertility. Thus, genetic interactions between the two autosomal regions and the X chromosome have a crucial role in proper sperm differentiation, and their disruption causes hybrid breakdown. Intracytoplasmic sperm injection and zona-free in vitro fertilization showed that the C57BL/6J-ChrXMSM spermatozoa have a defect in penetration of the extracellular zona pellucida. Moreover, two-

dimensional electrophoretic proteome study of whole proteins from sperms provided considerable candidates responsible for the sterility of C57BL/6J-ChrXMSM males.

(6) QTL analysis of hereditary predisposition of obesity based on inter-subspecific cross of C57BL/6J and MSM/Ms strains

Akiteru Maeno, Hideko Watanabe, Akihiko Mita, Ayako Oka and Toshihiko Shiroishi

Obesity is a highly heritable and genetically complex trait with hundreds of potential loci identified. In order to elucidate the genetic determinants of this disease, we are taking approach to use mouse models for heritable obesity. In this study, we conducted genetic analysis of obesity-related quantitative traits based on the cross between a standard laboratory mouse strain C57BL/6J (B6) and a Japanese wild mouse-derived strain MSM/Ms (MSM). The quantitative traits that we analyzed in this study are followings: body weight, body weight that excludes total fat pat weight (lean body weight), percentage of fat pat surrounding each of three visceral tissues (gonad, retroperitoneum and mesenterium) to lean body weight, percentage of sum of the above three visceral fad pat weight to lean body weight, percentage of subcutaneous fad pat weight to lean body weight and total fat pat weight to lean body weight (adiposity index: A.I.).
MSM has higher A.I. value than that of B6 at ten weeks of age, and this tendency became more prominent as age proceeded. This suggests that MSM shows higher predisposition to obesity as compared with B6. For the quantitative trait loci (QTL) analysis, we crossed B6 and MSM mice and generated F1 hybirds, and subsequently intercrossed the F1 mice and obtained totally 272 F2 progeny. Then, we carried out QTL analysis to identify loci responsible for eight obesity-related traits described above. First, single-locus genome scans analysis identified four QTLs on Chr 2, 6, 9 and 13, all of which control A.I. value. All these QTLs showed sex-dependent effect. For the three QTLs on Chr 6, 9 and 13, MSM alleles increase A.I. value, while B6 allele increases the A.I. value for the QTL on Chr 2. Because all four QTLs explain relatively small proportion of the variance observed in the F2 progeny (only 9 to 11% of the total variance), many other minor QTLs and epistatic interaction of two independent loci were expected to be contributed to the genetic variance. Therefore, we implemented pairwise genome scan analysis for the same data set of the 272 F2 progeny. As a result, we identified a significant epistatic interaction between two loci on Chr 9 and 13.
QTL analyses with Multiple Interval Mapping (MIM) and Bayesian Interval Mapping (BIM) are thought to be more suitable for the cases in which multiple QTLs are responsible complex traits. We need further studies using the above analyses to reveal hidden QTLs that were not detected in this study.

(7) Genetic dissection of obesity using mouse consomic strains

Toyoyuki Takada, Akiteru Maeno and Toshihiko Shiroishi

Obesity is a common disease and a major risk to develop type 2 diabetes mellitus and metabolic syndrome. Genetic obesity is generally thought to be multifactorial disease, which is caused by multiple genetic determinants and influence of environmental factors. To understand pathology of obesity, genetic analysis of responsible genes for this complex trait has been prominent issue as in many common human diseases. We are taking approach to use mouse models for obesity. C57BL/6J-ChrMSM consomic strains were constructed by transferring individual chromosomes from MSM/Ms strain, derived from Japanese wild mouse, Mus musuculs molossinus, into the genetic background of a standard laboratory strain C57BL/6J, which was derived from west European wild mouse, M. m. domesticus. These consomic strains are strikingly useful for chromosome mapping of various phenotypes, because above two mouse strains showed extremely large extent of phenotypic variations based on vast amount of genomic differences (~ 1% SNP). Our preliminary phenotyping of the consomic strains indicated a variety of range in susceptibility or resistance to obesity or obesity-related phenotypes among the strains. Based upon the

strain difference, we intend to explore genes and genetic pathways underlying the polygenic obesity. At the first step, now we are conducting more detailed characterization of the phenotype of each consomic strain using following tests: 1) measurement of consumption of foods (normal chaw and high fat diet, etc.) and body weight, 2) detection of metabolism-related parameters (activity, body fat content, blood and hepatic lipid content, plasma insulin and leptin levels, etc), 3) radiographical measurement of adipose tissue mass using computer tomography (CT) scanning, 4) transcriptome analysis of metabolism-related tissue of all consomic strains.

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OTHERS

1．城石俊彦 , 1 , 遺伝学会企画集会幹事
2．城石俊彦 , 1 , 実験動物学会評議委員
3．城石俊彦 , 1 , Editorial boad of Mammalian Genome
4．城石俊彦 , 1 , Editor of Genes & Genetic Systems
5．城石俊彦 , 1 , "The Scientific World" Associate editor for Genetics
6．城石俊彦 , 1 , Editor of DNA Research
7．城石俊彦 , 3 , 文部科学省科学技術政策研究所科学技術動向センター専門調査員
8．城石俊彦 , 3 , (独)理化学研究所バイオリソースセンター検討委員会委員
9．城石俊彦 , 3 , (財)遺伝学普及会常任理事
10．城石俊彦 , 3 , 日本学術振興会ゲノムテクノロジー第164委員会委員
11．城石俊彦 , 3 , 日米科学技術協力事業組み換えDNA研究計画委員会委員
12．城石俊彦 , 3 , (財)順天堂災害医学研究所理事

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F. GENETIC STRAINS RESEARCH CENTER
F-b. Mammalian Development Laboratory
Yumiko Saga

RESEARCH ACTIVITIES

Mammalian Development Laboratory

RESEARCH ACTIBITIES

(1) Molecular mechanism of somite segmentation

Mitsuru MORIMOTO, Nobuo SASAKI, Makoto KISO and Yumiko SAGA

We have been investigating the in vivo function of the bHLH transcription factor, Mesp2, for which the periodic expression of both mRNA and protein appears in the anterior PSM. Mesp2 plays key roles in the anterior PSM, at the point of transition of the paraxial mesodermal cells from the PSM to somites. In addition, we have previously shown that Mesp1 is a closely related member of the Mesp-family of genes, which share significant sequence homology in their bHLH regions. We have attempted to define the functional domains of the Mesp2 protein by focusing on the vertebral development reflecting rostro-caudal properties of somites in vivo. We find that Mesp2 contains a degradation domain, which acts as a target of proteasome-mediated proteolysis and appears to play this role in vivo. We have also defined the nuclear localization signals (NLS) and constructed a minimum Mesp2 protein (P2-HD) composed of the NLS, bHLH and the degradation domains. The ability of the P2-HD as a transcription factor in vivo was examined. Some of the defects that had been previously observed in the Mesp2-null mice were rescued in the knock-in mice but only in the posterior half of the body, indicating differential effects of P2-HD along the anterior-posterior (AP) axis. In addition, quantitative analysis of the expression along the AP-axis revealed that the relative levels of Mesp2 increased, whereas Mesp1 is down-regulated in the later stages of development by the activities of Mesp2 in the wild-type embryo. Moreover, we have found that somitogenesis in the early stages is more susceptible to changes in the Mesp gene dosage, indicating that a threshold level of Mesp activity must be required for the progression of normal somitogenesis.

(2) Regulation of Mesp2 gene expression

Mitsuru Morimoto, Masayuki OGINUMA, Nobuo Sasaki and Yumiko SAGA

The transcription factor, Mesp2 plays essential roles in the segmental border formation and establishing rostral-caudal patterning within somites. A possible Mesp2 target gene, Ripply2 is identified by microarray analysis as one of genes down-regulated in the Mesp2-null mouse. Ripply2 encodes a possible transcriptional co-repressor containing WRPW motif. We find that Mesp2 could bind to the enhancer of Ripply2 gene, indicating that Ripply2 is a direct target of Mesp2. We asked whether the Ripply2 is responsible for the repression of genes under the control of Mesp2 by generating the Ripply2 knockout mouse. Unexpectedly, Ripply2-null embryo showed rostralized phenotype that is contrastive to that of Mesp2-null mice. Gene expression studies together with genetic analyses revealed that Ripply2 turned out to be a negative regulator of Mesp2. The lack of Ripply2 results in the

prolonged expression of Mesp2, which leads to the rostralized phenotype via suppressing Notch signaling. The Mesp2/ Ripply2 double-null mutant shows almost similar phenotype to that of Mesp2-null mutant, confirming that Ripply2 functions exclusively thorough suppression of Mesp2.

(3) Functional analyses of Hesr1 and Hesr2 in the cardiovascular development
Hiroki KOKUBO, Raul VizcardoSakoda, and Yumiko SAGA
The establishment of chamber specificity is an essential requirement for cardiac morphogenesis and function. Hesr1 and Hesr2 are specifically expressed in the atrium and ventricle, respectively, implicating these genes in chamber specification. In our current study, we show that the forced expression of Hesr1 or Hesr2 in the entire cardiac lineage results in the reduction or loss of the atrioventricular (AV) canal. In the Hesr1-misexpressed heart, the boundaries of the AV canal have a poorly defined appearance, and the expression levels of specific markers of the AV myocardium, Bmp2 and Tbx2, are weakened or undetectable. More potent effects could be observed in Hesr2-misexpressed embryos, in which the AV canal appears to be absent entirely. These data suggest that Hesr1 and Hesr2 may prevent cells from expressing the AV canal specific genes that lead to the precise formation of the AV boundary. Our current findings further indicate the possibility that Tbx2 expression is directly suppressed by Hesr1 and Hesr2. Furthermore, we find that the expression of Hesr1 and Hesr2 is independent of Notch2 signaling. Taken together, our data thus demonstrate that Hesr1 and Hesr2 play crucial roles in AV boundary formation through a Notch independent pathway.

(4) Functional redundancy between Nanso2 and Nanos3
Atushi SUZUKI and Yumiko SAGA
The mouse Nanos proteins, Nanos2 and Nanos3, are required for germ cell development and share a highly conserved zinc finger domain. The expression patterns of these factors during development, however, differ from each other. Nanos3 expression in the mouse embryo commences in the primordial germ cells (PGCs) just after their formation and a loss of this protein results in the germ cell-less phenotype in both sexes. In contrast, Nanos2 expression begins only in male PGCs after their entry into the genital ridge and a loss of this protein results in a male germ cell deficiency, irrespective of the co-expression of Nanos3 in the these cells. These results indicate that these two Nanos proteins have distinct functions, depending on the time and place of their expression. To further elucidate this, we have generated transgenic mouse lines that express Nanos2 under the control of the Oct4ΔPE promoter and examined Nanos2 function in a Nanos3-null genetic background. We find that ectopically produced Nanos2 protein rescues the Nanos3-null defects as the germ cells fully develop in both sexes in the transgenic mice. This result indicates that Nanos2 can substitute for Nanos3 during early PGC development. In contrast, our current data show that Nanos3 does not rescue the defects in Nanos2-null mice. Our findings thus indicate that there are redundant functions of the Nanos proteins in early PGC development but that Nanos2 has a distinct function during male gem cell development in the mouse.

(5) Functional analysis of nanos3
Hitomi SUZUKI, Makoto KISO and Yumiko SAGA
In the Nanos3-null mice, the number of PGCs rapidly decreased during their migration, indicating that Nanos3 is responsible for the maintenance of PGCs rather than their generation. There are two possibilities for the loss of PGCs, apoptotic cell death or abnormal differentiation to somatic cells. By the immunostaining, we detected apoptosis in migrating PGCs in Nanos3-/-mice. In addition, we have generated the Nanos3-cre mouse in which the cre recombinase gene is knocked in the endogenous Nanos3 locus. By crossing with the Rosa26 reporter mouse, we are able to visualize Nanos3 expressing PGC cells by ・Γ-gal staining. In the presence of Nanos3, ・Γ-gal positive cells were incorporated into the genital ridge, indicating that these cells were PGCs. In addition, we observed ・Γ-gal positive cells in the tail bud. These cells were lost during development since they failed to enter PGC program. In the absence of Nanos3, although some cells in the tail bud showed ・Γ-gal activity, we could not observe any ・Γ-gal positive cells in the genital ridge. Importantly

we did not observe expansion of ･｢-gal positive somatic cells in any other cell lineages, which strongly indicates that Nanos3 is required for maintaining PGCs by preventing apoptosis and the lack of Nanos3 does not result in the cell fate change into the somatic cells.

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F-c. Mouse Genomics Resource Laboratory
Tsuyoshi Koide

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F. GENETIC STRAINS RESEARCH CENTER
F-d. Model Fish Genomics Resource

Noriyoshi Sakai

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F. GENETIC STRAINS RESEARCH CENTER
F-e. Plant Genetics Laboratory

Nori Kurata

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2．鈴木温, 永口貢, 佐藤光, 熊丸敏博, 長戸康郎, 倉田のり「イネ全遺伝子の突然変異検索法奸注up度変異系統群と簡易TILLING法の確立」，日本育種学会第110回講演会，松山，9/22-23
3．上田健治,豊澤恵子,野々村賢一,倉田のり,宮尾安藝雄,廣近洋彦,井上正保「イネ花粉形成突然変異体の選抜と解析」，日本植物学会第70回大会，熊本，9/14-16

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21．倉田のり「平成18年度特定領域研究発足案内」, 日本育種学会第110回講演会 , 松山 , 9/22-23
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25．川勝泰二, 伊藤純一, 三好一丸, 倉田のり, 長戸康郎「イネの葉間期と葉の発生成熟速度を変更するPlastochron2変異体の解析」, 日本育種学会第109回講演会 , 東京 , 3/28-30
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27．呉健忠, 江花薫子, 片桐敏, 細川聡美, 吉原里枝, 唐澤歩, 程朝陽, 徐健紅, 土本卓, 大坪久子, 大坪榮一, 宮林登志江, 倉田のり, 河瀬真琴, 井澤毅, 門脇光一, Duncan D. Vaughan, 奥野員敏, 並木信和, 佐々木卓治, 松本隆 「 p-SINEマーカーを用いた栽培及び野生種イネコレクションにおける詳細な系統解析 」, 日本育種学会第109回講演会 , 東京 , 3/28-30
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2．倉田のり 「植物ゲノム障壁」シンポジウム　特定領域公開シンポジウム　東京　10/2
3．倉田のり　植物の生殖過程におけるゲノム障壁　特定領域研究ワークショップ　三島　11/8-9
4．倉田のり 「植物ゲノム障壁」シンポジウム　特定領域研究公開シンポジウム　東京　10/2
5．倉田のり・渡辺正夫・松岡信　高等植物の生殖形質におけるゲノム障壁制御遺伝子の分子遺伝学的解析　国立遺伝学研究所研究集会（共催） 三島　11/8-9
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BOOK

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2．倉田のり（2006）まるごと生き物大集合ーバイオリソースプロジェクトーイネ　遺伝　36 - 37

OTHERS

1．野々村賢一，1，日本育種学会幹事
2．倉田のり，1，日本学術会議　育種学分科会幹事
3．倉田のり，1，日本学術会議　植物科学分科会員
4．倉田　のり，3，生物遺伝資源イネ小委員会委員長
5．倉田　のり，3，Rice Genetics Newsletter Editor
6．Nori Kurata，3，NSF project advisory committee member and project proposal reviewer

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F. GENETIC STRAINS RESEARCH CENTER
F-f. Microbial Genetics Laboratory

Hironori Niki

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1．仁木 宏典（2006）大腸菌，遺伝，60，52 - 53

POSTER PRESENTATIONS

1． Niki, H.「 Helical Structure of the SopA motor protein is independent of nucleoids and bacterial action, MreB 」， EMBO Workshop on “Cell cycle and Cytoskeletal Elements in Bacteria”，Copenhagen，8/23
2． 久田香織，仁木宏典「 呼吸鎖複合体I(Complex I)とそのサブユニットNuoGがバクテリアのセントロメア様領域migSの機能に果たす役割 」，第3回 21世紀大腸菌研究会2006，，近江八幡市
3． Hatano, T.,Yamaichi, Y.,and Niki, H.「 Dynamics of helix forming motor protein for plasmid partitioning, SopA 」， Molecular Genetics of Bacteria & Phages，米国 ニューヨーク，8/23
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6． 田口温子，仁木宏典「 動的に変化する核様体形態の3次元構築 」，第3回 21世紀大腸菌研究会，滋賀県近江八幡市，10/3
7． 田口温子,仁木宏典「 大腸菌の核様体形態変化から分配機能を探る 」，第3回生命科学合同セミナー，静岡県掛川市，10/31
8． 古谷寛治，仁木宏典「 分裂酵母DNAチェックポイントタンパク質Rad9の複製キナーゼHsk1によるリン酸化は複製フォーク損傷応答を制御する 」，複製分配ワークショップ，熱海，10/30

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F. GENETIC STRAINS RESEARCH CENTER
F-g. Invertebrate Genetics Laboratory

Ryu Ueda

RESEARCH ACTIVITIES

test

PUBLICATIONS

Papers

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3 . 上田龍 「 体系的RNAiによるショウジョウバエゲノム機能の解析 」, RNAi研究会2006 , 東京都 , 9/28
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OTHERS

1 . 上田龍 , 1 , 日本遺伝学会　選挙管理委員会　委員長
2 . 上田龍 , 3 , 独立行政法人・農業生物資源研究所・評価助言委員

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G. CENTER FOR GENETIC RESOURCE INFORMATION
G-a. Genetic Informatics Laboratory

Yukiko Yamazaki

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

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2．山崎由紀子「ナショナルバイオリソースプロジェクト「情報」研究活動を支援する双方リソースポータルサイト」，第53回日本実験動物学会，神戸，5/12-13
3．山崎由紀子「ナショナルバイオリソース「情報」」，遺伝学会第78回大会NBRPシンポジウム，つくば，9/27
4． 山崎由紀子 「ナショナルバイオリソースプロジェクト「情報」」， 遺伝学会第78回大会NBRPパネル展示，つくば，9/25-27
5． Hiroshi Ezura, Tsuyoshi Mizoguchi, Shin Watanabe, Yasutaka Kubo, Hitoshi Mori, Shunsuke Imanishi, Daisuke Shibata, Yukiko Yamazaki 「Tools Developed for Tomato Functional Genomics by Japanese Solanaceae Genomics Consortium (JSOL)」，International Workshop on Tomato Genomics，Hyderabad，11/12-14
6． Yukiko Yamazaki「Utilization of Biological Ontologies in Rice Database - Oryzabase」，Plant and Animal Genome XIV，San Diego，1/16

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DB SOFT

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20．Sakaniwa, S., Yamakawa, T., Kawachi, Kasai, F., Yamazaki, Y.， NBRP Algae 2006
http://shigen.lab.nig.ac.jp/algae/
21． Yamakawa, T., Yamakawa, T., K., Niki, H., Miki, T., Kato, J., Yamazaki, Y.， NBRP E.coli Strain 2006

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G. CENTER FOR GENETIC RESOURCE INFORMATION
G-b. Genome biology Laboratory
Yuji Kohara

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1 . Eiichi Shoguchi, Takeshi Kawashima, Yutaka Satou, Makoto Hamaguchi, Tadasu Sin-I, Yuji Kohara, Nik Putnam, Daniel S. Rokhsar and Nori Satoh (0) Chromosomal mapping of 170 BAC clones in the ascidian Ciona intestinalis , **Genome Research** , 16 , 297 - 303
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3 . Tetsuya Matsuno, Nobuyuki Tominaga, Koji Arizono, Taisen Iguchi and Yuji Kohara (0) Graphical gaussian modeling for gene association stuctures based on expression deviation patterns induced by various chemical stimuli. , **IEICE Trans. Inf. & Syst.** , E89-D , 1563 - 1574
4 . Terasaki, H., Murakami, R., Yasuhiko, Y., Shin-i, T., Kohara, Y., Saga, Y., and Takeda, H. (2006) Transgenic analysis of medaka mesp-b enhancer in somitogenesis. , **Development Growth and Differentiation** , 48 , 153 - 168

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H. STRUCTURAL BIOLOGY CENTER
H-a. Biological Macromolecules Laboratory
Makio Tokunaga

RESEARCH ACTIVITIES

PUBLICATIONS
Papers

1．椎名伸之，徳永万喜洋（2006）神経シナプス可塑性における局所的翻訳の制御機構，蛋白質･核酸･酵素，51，943 - 949
2．Miletic AV, Sakata-Sogawa K, Hiroshima M, Hamann MJ, Gomez TS, Ota N, Kloeppel T, Kanagawa O, Tokunaga M, Billadeau DD, Swat W （2006） Vav1 Acidic Region Tyrosine 174 Is Required for the Formation of T Cell Receptor-induced Microclusters and Is Essential in T Cell Development and Activation.，**J Biol Chem**，281，38257 - 38265
3．Yamasaki S., Ishikawa, E., Sakuma, M., Ogata, K., Sakata-Sogawa K., Hiroshima, M., Wiest, D. L., Tokunaga M., Saito T.（0）Mechanistic basis of pre-T cell receptor-mediated autonomous signaling critical for thymocyte development.，**Nature Immunol**，7，67 - 75

ORAL PRESENTATION

1． Tokunaga, M., Sakata-Sogawa, K. Visualization and single molecule analysis of molecular functions in linving cells CBR Seminar Center for Blood Research, Harvard Medical School 6/26
2．徳永万喜洋 1分子イメージングと定量解析 — 分子からシステムへ — 2006宇宙ライフサイエンス･生物物理若手の会共催 夏の学校 神戸市立セミナーハウス 7/30
3．徳永万喜洋 1分子力計測と1分子イメージング･定量解析 — 分子からシステムへ — 平成18年度文部科学省ナノバイオサマースクール「生命活動を観る」 人材開発センター富士研修所 8/30
4．徳永万喜洋 全反射･薄層斜光照明顕微鏡による細胞1分子イメージングと定量 — 分子からシステムへ — NEDOプロジェクト「細胞内ネットワークのダイナミズム解析技術開発」機器開発･成果の公開ワークショップ エムプラス，丸の内 9/12
5．徳永万喜洋，椎名伸之，廣島通夫，十川久美子 核構造とシナプス局所的翻訳の分子イメージング解析 2006年度生理学研究所研究会「細胞シグナリングの時空間統御機構解明への方略探索」 岡崎コンファレンスセンター 10/5
6．徳永万喜洋 1分子イメージングに使うカメラをもっと良くして欲しい EABS&BSJ2006浜松ホトニクス･ランチョンセミナー「1分子イメージングのさらなる飛躍を目指して ～より高精細に、より高感度に～」 沖縄コンベンションセンター 11/13
7．徳永万喜洋 in vivo 細胞イメージングの最前線 1分子イメージング バイオファイナンスギルド(日経BP)「投資対象となるセロームとは何か？」 ダイヤハ重洲ロビル 12/21

POSTER PRESENTATIONS

1．椎名伸之，新倉和美，徳永万喜洋「 神経局所的翻訳に関わるmRNA結合タンパク質の機

能とイメージング」, 第83回日本生理学会大会シンポジウム , 前橋 , 3/28-30
2 . Shiina N., Shinkura K., Tokunaga, M.「An RNA-binding protein RNG105 in neuronal RNA granules: regulatory machinery for local translation and synaptic plasticity.」, 20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress , Kyoto , 6/18-23
3 . Shiina N., Shinkura, K., Tokunaga, M.「RNG105 in neuronal RNA granules: Involvement in local translation and synapse formation」, East Asian Biophysics Symposium & Forty-Fourth Annual Meeting of the Biophysical Society of Japan , Ginowan , 11/12-16
4 . 椎名伸之「神経シナプス可塑性における局所的翻訳の制御と機能」, 国立遺伝学研究所研究会 , 東京 , 6/24
5 . Tokunaga, M.「Visualization of dynamics of signaling, Molecular quantification and modeling of nuclear import using single molecule imaging in cells.」, The 9th Membrane Research Forum , Kyoto , 3/15
6 . Tokunaga, M., Imamoto, N.「Kinetic Quantification and Modelling of Nuclear Transport in Cells using Single Molecule Imaging.」, Gordon Research Conference Single Molecule Approaches To Biology , New Hampshire , 6/18
7 . Sakata-Sogawa, K., Yokosuka T.,Hiroshima, M., Saito, T., TOKUNAGA, M.「Molecular imaging and analysis of microclusters responsible for initiating T cell receptor signaling.」, Gordon Research Conference Single Molecule Approaches To Biology , New Hampshire , 6/18
8 . Hiroshima M., Tokunaga, M.,「Single hydrogen bonds of DNA base pairs detected by intermolecular force microscopy」, Gordon Research Conference Single Molecule Approaches To Biology , New Hampshire , 6/18
9 . Sakata-Sogawa K., Yokosuka, T., Hiroshima, M., Saito, T., Tokunaga, M.「Molecular imaging and analysis of microclusters responsible for initiating T cell receptor signaling」, East Asian Biophysics Symposium & Forty-Fourth Annual Meeting of the Biophysical Society of Japan , Ginowan , 11/12
10 . Shinkura K., Sakata-Sogawa, K., Hiroshima, M., Tokunaga, M.「Multi-color molecular imaging of transcription factors」, East Asian Biophysics Symposium & Forty-Fourth Annual Meeting of the Biophysical Society of Japan , Ginowan , 11/12
11 . Hiroshima M., Tokunaga, M.「Single hydrogen bonds of DNA base pairs detected by intermolecular force microscopy」, East Asian Biophysics Symposium & Forty-Fourth Annual Meeting of the Biophysical Society of Japan , Ginowan , 11/12
12 . Fukagawa A., Hiroshima, M., Kuwajima, K., Tokunaga, M.「Detection of substructural unfolding of SNase by intermolecular force microscopy」, East Asian Biophysics Symposium & Forty-Fourth Annual Meeting of the Biophysical Society of Japan , Ginowan , 11/12
13 . 徳永万喜洋 「新しい細胞内1分子イメージング顕微鏡創出による生体分子定量解析技術の開発」, ダイナミックバイオH17年度・第2回研究開発委員会 , 東京 , 3/3
14 . 徳永万喜洋 「新しい細胞内1分子イメージング顕微鏡創出による生体分子定量解析技術の開発」, ダイナミックバイオH18年度・第1回研究開発委員会 , 東京 , 9/1

BOOK

1 . 徳永万喜洋 (2006) 巻頭言「必ず出来る」 生物 241 - 241

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H. STRUCTURAL BIOLOGY CENTER
H-b. Molecular Biomechanism Laboratory
Nobuo Shimamoto

RESEARCH ACTIVITIES

(1) Single-molecule dynamics of translation termination.

Hideki NAKAYAMA, Kouichi ITO, and Nobuo SHIMAMOTO

Single-molecule analysis has not been much applied to translation, although it can provide critical conclusions to several important problems such as order of association/dissociation of components. Therefore, we are challenging to solve a long-standing problem in termination: whether mRNA dissociates from 70S or from 30S subparticle. If it dissociates from 70S, genes on the same mRNA can be translated in cis by sliding of 70S, but if not, the whole initiation process has to be repeated. Furthermore, the growth-phase control of conversion from 70S into 100S inactive particles should have different pathways depending on the termination mechanism.
At first, we have developed a surface treatment of glass sides that has NTA residues but does not adsorb nonspecific substance in an extract prepared from *E. coli*. Next, we tethered ribosome at its 30S through the binding between NTA and his tag introduced in an Rps protein. The 50S of this ribosome has an Rpl protein fused with GFP and thus the locations of ribosome molecules were identified by its fluorescence. The tethering of individual ribosome molecules was shown by a single-step photo bleaching of the GFP. We prepared an mRNA encoding Lumio-his-tag, and the RNA is labeled with ca. 10 Texas Red moieties at its 5'-end. The translational product was fixed on the NTA surface and detected by Lumio Green, proving the activity of the tethered ribosome molecules. The movements of GFP and Texas Red spots should yield the conclusion. A preliminary experiment showed the presence of dissociation of mRNA from 70S, and now the fraction of that from 30S are under examination.

(2) Construction of DNA library by PCR with a single primer.

Hideki NAKAYAMA, Ryusuke FUJITA and Nobuo SHIMAMOTO

For studies of bacterial infection and cloning from an environment, there are cases where only an amount of DNA as small as direct PCR is available to target DNA segments in constructing a DNA library. PCR with primers of random sequences are used in such a case but is often unsatisfactory because of poor and/or biased amplification. We have developed a complementary method of PCR to use a single primer. This method was

successful for 0.1-1 ng of *E. coli* DNA and examination at 30 loci showed less than 100-fold differences in amplification. The core heart of this method is the selection of the primer. We screened the best 10 base primer and found that the 6 base at 3'-end must reflect the most frequent hexamer sequences in the genome, while the 4 base at 5'-end does not affect the amplification in our PCR condition. The drawback of this efficient construction of library is the formation of recombinants of two or more loci during the amplification. However, this is not very harmful for the search for positive functions or if the genome information of itself or a close relative is rich enough to indicate the recombination.

(3) Genetic and biophysical study on σ^{70} of *E. coli* RNA polymerase.

Suganthan Rajan Babu, Akiko Hatakeyama, and Nobuo Shimamoto

σ^{70} is a subunit of *E. coli* RNA polymerase and mainly interact with a promoter. Its fusion with GFP tends to be cleaved in cells and thus GFP must be inserted in σ^{70}. One of such mutant σ^{70} showed a distinct cleavage at the middle of Region 2.4 of σ^{70}, leaving the N-terminus fragment containing GFP and Regions from 1.1 to 2.3. The C-terminus fragment was not significantly accumulated in the cell. We quantitative analyses of the activity of the purified enzyme and the fraction of the cleavage fragment, there is possibility that the N-terminus fragment is bound to core RNA polymerase. We are analyzing the activity of the enzyme harboring the N-terminus fragment.
We have found that an *E. coli* strain with *rpoD*(the gene encoding σ^{70}) can grow 2°C higher temperature than the wild type, when it harbor on a plasmid a chimeric *rpoD* with its Region 4.2 is replaced that of *sigA* of *T. thermophilus*. To clarify the relationship with *ropD* and upper limit of the growing temperature of an *E. coli* strain, we have constructing mutants of *rpoD*.

(4) Immobilization of protein and nucleic acid on diamond needle.

Yosuke Amemiya and Nobuo Shimamoto

To inject a substance in a cell, glass capillaries are conventionally used and its technology has been matured to show clear limitations on the size of cells and the size of needles. Only large eukaryotic cells like oosites are available to the technique and the cells cannot stand for multiple injections. The finer the needles, the better the viability of cells after injection. Therefore, finer needles are expected to give better results but the material is limited because of the stiffness. Diamond is the hardest material and biologically inactive, and thus expected to a new material for finer needles to carry a substance in or take a biological materials out of the cells. Therefore, it is essential to develop a good surface of diamond that can immobilize various biological molecules. We are challenging to make such surface in collaboration with the Diamond Group of AIST and a Group of Olympus.

PUBLICATIONS

Papers

1．Susa, M., Kubori, T. and Shimamoto, N.（2005）A pathway branching in transcription initiation in Escherichia coil，**Molec.Microbiol.**，59，1807 - 1817
2．Shimamoto, N. and Tomizawa, J.（2006）Biologyにおけるkinetic stateとthermodynamic state，物性研究，85，635 - 646
3．Vuthichai Ampornarambeth, Tao Zhang, Ana Hadiana, Shimamoto,N., and Ueno,H（2006）A Web-Based e-Learning Platform for Postgraduate Education，**Proc. Fifth IASTED International Conference on Web-Based Education**，，388 - 393

ORAL PRESENTATION

1．嶋本伸雄　Introduction of Nanobiology　産業技術総合研究所・ダイヤモンド研究センター　5/24
2．嶋本伸雄　Single-molecule dynamics, chemical kinetics, and fluorescence technologies in nanobiology　産業技術総合研究所・ダイヤモンド研究センター　5/24
3．嶋本伸雄　ナノバイオロジー　北海道大学・理学研究科　5/10-5/12
4．嶋本伸雄　基礎から学ぶ分子細胞生物学コース　機能分子としてのﾀﾝﾊﾟｸ質　KAST教育講座　東京大学医科学研究所　5/23
5．Shimamoto, N.　Secrets of biological nanomachines: The difference between artificial devises and biological molecular machines　Miami International University, Faculty of Engineering　3/31
6．嶋本伸雄　ナノバイオの光と陰　IBM ライフサイエンス天城セミナー　IBM天城ホームステッド　7/19

POSTER PRESENTATIONS

1．宮本貴史、嶋本伸雄「Coupling between transcription initiation and DNA damage」，第20回国際生化学・分子生物学会，京都市，6/18～23
2．宮本貴史、嶋本伸雄「DNAのUV損傷による転写スイッチ」，第8回RNAミーティング，淡路市，7/18～20
3．宮本貴史、嶋本伸雄「DNAのUV損傷による転写スイッチ」，特定領域「RNA情報網」第4回サテライトミーティング，裾野市，9/11～13
4．雨宮陽介、嶋本伸雄「Surface modification of diamond to prevent nonspecific protein adsorption toward the selective immobilization of target biomolecules」，EABS & BSJ 2006（日本生物物理学会），沖縄県宜野湾市，11/12～16
5．宮本貴史、嶋本伸雄「The switch of transcription induced by UV-damaged DNA」，EABS & BSJ 2006（日本生物物理学会），沖縄県宜野湾市，11/12～16
6．畠山明子、嶋本伸雄「Correlation between rpoD alleles and upper limits of growing temperature」，EABS & BSJ 2006（日本生物物理学会），沖縄県宜野湾市，11/12～16
7．Suganthan Rajan Babu, Shimamoto,N.「Necessity of C-terminus half of E. coli sigma-70 in its function」，EABS & BSJ 2006（日本生物物理学会），沖縄市宜野湾市，11/12～16
8．中山秀喜、嶋本伸雄、伊藤耕一「翻訳終結過程の1分子ダイナミックス」，第8回RNAミーティング，淡路市，7/18～20
9．中山秀喜、嶋本伸雄「ナノXYステージを用いた翻訳の一分子検出」，第58回日本生物工学会大会，大阪市，9/11～13
10．Nakayama,H.,Ito,K.,Shimamoto,N.「Single-molecule observation of a translation termination」，RNA 2006 Izu国際シンポジウム，伊豆の国市，12/3～7
11．畠山明子,嶋本伸雄「大腸菌転写開始因子σ70による環境応答機構の解明」，特定領域「RNA情報網」第4回サテライトミーティング，裾野市，9/11～13
12．嶋本伸雄、中山秀喜、伊藤耕一「Single-molecule observation of a translational process」，第20回国際生化学・分子生物学会，京都市，6/19
13．Shimamoto, N.「Molecular memory of transcription machinery and transcriptional regulation by it」，The Biological Sciences Seminar Series of Miami International University，Miami, USA，3/28

PATENT

1．2006-110713，マルチウェルインキュベーション装置及びこれを用いた分析方法，嶋本伸雄，情報・システム研究機構

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H. STRUCTURAL BIOLOGY CENTER
H-c. Multicellular Organization Laboratory
Isao Katsura

RESEARCH ACTIVITIES

(1) Enhancement of chemotaxis by pre-exposure to odorants and food in the nematode *C. elegans*

Ichiro TORAYAMA, Hiroshi ICHIJO, Kotaro KIMURA, Takeshi ISHIHARA[1] and Isao KATSURA ([1]Kyushu University)

We have found that *C. elegans* specifically enhances chemotaxis to butanone, but not to benzaldehyde, by pre-exposure to butanone and food. This odor-specific plasticity, which we call butanone enhancement, is different from the already known inhibition of olfactory adaptation by food. In the latter case, the chemotaxis index never exceeds that of naive animals, and food can be replaced by serotonin, which is not true for butanone enhancement. To elucidate the molecular mechanism, we isolated ten mutants that showed abnormality in this plasticity. Of these mutants, *olrn-1(ut305)* and *olrn-2(ut306)* were studied in detail. The *olrn-1* gene encoded a novel protein containing predicted transmembrane domains and acted in AWC olfactory neurons for butanone enhancement and for the AWC neuronal asymmetry. Namely, while the wild-type animal is known to express *str-2* gene in only one of the two AWC neurons, the *olrn-1(ut305)* mutant expressed *str-2* in neither of them. We then hypothesized that the absence of the *str-2*-expressing AWC neuron (AWC^{ON} neuron) is the reason for the defect in butanone adaptation, and proved it by various experiments, including the butanone enhancement assay of AWC^{ON}-killed wild type animals. We also cloned the *olrn-2* gene and found that it was allelic to *bbs-8*, one of the Bardet-Biedl syndrome (*bbs*) genes. The *olrn-2(ut306)* mutant showed the wild-type phenotype in the AWC asymmetry, and the *olrn-2* gene was required in the AWC^{ON} neuron for butanone enhancement. The *olrn-2(ut306)* mutant showed structural defects in sensory cilia like known *bbs* mutants. We therefore tested many cilium structure mutants for butanone enhancement. The results revealed that all the Bardet-Biedl syndrome mutants tested were abnormal, while other cilium structure mutants were normal in butanone enhancement. Besides butanone enhancement, we found similar plasticity with isoamyl alcohol.

In 2006, we found that pre-exposure to butanone and the odor of food enhances chemotaxis to butanone. This result shows that AWC neurons are strong candidates of neurons that sense food for butanone enhancement, because butanone enhancement was not impaired by mutations that block the sensation of other known olfactory neurons (*lim-4* for AWB and *osm-9* for AWA, ASH, and ADL). We also found behavioral plasticity similar to butanone

enhancement with 2,3-pentanedione. We are now investigating the relationship between this plasticity and the plasticity with butanone and isoamyl alcohol.

(2) Genetic analysis of the plasticity of avoidance behaviors in *C. elegans*

Kotaro KIMURA and Isao KATSURA

We have recently discovered a novel type of plasticity in the avoidance response of *C. elegans*: The avoidance response of the animal to repellent odors was enhanced, rather than being reduced, after preceded exposure to the odor. It was somewhat surprising because almost all of the previously known stimuli (including other repellent stimuli) to the animals cause adaptation, i.e., the reduction of the sensory response after preceded exposure. In general, adaptation has been extensively studied in various sensory systems. However, the enhancement of the sensory response has been far less studied, particularly at the molecular level, with an exception of mammalian pain sensation and gill-withdrawal reflex in *Aplysia*. Therefore, analyzing the enhancement of the avoidance response of *C. elegans* may lead to the identification of a novel regulatory mechanism of the sensory response enhancement in general.

To gain insight into the molecular mechanism of the enhancement of 2-nonanone avoidance behavior, we have carried out a candidate screening and found that several mutants showed specific defects in the enhancement of avoidance behavior. We are currently analyzing the details of the phenotypes of the mutants.

In addition, we are developing a quantitative analysis system for the animals' movement. Preliminary results suggest that there are differences in the direction and in the speed between the avoidance behaviors to 2-nonanone and 1-octanol, two repulsive odors mainly sensed by different types of sensory neurons, AWB and ADL, respectively.

(3) Class 1 *flr* mutants of the nematode *Caenorhabditis elegans*

Yuri KOBAYASHI, Kotaro KIMURA and Isao KATSURA

Class 1 *flr* mutants of C. elegans, which map in *flr-1*, *flr-3* and *flr-4*, were isolated originally by resistance to 0.4 mg/ml NaF (Katsura, I. *et al*.: Genetics **136,** 145-154, 1994). They also showed many other phenotypes including slow growth, short defecation cycle periods (Dec-s), frequent skip of the expulsion step of defecation, synthetic abnormality in dauer larva formation, weak tendency to stay on food, and hypersensitivity to serotonin. The *flr-1* gene encoded a cation channel of the DEG/ENaC superfamily, while *flr-4* and *flr-3* coded for a novel Ser/Thr protein kinase and a kinase-like molecule, respectively, both having a hydrophobic domain at the carboxyl terminus. They were expressed essentially in the intestinal cells, except that *flr-4* was expressed also in the isthmus of the pharynx and in a pair of head neurons called AUA. We consider that class 1 *flr* genes constitute a regulatory system that acts in differentiated intestinal cells.

In 2006 we continued the following experiments. To reveal the mechanism of the regulation of defecation cycle periods, we looked for genes, the RNAi of which suppress the Dec-s phenotype of the *flr-1(ut11)* mutant or the Dec-l phenotype of animals expressing the FLR-1 ion channel lacking the C-terminal cytoplasmic domain (FLR-1ΔC). We also investigated the role of the C-terminal cytoplasmic domain by making various deletion mutants in this region. The C-terminal domain is exceptionally large for an ion channel of the DEG/ENaC family and contains many putative phosphorylation sites.

(4) Class 2 *flr* mutants of the nematode *Caenorhabditis elegans*

Akane OISHI, Kotaro KIMURA, Takeshi ISHIHARA[1] and Isao KATSURA ([1]Kyushu University)

Class 2 *flr* mutations were isolated first as a weak fluoride-resistant mutation and then as suppressors of the slow growth or serotonin-hypersensitivity of class 1 *flr* mutations. Besides these phenotypes, they also suppressed the dauer larva formation abnormality and weak tendency to stay on food, but not the defecation abnormalities or strong fluoride-resistance. The phenotypes suggest two possibilities on the relationship between class 1 and class 2 *flr* genes. (a) Class 2 *flr* genes may act downstream of the class 1 regulatory pathway. At the downstream, the regulatory pathway may bifurcate into two branches, the growth/dauer/chemosensory branch and the defecation/fluoride sensitivity branch, while class 2 genes act in the former branch and not the latter. (b) Class 2 *flr* genes may act antagonistically to class 1 genes, while the threshold is different for the growth/dauer/chemosensory phenotypes and the defecation/fluoride sensitivity phenotypes. Class 2 mutations mapped in four genes, *flr-2*, *flr-5*, *flr-6* and *flr-7*, of which only *flr-2* has been cloned. *flr-2* encoded a secretory protein belonging to the gremlin/DAN/cerberus family. A functional *flr-2*::GFP fusion gene was expressed in some neurons in the head and the tail as well as many pharyngeal neurons. We found that FLR-2 interacts in vitro with a secretory protein encoded by the ZK20.1 gene and isolated a deletion mutant in this gene. A ZK20.1::GFP fusion gene was expressed in the intestine and body wall muscles.

In 2006, we continued the study on the role of ZK20.1 in defecation cycle length regulation. Both the deletion mutation and RNAi of ZK20.1 did not change defecation cycle length of wild type animals, but they increased that of *flr-2;flr-4* double mutants and a weak *flr-4* mutant (*n2259*). We are also trying to clone *flr-6* and *flr-7* despite the technical difficulty of the rescue experiments.

(5) Analysis of synthetic dauer-constitutive mutants in the nematode *Caenorhabditis elegans*

Norio SUZUKI[1], Takeshi ISHIHARA[2] and Isao KATSURA ([1]Riken CDB, [2]Kyushu University)

If newly hatched larvae of *C. elegans* are in a crowded state and given a limited food supply, they sense the environmental signal of pheromone and food with a head sensory organ called amphid, and deviate from the normal life cycle, ending in non-feeding larvae called dauer larvae. We are investigating synthetic dauer-constitutive (synDaf) mutants, i.e., mutants that form dauer larva in a certain mutant background even in the presence of plenty food and at low population density. We found that mutations in more than 50 known neural genes show synDaf phenotypes. We are studying the combinations of mutations for the synDaf phenotype and the pattern of suppression of the synDaf phenotype by various suppressor mutations. In this way we hope to elucidate the detailed regulatory pathway for dauer larva formation.

Furthermore, to identify new genes for the regulation of dauer larva formation, we have isolated and mapped 44 mutations that show the synDaf phenotype in the *unc-31(e169)* background, where *unc-31* gene encodes CAPS protein, which is thought to act in the secretion of biogenic amines and peptides. These mutations mapped at least to 17 genes, of which *sdf-9*, *sdf-13*, and *sdf-14* have been cloned. *sdf-9* encoded a protein tyrosine phosphatase-like molecule, was expressed in a pair of neuron-associated cells called XXXL/R, and regulated dauer larva formation in the steroid hormone signaling pathway. *sdf-13* encoded a homologue of the transcription factors Tbx2 andTbx3 and controlled olfactory adaptation in AWC and dauer larva formation in cells other than AWC (possibly ASJ) neurons. *sdf-14* was allelic to *mrp-1*, a homolog of the MRP1 (multidrug resistance-associated protein 1) gene, which acted in neurons, pharyngeal muscles and intestinal cells for dauer regulation. Interestingly, human MRP1 could substitute for *C. elegans* MRP-1 in

dauer larva regulation, and an inhibitor of the human MRP1 export activity impaired this function, showing that the export activity is required for normal dauer larva regulation.

In 2006, we examined a huge amount of data on the synDaf phenotypes of known mutations to find rules. We plan to write a paper using these data and those on the mapping and initial characterization of the mutants we isolated.

PUBLICATIONS

Papers

1． Kodama, E., Kuhara, A., Mohri-Shiomi, A., Okumura, M., Kimura, K. D., Tomioka, Y., Iino, Y., and Mori, I. （2006） Insulin-like signaling and the neural circuit for integrative behavior in C. elegans. , **Genes Gev.** , 20 , 2955 - 2960

ORAL PRESENTATION

1．桂　勲　生命分子科学特論Ⅳ 真核生物の分子細胞生物学　学習院大学・理学部　9/6
2．桂　勲　線虫C.elegansの嗅覚学習の分子遺伝学的解析　学習院大学・理学部　9/6
3．桂　勲　生命情報工学科特別講義 線虫C.elegansの行動の分子生物学　創価大学・工学部　7/31

POSTER PRESENTATIONS

1． Torayama, I.,Ishihara, T.,Katsura, I.「 Odor-specific peripheral sensitization integrates the signal of butanone and food to change behavior in the nematode *Caenorhabditis elegans*. 」, 20th IUBMB Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress , Kyoto , 6/18-23
2． Kobayashi, Y.,Kimura, K.,Katsura, I.「 The carboxyl-terminal cytoplasmic domain of the FLR-1 ion channel regulates defecation cycle periods. 」, 2nd East Asia C.elegans Meeting , Seoul , 11/15-18
3． Ichijo, H.,Kimura, K.,Torayama, I.,Katsura, I.「 Analysis of mutants defective in olfactory learning induced by AWC-sensed odorants 」, 2nd East Asia C.elegans Meeting , Seoul , 11/15-18
4．木村幸太郎, 桂勲「 事前暴露により増強される線虫C.elegansの匂い忌避行動 」, 日本分子生物学会2006フォーラム「分子生物学の未来」, 名古屋 , 12/6-8

EDUCATION

1．木村幸太郎、小田洋一　脳のはたらきの統合的理解：遺伝子～神経回路～行動　日本分子生物学会2006フォーラム「分子生物学の未来」シンポジウム　名古屋　12/8

OTHERS

1．桂　勲 , 1 , Genes to Cells, Associate Edditor
2．桂　勲 , 1 , 日本分子生物学会、広報幹事

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H. STRUCTURAL BIOLOGY CENTER
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H-d. Biomolecular Structure Laboratory

Yasuo Shirakihara

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1 . Yoshimune,K.,Shirakihara, Y., Shiratori, A., Wakayama,M., Chantawannakul. P.,Moriguchi,M. (0) Crystal structure of a major fragment of the salt-tolerant glutaminase from Micrococcus luteus K-3 , **BioChem Biophys Res Commun.** , 346 , 1118 - 1124
2 . Shiroishi,M., Kuroki,K., Tsumoto, K., Yokota,A., Sasaki,T., Amano,K., Shimojima, T., Shirakihara,Y., Rasubala,L., P. Anton van der Merwe,Kumagai,I., Kohda,D., Maenaka,K. (0) Entropically-driven MHC class I recognition by human inhibitory receptor Leukocyte Ig-like receptor B1 (LILRB1/ILT2/CD85j) , **J Mol Biol** , 355 , 237 - 248

POSTER PRESENTATIONS

1 . Shirakihara, Y.,Shiratori A., Murakami S., Suzuki T., Yoshida M. 「 Improvement and analysis of ATP synthase crystals 」, EABS & BSJ 2006 , Okinawa , 11/12-11/16
2 . Gao, YG., Hayashi, T., Sakai, N., Itou, H., Yao, M., Watanabe, N., Tamura, T., Tanaka, I., 「 タンパク3000プロジェクト「転写・翻訳」拠点の成果（5） 有用細菌由来転写因子の立体構造解析 」, 日本蛋白質科学会2006年年会 , 京都府京都市 , 4/24
3 . Itou, H., Okada, U., Suzuki, H., Yao, M., Wachi, M., Watanabe, N., Shirakihara, Y., Tanaka, I.「 ゲノム解析により見いだされた新規タンパク質Corynebacterium glutamicum由来CGL2612タンパク質は薬剤耐性に関与する転写抑制因子である 」, 日本蛋白質科学会2006年年会 , 京都府、京都市 , 4/24 - 4/26
4 . Itou, H., Okada, U., Suzuki, H., Wachi, M., Yao, M., Watanabe, N., Shirakihara, Y., Tanaka, I.「 The CGL2612 protein, a newly identified protein by genomic DNA analysis on Corynebacterium glutamicum, is a drug resistance-related transcriptional repressor 」, 20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress , Kyoto , 6/18-23

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H. STRUCTURAL BIOLOGY CENTER
H-e. Gene Network Laboratory
Emiko Suzuki

RESEARCH ACTIVITIES

PUBLICATIONS

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Kobayashi,M.,Michaut,L.,Ino,A.,Homjo,K.,Nakajima,T.,Maruyama,Y.,Mochizuki,H.,Ando,M.,Ghangrekar,I.,Takahashi,K,.Saigo,K.,Ueda,R.,Gehring,WJ.,
Furukubo-Tokunaga,K.（2006）Differntial microarray analysis of *Drosophila* mushroom body transcripts using chemical ablation，**PNAS**，103，144
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2． Kuranaga,E., Kanuka,H., Tonoki,A., Takemoto,K., Tomioka,T., Kobayashi,M., Hayashi,S.,and Miura,M.（2006）*Drosophila* IKK-related kina
regulates nonapoptotic function of caspases via degradation of IAPs.，**cell**，126，583 - 596

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1．鈴木えみ子、来栖光彦、Carrero-Martinez,F.「神経ネットワーク形成の分子基盤」，国立遺伝学研究所研究会シンポジウム，東京都，6/24
2． Carrero-Martinez,F.,Furrer,M.,Suzuki,E.Chiba,A.「The "Filopodial Scaffolding" Hypothesis :Synaptogenesis in *Drosophila* Embryo Requi
Corroboration of Both Filopodial Clustering and Postsynaptic Scaffolding Protein Dlg」，46th Annual Meeting of the American Society for Cell Biolog
San Diego，12/9-13
3． Toda, H.,Mochizuki,H.,Suzuki,E.,Tomoda T.Furukubo-Tokunaga,K.「The Conserved Ser-Thr Kinase UNC51 Functions with UNC-76 to Regul
Axonal Transport in *Drosophila*」，47th Annual Drosophila Research Conference，Houston，3/29-4/2
4． Nishiwaki,Y.,Komori,A.Manabe,T.,Hosoya,T.,Sagara,H.,Suzuki,E.,Okamoto,H.,Masai,I.「The *eclipse* mutation affects visual performance in b
mutant and heterozygous larvae」，The International Meeting on Zebrafish Development and Genetics，Madison，6/14-18
5．鈴木えみ子,来栖光彦,F.Carrero-Martinez「神経ネットワーク形成の分子基盤」，国立遺伝学研究所研究会，東京，6/24
6． Mochizuki,H.,Toda,H.,Suzuki,E.,Tomoda,T.Furukubo-Tokunaga,K.「The Conserved Ser/Thr Kinase UNC51 Functions with UNC-76 to Regul
Axonal transport in *Drosophila*」，第29回日本神経科学大会，京都，7/19-21
7． Ino,A., Kobayashi,M., Nakajima,T., Michaut,L., Ghangrekar,I., Takahashi,K., Ueda,R., Saigo,K., Gehring,WJ., Furukubo-Tokunaga,K.「PS2P-EC
Differential microarray analysis of mushroom body transcripts using chemical ablation」，第29回日本神経科学大会 国立京都国際会議，京都，2/19-
8． Kurusu,M.,Suzuki,E.,Zinn,K.「Exclusive expression of N-CADHERIN and Fasciclin 2 is required for the formation of concentric axonal layers
Drosophila Mushroom body」，The 4th annual CDB Symposium，神戸，4/10-12
9． Nishiwaki,Y.,Komori,A.,Hosoya,T.,Sagara,H.,Suzuki,E.,Okamoto,H.,Masai,I.「ゼブラフィッシュ突然変異体*eclipse*の視覚行動」，第29回日本神経
学大会，京都，7/19-21

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I. CENTER FOR INFORMATION BIOLOGY AND DNA DATA BANK OF JAPAN
I-a. Laboratory for DNA Data Analysis

Takashi Gojobori

RESEARCH ACTIVITIES

Wide scale gene family analysis under the point of view of expression.
Andrea Cornero, Margherita Squillario, Kazuho Ikeo and Takashi Gojobori.
In order to discover new details about how the mechanism of transciption works, a wide-scale analysis of heterogeneous data regarding gene families in both human and mouse has been performed. Studying different kinds of data (such as expression data, sequences data, transcription starting site distributions, etc.), can reveal important relationship between the characteristic of the genes and of their promoters. These relationships can then give us some new information about the complex regulation of the transcriptional process.
Preliminary result showed that genes with similar distribution and number of transcription starting site have also a similar profile of expression. Further analysis revealed that there's no apparent relationship between the similarity of the aminoacidic sequence of the genes and the similarity of their expression profiles. From this preliminary result, it is possible to assume that the evolutionary process of the promoter and the coding regions is independent.

The sensory apparatus of hydra.
Hwang Jung Shan, Yasuharu Takaku, Kazuho Ikeo and Takashi Gojobori
Nematocyte is the stinging cell present in all cnidarians. They are specialized for the prey capture, the defense and the attachment on substances. Nematocyte can be triggered and releases its ‘explosive’ nematocyst that subsequently kills its preys. Early investigations indicated that ciliary structures on the apical surface of nematocyte react to the mechanical stimuli and it was later named cnidocil apparatus. To understand the molecular structures of cnidocil apparatus and its evolutionary perspective, we collected genes with expressions at the late differentiation of nematocyte (the stage when cnidocil apparatus is assembled). As a result, we identified four genes expressed at the late differentiation by whole mount in situ hybridization. We also performed immuno-fluorescent method with antibodies raised against these gene products. Two proteins are structurally crucial for the formation of cnidocil apparatus and they both contain intermediate filament domains. The other two are cytoplasmic proteins which interact with calcium ions. Homologues of these calcium-binding proteins were found to express in the vertebrate inner ear hair cell and play a role in calcium-dependent signal transduction. This leads us to the conclusion that cnidarians and vertebrates might share a common origin of mechanosensory apparatus and likely both mechanosensory systems play similar roles in response to external stimuli.

The Evolutionary Origin of Mammalian Neocortex
Ikuo Suzuki, Tatsumi Hirata, and Takashi Gojobori
Neocortex of the mammalian brain is known to control highly integrated functions such as logical consideration and speech of a language. Because only mammals including humans

have a laminated structure of the neocortex, this well-organized structure may be needed for constructing the neural circuits by which enormously complex information can be precisely processed. However, the molecular backgrounds of how mammalian laminated neocortex evolved have been totally unknown. With the aim of elucidating the evolutionary origin and process of the mammalian laminated neocortex at the molecular level, I conducted a comparative study of developmental processes between the mammalian neocortex and the non-mammalian corresponding region, the pallium. In the present study, I took a chick pallium as a non-mammalian model, because the chick brain is relatively easy to handle experimentally. In order to know the cellular organization, I examined the expression patterns of several molecular markers in the chick pallium. The molecular markers were chosen from the genes specifically expressed in particular cellular layers of mammalian neocortex. As a result, the expression patterns of those molecular markers in chickens did not show any obvious layer structure as seen in mammals, though they clearly indicated regional distinctions. The expressions of markers for mammalian upper cortical layer were located in the mesopallium of the chick telencephalon and those for the deep layer were in the hyperpallium. From this kind of study, I would speculate the developmental program of the common ancestor's pallium and the evolutionary events, which make the uniqueness of the mammalian neocortex.

Evolutionary origin of sex-related genes in the mouse brain
Kazuya Yuge, Kazuho Ikeo and Takashi Gojobori
With the aim of elucidating the evolutionary process of sexual dimorphism in the brain at the molecular level, we conducted genomic comparisons of a set of genes expressed in a sexually different manner in the mouse brain with all genes from other species of eukaryotes. First, we obtained the protein-coding genes whose levels of mRNA expression in the brain differed between male and female mice according to the currently available microarray data, and designated these genes operationally as "sex-related genes in the mouse brain". Next, we estimated the time when these sex-related genes in the mouse brain emerged in the evolutionary process of eukaryotes by examining the presence or absence of the orthologues in the eukaryotic species whose genome sequences are available. As a result, we found that about 60-75% of sex-related genes in the mouse brain emerged after the divergence of urochordates and mammals whereas about 50% of all the mouse genes emerged during the same period of time. In particular, about 30% of these sex-related genes in the mouse brain emerged just before the evolutionary appearance of bony fish. It looks apparent that the orthologues of these sex-related genes in the mouse brain appeared with a larger amount at almost the same time as the emergence of phenotypic sex differences in the brain. Moreover, 30% of sex-related genes in the mouse brain that emerged after the divergence of urochordates showed protein binding functions, compared to none of these genes that emerged before the divergence of urochordates. These findings therefore suggest that the formation of new protein-protein interactions through binding functions in vertebrates may have influenced the evolution of sexual dimorphism in the brain at the molecular level.

Transcriptional interferences in *cis* natural antisense transcripts of human and mouse
Naoki Osato, Yoshiyuki Suzuki, Kazuho Ikeo, Takashi Gojobori
For a significant fraction of mRNAs, their expression is regulated by other RNAs including *cis* natural antisense transcripts (*cis*-NATs) that are complementary mRNAs transcribed from opposite strands of DNA at the same genomic locus. The regulatory mechanism of mRNA expression by *cis*-NATs is unknown, though a few possible explanations have been proposed. To understand this regulatory mechanism, we conducted a large-scale analysis of the currently available data and examined how the overlapping arrangements of *cis*-NATs

affect their expression level. Here, we show that for both human and mouse the expression level of *cis*-NATs decreases as the length of the overlapping region increases. In particular, the proportions of the highly expressed *cis*-NATs in all *cis*-NATs examined were about 36% and 47% for human and mouse, respectively, when the overlapping region was less than 200 bp. However, both proportions decreased virtually to zero when the overlapping regions are more than 2,000 bp in length. Moreover, the distribution of the expression level of *cis*-NATs changes according to different types of the overlapping pattern of *cis*-NATs in the genome. These results are consistent with the transcriptional collision model for the regulatory mechanism of gene expression by *cis*-NATs.

Evolutionary analysis of the blind cavefish of Mexican tetra, *Astyanax mexicanus*, by cDNA microarrays

Nobuhiko Tanaka, Shozo Yokoyama, Kazuho Ikeo, Takashi Gojobori

Mexican tetra (*Astyanax mexicanus*), a single species with eyed surface (surface fish) and eyeless cave (cavefish) dwelling forms, gives unique opportunities for studying the genetics of speciation processes because the direction of evolutionary processes is known with certainty: cavefish are derived from surface-dwelling ancestors. In this study, to extensively find genes that can differentiate evolutionary changes between the surface fish and the cavefish, we conducted cDNA microarray analyses. Each of the microarrays has 3,070 non-redundant genes from an entire body of an adult surface fish. Target genes for the microarrays were made from an entire body of each a surface fish and a cavefish. As a result of four-time array analyses, 209 genes out of the 3,070 genes were found with significant differential expression (p-value < 0.01): 122 genes and 87 genes were under-expressed genes and over-expressed genes in the cavefish, respectively. Functional information on the differentially expressed 209 genes suggested behavioral, physiological, and morphological changes between the surface fish and the cavefish. The differentially expressed genes with functional information could be candidates for further analyses to understand a mechanism of the differences of gene expression pattern between the two dwelling forms. This is the first report that differences of gene expression between the surface fish and the cavefish are extensively examined throughout a whole body.

Compensatory change of interacting amino acids in the coevolution of transcriptional coactivator MBF1 and TATA-box binding protein TBP

Qing-Xin Liu, Naomi Nakashima-Kamimura, Kazuho Ikeo, Susumu Hirose and Takashi Gojobor

To elucidate the transcriptional regulation in eukaryotic genome network, it is important to understand coevolution of transcription factors, transcriptional coactivators and TATA-box binding protein TBP. In this study, coevolution of transcriptional coactivator MBF1 and its interacting target TBP was first evaluated experimentally by examining if compensatory amino acid changes took place at interacting sites of both proteins. The experiments were conducted by identifying interaction sites and comparing the amino acids at these sites among different organisms. Here we provide evidence for compensatory changes of transcription coactivator and its interacting target, presenting the first report that transcription coactivator may have undergone coevolution with TBP.

Functional analysis of *Drosophila* TDF during the neuronal development

Qing-Xin Liu, Kazuho Ikeo, Yasushi Hiromi, Susumu Hirose and Takashi Gojobori

In *Drosophila*, the *tracheas defective* (*tdf*) gene encodes a bZIP protein that required for the development of trachea, heart, head and neural system. TDF is highly expressed in the cells of the morphogenetic furrow (MF) region. Loss of TDF function causes defects in the eye development. Overexpression of TDF in the eye disc induced abnormal eyes. Moreover, overexpression of TDF in the leg disc resulted in lack of tarsus. The targets of *tdf* responsible for these responses have not been identified. To identify *tdf* downstream genes in a comprehensive manner, we used genome-wide oligonucleotide arrays and analyzed differential gene expression in wild-type embryos versus *tdf* mutant embryos. Upon knockout of *tdf* function, expression of 340 genes decreased and 338 genes increased.

Many of these genes can be assigned to specific aspects of the tracheal and neural system development. We also discovered *tdf* target genes that are likely to play specific roles in eye morphogenesis.

Functional importance of pathfinding of neurons inferred from evolutionary conservation of Tbx20
Qing-Xin Liu, Masaki Hiramoto, Hitoshi Ueda, Takashi Gojobori, Yasushi Hiromi and Susumu Hirose
The T-box transcription factors are a family of developmentally regulated DNA-binding proteins that play an important role in organogenesis. In fact, they are involved with developmental processes such as cell lineage choices, terminal differentiation and proliferation. However, the function of T-box transcription factors in neural development is poorly understood. With the aim of examining functional significance of Tbx20 in the process of pathfinding of neurons, we have first identified the *midline* gene, a *Drosophila* ortholog of Tbx20, which is a master control gene for neuronal pathfinding. We then determined the binding sequence of Midline using the in vitro binding site selection method. As a result, we found that the binding sequence of Midline existed in the upstream regions or an intron of slit, frazzled and robo. Chromatin immunopreciptation also showed that Midline directed binding of Midline to the binding sites of all three genes. Using comparative genomics, the binding sequence of Midline was also found in the regulating regions of slit, frazzled and robo in the genomes of zebrafish, mouse and human. Thus, the role of Tbx20 in the pathfinding of neurons is very much important, because its orthologs of human, mouse and zebrafish are also expressed in motor neurons.

Search for the evolutionary origin of protozoan lens-eye
Shiho Hayakawa, Hwang Jung Shan, Yasuharu Takaku, Satoshi Nagai, Takeo Horiguchi, Hiroshi Suga, Kazuho Ikeo, Walter Gehring and Takashi Gojobori
The dinoflagellates (division Pyrrhophyta, class Dinophyceae) are a group of unicellular phytoplankton in marine and fresh waters, which are composed of more than 2,000 species. More than a half of them are photosynthetic while the rest of them are heterotrophic. One of families in dinoflagellates, Warnowiaceae, consists of three heterotrophic genera, *Warnowia*, *Erythropsis* and *Nematodinium*, which are identified by distinct structures such as cingulum, sulcus and “ocellus”. In particular, “ocellus” is an organelle of the lens-like structure which exists only in this family. With the aim of examining if this protozoan lens-eye is actually the evolutionary origin of human camera-eyes, we attempted to identify the genes that may be involved with the formation and function of the ocellus. In practice, we collected samples of the species for the three genera of Warnowiaceae, which were carefully identified by morphological traits, from the sea near Japan as well as the Mediterranean Sea. Isolating DNAs from those samples, we first confirmed species identification by constructing molecular phylogenetic tree of SSU rDNAs and mitochondrial genes. Then, we constructed cDNA libraries and sequenced cDNA clones. When we made the annotation on those clone sequences, we found that there were homologues for photoreceptor-related genes such as rhodopsin and plastid-targeting proteins. More interestingly, we also found a number of gene homologues that can be apparently related to morphogenesis of the ocellus and retina. From these reasons, we think it reasonable to conclude that at least some genes in protozoan ocellus shared the common ancestry with mammalian camera-eyes. The coming issue will be to know by which mechanisms this can be brought, straightforward evolution or horizontal gene transfer.

To search the origin of neural tube: Gene expression analysis of ciliary band in sea urchin embryo
Sonoko Kinjo, Kazuho Ikeo and Takashi Gojobori
Sea urchin, a member of echinoderm, has radial nervous system although it is close relatives of vertebrates that have centralized nervous system. It is being accepted that neural tube, the central nervous system (CNS) of vertebrates, originated from protostome CNS because of the similarity of Hox genes expression between vertebrates and protostomes. However, this theory

cannot explain how echinoderm establishes its unique nervous system. Because molecular mechanism of nervous system of sea urchin is largely unknown, first we investigated the genes concerning nervous system of sea urchin. We constructed cDNA library of ciliary band, a nervous system of sea urchin larva, and sequenced around 5,000 expressed sequence tags (ESTs) so far. For the 1,000 ESTs, annotation via homology search was conducted and 40% of ESTs matched to known genes. More than half of matched genes were mitochondrial genes. In the remaining matched genes, there were actin and tubulin that relate to ciliary movement. In addition, we found ESTs that shows high similarity with BAC clone of sea urchin that contain Hox cluster genes. At the current situation, there are few genes functionary annotated enough and 60% of ESTs did not match any known genes. Further we would like to conduct more detail annotation.

Ancient positive selection on CD155 as a possible cause for susceptibility to poliovirus infection in simians
Yoshiyuki Suzuki
Poliovirus is the etiological agent of poliomyelitis. From the observations that only simians are susceptible to poliovirus infection and that 37 amino acid sites (the poliovirus-binding associated [PBA] sites) in the domain D1 of CD155 are involved in the binding to poliovirus, it is considered that the susceptibility to poliovirus infection evolved through amino acid substitutions that occurred at the PBA sites on the ancestral branch of simians. Here it is shown that positive selection has operated on these substitutions by analyzing the nucleotide sequences encoding almost the entire region of D1 in humans, non-human hominoids (chimpanzees and gorillas), Old World monkeys (African green monkeys), New World monkeys (brown capuchins, squirrel monkeys, and marmosets), prosimians (ring-tailed lemurs), and non-primate mammals (rabbits). Positive selection is unlikely to have operated on the susceptibility to poliovirus infection, but possibly on the binding to another molecule. Elimination of susceptibility to poliovirus infection in simians may be difficult, because it also requires elimination of advantageous effects that have been exerted by CD155.

Natural selection on the influenza virus genome
Yoshiyuki Suzuki
Influenza viruses are the etiological agents of influenza. Although vaccines and drugs are available for the prophylaxis and treatment of influenza virus infections, the generation of escape mutants has been reported. To develop vaccines and drugs that are less susceptible to the generation of escape mutants, it is important to understand the evolutionary mechanisms of the viruses. Here natural selection operating on all the proteins encoded by the H3N2 human influenza A virus genome was inferred by comparing the numbers of synonymous (dS [DS]) and nonsynonymous (dN [DN]) substitutions per site. Natural selection was also inferred for the groups of functional amino acid sites involved in B-cell epitopes (BCEs), T-cell epitopes (TCEs), drug resistance, and growth in eggs. The entire region of PB1-F2 was positively selected, and positive selection also appeared to operate on BCEs, TCEs, and growth in eggs. The frequency of escape mutant generation appeared to be positively correlated with the dN/dS (DN/DS) values for the targets of vaccines and drugs, suggesting that the amino acid sites under strong functional constraint are suitable targets. In particular, TCEs may represent candidate targets, since the dN/dS (DN/DS) values were small and negative selection was inferred for many of them.

Statistical properties of the methods for detecting positively selected amino acid sites

Yoshiyuki Suzuki
Parsimony and Bayesian methods have been developed for detecting positively selected amino acid sites. It has been reported that the parsimony method is generally conservative. In contrast, the Bayesian method is known to identify more positively selected sites than the parsimony method, especially when the number of sequences analyzed is small, although the interpretation of results obtained from the former method is controversial. Here I show that the likelihood-ratio test (LRT) of the Bayesian method corresponds to the parsimony method with window analysis, by analyzing the nucleotide sequences encoding the trans-activator (tax) gene of human T-cell lymphotropic virus type I (HTLV-I). It is also indicated that in the parsimony method, the test of selective neutrality using the binomial probability tends to be conservative, but the Monte Carlo simulation is useful for solving this problem. In addition, in the Bayesian method, the bootstrap method appears to produce similar results to the LRT. This information may be useful for improving the methods for detecting positively selected amino acid sites.

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ORAL PRESENTATION

1．Ikeo,K.　FASTA BLASTの使い方　　国立遺伝学研究所　生命情報・DDBJ研究センター　6/15

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3．Gojobori T.　INSD International Nucleotide Sequence Database: History of INSD, What is DDBJ　Bioinformatics and DDBJ Training Course　Jakarta, Indonesia　3/7

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7．五條堀孝　遺伝子発現から見た生物進化　お茶の水女子大学総合生命科学講義　東京　3/17
8．五條堀孝　夏の学校3「階層性について」 日本進化学会2006年大会　東京　8/31
9．五條堀孝　生命情報論講演　慶応義塾大学生命情報論　慶應義塾大学・藤沢キャンパス　12/19
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3．Ikeo,K.「Comparative study of tunicate genome sequences to understand evolution of cis-element」, Marine Genomics , Sorrento, Italy , 10/28-11/1
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13．美濃部純子, 金林明奈, 早川志帆, 藤澤千笑, 五條堀孝, 小早川義尚,小泉修, 藤澤敏孝「ヒドラのnoggin様遺伝子(HyNog)の発現パターン」, 日本動物学会第77回大会 , 松江 , 9/21-24
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17．五條堀孝「統合データベースプロジェクト」, ライフサイエンス合同シンポジウム2006 ,

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18．五條堀孝「統合データベースプロジェクト」，ライフサイエンス合同シンポジウム2006，大阪，3/23
19．五條堀孝「ゲノム研究における超高速計算システムの活用」，第2回「計算科学による新たな知の発見・統合・創出」シンポジウム，茨城県つくば市，4/5
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22．五條堀孝「ポストゲノムと臨床情報研究」，東海大学シンポジウム「ポストゲノム時代の臨床研究について」，東京，7/27
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24．五條堀孝「生命システムの進化-脳・神経系の進化過程のゲノム的研究」，日本進化学会2006年大会，東京，8/31
25．五條堀孝「ヒト遺伝子統合データベース」“An Integrated Databese of Human Genes”，BioJapan 2006，大阪，9/13
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27．五條堀孝「An Integrated Database of Human Genes」，DNAチップ研究所にて，神奈川，9/26
28．五條堀孝「バイオ分野からワイヤレスセンサーに対する期待～ゲノム情報を用いた健康情報産業に関する今後の展望～」，第10回「ワイヤレス・センサー・ネットワーク社会に向けたナノメートルCMOSシステムとその要素技術の研究」に関する先導的研究開発委員会，東京，9/29
29．Gojobori, T.「DNA Variation and Phenotype Data in the H-Invitational Human Gene」，標準化国際Workshop，東京，10/17
30．Gojobori, T.「Explosive emergence of central nervous system-specific genes during genomic evolution of body fish」，Marine Genomics International Conference，Sorrento, Italy，10/31
31．五條堀孝「ヒトゲノムネットワーク情報システムの構築」，GNP第2回研究報告会，神奈川，11/7
32．五條堀孝「Genomic evolution of human nervous system-specific genes and its implication to methods for hunting neuropathological disease-sensitive genes」，応用ゲノムサテライトシンポジウム「Human genome, evolution, and disease」，東京，12/16
33．五條堀孝「疾患関連遺伝子同定支援システム、遺伝子多様性DBの構築」，データベース・解析部門、平成17年度遺伝子多様性モデル解析事業全体会議，東京，1/25
34．五條堀孝「ゲノムネットワークプラットフォームの構築とヒトトランスクリプトームから見た遺伝子構造の統一的理解への活用」，転写制御ネットワーク解析の最前線，東京，1/26
35．五條堀孝「病態のシステム的理解と疾患情報モデルの構築」，「応用ゲノム」CO1・CO2計画研究・公募研究班会議，東京，2/16
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37．五條堀孝「ダーウィンを越えた日本人-木村資生博士の研究」，公益信託進化学振興木村資生基金第1回木村資生記念講演会「生物進化の最近の発展」，愛知県岡崎市，3/4
38．Hwang J. S., Ikeo K., Fujisawa T., Gojobori, T.「The cnidocil apparatus of hydra: a progenitor of metazoan sensory receptor?」，日本進化学会2006年大会，東京，8/29-8/31
39．Q-X. Liu「Functional importance of pathfinding of neurons inferred from evolutionary conservation of Tbx20」，The 78th annual Meeting of the Genetics Society of Japan，Tukuba，9/25-27
40．Qing-Xin Liu, Naomi Nakashima-Kamimura, Kazuho Ikeo, Susumu Hirose and Takashi Gojobor「Compensatory change of interacting amino acids in the coevolution of transcriptional coactivator MBF1 and TATA-box binding protein TBP」，The 20th IUBMB International Congress of Biochemistry and Molecular Biology and 11th FAOBMB Congress，Kyoto，6/18-23

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EDUCATION

1．五條堀孝　H-Invitational Disease Edition Meeting　東京都江東区　2/13
2． LIPI and DDBJ (Gojobori T.)　Bioinformatics and DDBJ Training Course　Jakarta, Indonesia　3/6-8
3．五條堀孝　All Human Genes FA Strategic Meeting　東京都江東区　7/20
4．五條堀孝　日本進化学会2006年大会（大会委員長）　東京都渋谷区　8/29-31
5．五條堀孝　Disease Edition Cancer Edition Peparatory Meeting　東京都江東区　10/16
6．五條堀孝　AHG FA 2006 Strategic Meeting #2　東京都江東区　10/24-25
7．佐々木卓司、Rod A. Wing、五條堀孝　Rap 3 (イネゲノム国際会議）　茨城県つくば市　12/9-10

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OTHERS

1．五條堀　孝，1，Editorial Board of Gene Therapy and Molecular Biology
2．五條堀　孝，1，Editorial Board of BMC Genomics
3．五條堀　孝，1，(財)遺伝学普及会常務理事
4．五條堀　孝，1，Associate Editor of PLoS Genetics
5．五條堀　孝，1，Associate Editor of Molecular Biology and Evolution
6．五條堀　孝，1，Editor of GENE
7．五條堀　孝，1，Editor of FEBS Letters
8．五條堀　孝，1，日本進化学会2006年大会実行委員長
9． 五條堀　孝， 2， 全米芸術科学アカデミー外国人名誉会員(AAAS Foreign Honorary Member: AMERICAN ACADEMY OF ARTS & SCIENCES)
10．五條堀　孝，3，日本学術会議連携会員
11．五條堀　孝，3，文部科学省科学技術・学術審議会専門委員
12．五條堀　孝，3，経済産業省産業構造審議会臨時委員
13．五條堀　孝，1，Vice-Chairman of the International　Society of Molecular Evolution
14．五條堀　孝，1，日本遺伝学会評議員
15．鈴木　善幸，2，日本遺伝学会奨励賞
16．鈴木　善幸，2，日本進化学会研究奨励賞

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I. CENTER FOR INFORMATION BIOLOGY AND DNA DATA BANK OF JAPAN
I-b. Laboratory for Gene-Product Informatics
Ken Nishikawa

RESEARCH ACTIVITIES

(1) Intrinsically disordered loops inserted into the structural domains of human proteins

Fukuchi, S., Homma, K., Minezaki, Y. and Nishikawa, K.

Much attention has been paid recently to proteins with partially or fully disordered structures, which are found to exist mostly in eukaryotes and are involved mainly in pivotal cellular processes such as transcriptional regulation, translation and cellular signal transduction. Long disordered sequences are sometimes inserted within the single structural domains of proteins, forming loops from the molecular surface. Such intrinsically disordered loops (IDLs) either are invisible in X-ray crystallography, or hamper protein crystallization itself due to great flexibility. Perhaps because of this, such long disordered sequences have not been characterized adequately. Here, we propose an informational method that stringently identifies IDLs in the structural domains of proteins using the amino acid sequence alone. A genome-wide survey of human proteins conducted with the method identified 50 IDL-containing proteins, several of which have experimentally determined 3D structures. Similar searches in other entirely sequenced organisms revealed that IDLs are prevalent in eukaryotes, while they are much less so in prokaryotes. As there is a statistically significant coincidence between the boundaries of IDLs and those of exons, we suggest that IDLs were produced mainly by exon addition in eukaryotes. IDLs are almost always located at the surface of proteins and are enriched with hydrophilic residues, and IDL-containing proteins tend to be intracellular. Some of the well-characterized proteins with IDLs illustrate that IDLs play pivotal roles in the switching of intracellular signaling or regulatory functions, suggesting that IDL insertion is an effective way to create functionally different domain variants.

(2) Human transcription factors contain a high fraction of intrinsically disordered regions essential for transcriptional regulation

Minezaki, Y., Homma, K., Kinjo, A.R. and Nishikawa, K.

Human transcriptional regulation factors, such as activators, repressors, and enhancer-binding factors are quite different from their prokaryotic counterparts in two respects: the average sequence in human is more than twice as long as that in prokaryotes, while the fraction of sequence aligned to domains of known structure is 31% in human transcription factors (TFs), less than half of that in bacterial TFs (72%). Intrinsically disordered (ID) regions were identified by a disorder-prediction program, and were found to be in good agreement with available experimental data. Analysis of 401 human TFs with experimental evidence from the Swiss-Prot database showed that as high as 49% of the entire sequence of human TFs is occupied by ID regions. More than half of the human TFs consist of a small DNA binding domain (DBD) and long ID regions frequently sandwiching unassigned regions. The remaining TFs have structural domains in addition to DBDs and ID regions. Experimental studies, particularly those with NMR, revealed that the transactivation domains

in unbound TFs are usually unstructured, but become structured upon binding to their partners. The sequences of human and mouse TF orthologues are 90.5% identical despite a high incidence of ID regions, probably reflecting important functional roles played by ID regions. In general ID regions occupy a high fraction in TFs of eukaryotes, but not in prokaryotes. Implications of this dichotomy are discussed in connection with their functional roles in transcriptional regulation and evolution.

(3) CRNPRED: highly accurate prediction of one-dimensional protein structure by large-scale Critical Random Networks

Kinjo, A.R. and Nishikawa, K.

One-dimensional protein structures such as secondary structures or contact numbers are useful for three-dimensional structure prediction and helpful for intuitive understanding of the sequence-structure relationship. Accurate prediction methods will serve as a basis for these and other purposes. We implemented a program CRNPRED which predicts secondary structures, contact numbers and residue-wise contact orders. This program is based on a novel machine learning scheme called critical random networks. Unlike most conventional one-dimensional structure prediction methods which are based on local windows of an amino acid sequence, CRNPRED takes into account the whole sequence. CRNPRED achieves, on average per chain, Q3 = 81% for secondary structure prediction, and correlation coefficients of 0.75 and 0.61 for contact number and residue-wise contact order predictions, respectively. CRNPRED will be a useful tool for computational as well as experimental biologists who need accurate one-dimensional protein structure predictions.

(4) Gene cluster analysis method identifies horizontally transferred genes with high reliability and indicates that they provide the main mechanism of operon gain in eight species of gamma-proteobacteria

Homma, K., Fukuchi, S., Nakamura, Y., Gojobori, T. and Nishikawa, K.

The formation mechanism of operons remains unresolved: operons may form by rearrangements within a genome or by acquisition of genes from other species, that is, horizontal gene transfer (HGT). One hindrance to its elucidation is the unavailability of a method to accurately identify HGT, although it is generally considered to occur. It is critically important first to select horizontally transferred (HT) genes reliably and then to determine the extent to which HGT is involved in operon formation. For this purpose, we considered indels in terms of gene clusters instead of individual genes and chose candidates of HT genes in 8 species of Escherichia, Shigella, and Salmonella based on the minimization of indels. To select a benchmark set of positively HT genes against which we can evaluate the candidate set, we devised another procedure using intergenetic alignments. Comparison with the benchmark set demonstrated the absence of a significant number of false positives in the candidate set, showing the high reliability of the method. Analyses of *Escherichia coli* K-12 operons revealed that although approximately 20 operons were probably gained from the last common ancestor of the 8 gamma-proteobacteria, deletion of intervening genes accounts for the formation of no operons, whereas horizontal transfer expanded 2 operons and introduced 4 entire operons. Based on these observations and reasoning, we suggest that the main mechanism of operon gain is HGT rather than intragenomic rearrangements. We propose that genes with related essential functions tend to reside in conserved operons, whereas genes in nonconserved operons mostly confer slight advantage to the organisms and frequently undergo horizontal transfer and decay. HT genes constitute at least 5.5% of the genes in the 8 species and approximately 45% of which originate from other gamma-proteobacteria. Genes involved in viral functions and mobile and extrachromosomal element functions are HT more often than expected. This finding indicates frequent mediation of HGT by bacteriophages. On the other hand, not only informational genes (those involved in transcription, translation, and related processes) but also operational genes (those involved in housekeeping) are HT less frequently than expected.

(5) Intrinsically disordered regions of human plasma membrane proteins preferentially occur in the cytoplasmic segment

Minezaki, Y., Homma, K., and Nishikawa, K.
A systematic survey of intrinsically disordered (ID) regions was carried out in 2109 human plasma membrane proteins with full assignment of the transmembrane topology with respect to the lipid bilayer. ID regions with 30 consecutive residues or more were detected in 41.0% of the human proteins, much higher than the corresponding figure (4.7%) for inner membrane proteins of *Escherichia coli*. The domain organization of each of the membrane protein in terms of transmembrane helices, structural domains, ID and unassigned regions as well as the distinction of inside or outside of the cell was determined. Long ID regions constitute 13.3% and 3.5% of the human plasma membrane proteins on the inside and outside of the cell, respectively, showing that they preferentially occur on the cytoplasmic side. We interpret this phenomenon as reflection of the general scarcity of ID regions on the extracellular side and their relative abundance on the cytoplasmic side in multicellular eukaryotic organisms.

(6) A tree of life based on protein domain organizations
Fukami-Kobayashi, K., Minezaki, Y., Tateno, Y. and Nishikawa, K.
It is desirable to estimate a tree of life, a species tree including all available species in the three superkingdoms, Archaea, Bacteria and Eukaryota, using not a limited number of genes but full-scale genome information. Here we report a new method for constructing a tree of life based on protein domain organizations, i.e. sequential order of domains in a protein, of all proteins detected in a genome of an organism. The new method is free from the identification of orthologous gene sets and therefore does not require the burdensome and error-prone computation. By pairwise comparisons of the repertoires of protein domain organizations of 17 archaeal, 136 bacterial and 14 eukaryotic organisms, we computed evolutionary distances among them and constructed a tree of life. Our tree shows monophyly in Archaea, Bacteria and Eukaryota, and then monophyly in each of eukaryotic kingdoms and in most bacterial phyla. In addition the branching pattern of the bacterial phyla in our tree is consistent with the widely accepted bacterial taxonomy, and is very close to other genome-based trees. A couple of inconsistent aspects between the traditional trees and the genome-based trees including ours, however, would perhaps urge to revise the conventional view, particularly on the phylogenetic positions of hyperthermophiles.

PUBLICATIONS

Papers

1．金城玲（2006）タンパク質の立体構造情報はどのようにアミノ酸配列に埋めこまれているか？，生物物理，46，37 - 40
2． Fukuchi, S., Homma, K., Minezaki, Y. and Nishikawa, K. （2006） Intrinsically disordered loops inserted into the structural domains of human proteins， **J. Mol. Biol.**，355，845 - 857
3． Minezaki, Y., Homma, K., Kinjo, A.R. and Nishikawa, K.（2006） Human transcription factors contain a high fraction of intrinsically disordered regions essential for transcriptional regulation.，**J. Mol. Biol.**，359，1137 - 1149
4． Kinjo, A.R. and Nishikawa, K.（2006） CRNPRED: Highly accurate prediction of one-dimensional protein structure by large-scale Critical Random Networks.， **BMC Bioinformatics**，7，401 - 0
5． Ohta, T., Kawabata, T., Nishikawa, K., Tani, A., Kimbara, K. and Kawai, F.（2006） Analysis of amino acid residues involved in the catalysis of polyethylene glycol dehydrogenase from Sphingomonas terrae using three-dimensional molecular modeling-based kinetic characterization of mutants.，**Appl. Environ. Microbiol.**，72，4388 - 4396
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1．Nishikawa, K.「Protein-protein interactions mediated by intrinsically unstructured regions in human transcription factors.」, The 20th IUBMB International Congress , Kyoto , 6
2．西川建「タンパク質構造のパラダイムシフト:ヒト転写因子にみられる長大な不規則領域の意味とは？」, 第8回日本進化学会年会 , 東京 , 8
3．Nishikawa, K.「Genome-wide information analyses on human transcription factors and plasma membrane proteins.」, NMR Association for Structural Biology Meeting , Yokohama , 11
4．本間桂一、福地佐斗志、西川建「オペロンは一般に遺伝子の水平移動により生成する」, 本分子生物学会2006フォーラム , 名古屋 , 12
5．峯崎善章、西川建「タンパク3000プロジェクト「転写・翻訳」拠点の成果(4):転写因子の比較ゲノム解析」, 第6回日本蛋白質科学会年会 , 京都 , 4
6．丹谷恵子、太田元規、西川建「ドメイン構成に基づく酵素の比較ゲノム解析」, 第6回日本蛋白質科学会年会 , 京都 , 4
7．金城玲、西川建「タンパク質の1次元構造予測法の改良」, 第6回日本蛋白質科学会年会 , 京都 , 4
8．峯崎善章、西川建「Intrinsically disordered regions of human membrane proteins.」, 第44回日本生物物理学会年会 , 沖縄 , 11
9．丹谷恵子、太田元規、西川建「tructural and functional diversities of enzymes with the common catalytic domain.」, 第44回日本生物物理学会年会 , 沖縄 , 11
10．長島剛宏、金城玲、三井崇志、西川建「Efficient search of protein low-energy conformational space with a newly devised Wang-Landau molecular dynamic technique.」, 第44回日本生物物理学会年会 , 沖縄 , 11
11．峯崎善章、西川建「ディスオーダー領域をもつタンパク質の細胞局在性」, 日本分子生物学会2006フォーラム , 名古屋 , 12

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I. CENTER FOR INFORMATION BIOLOGY AND DNA DATA BANK OF JAPAN
I-c. Laboratory for Gene Function Research

Yoshio Tateno

RESEARCH ACTIVITIES

The laboratory consists of five members: Dr. Yoshio Tateno (Professor), Dr. Roberto Antonio Barrero Gumiel (Assistant Professor), Dr. Atsushi Ogura (Postdoc), Dr. Yasuharu Takaku (Postdoc) and Ms. Naoko Murakata (Secretary). We aim at the elucidation of the origin, evolution and function of genes and proteins in view of molecular evolution, structural biology and information biology in collaboration with other research groups in the institute and out. Besides the research activities summarized below, we take part in the DDBJ activity in particular in the database construction and public relations.

RESEARCH ACTIVITY

(1) DDBJ in preparation for overview of research activities behind data submissions
Okubo, K., Sugawara, H., Gojobori, T. and Tateno, Y.

In the past year, DDBJ (http://www.ddbj.nig.ac.jp) collected and released 1,956,826 entries or 1,741,313,111 bases. The released data include approximately 90,000 ESTs and cDNAs of Macaca fascicularis, and 280 million bases of mouse GSS. In addition to the data collection, we have indexed the submitted data to the International Nucleotide Sequence Database Collaboration (INSDC, http://www.insdc.org) to classify the entries into research projects behind data submissions. They are expected to be useful to the data submitters and users for enhancing the data submission, retrieval and systematic data analyses at INSDC. The results of indexing also allow one to grasp research projects in life sciences that promoted and produced the DNA sequences submitted to INSDC. (Okubo, K. et al., 2006)

(2) Evidence standards in experimental and inferential INSDC Third Party Annotation data.
Cochrane, G., Bates, K., Apweiler, R., Tateno, Y., Mashima, J., Kosuge, T., Mizrachi, I., Schafer, S. and Fetchko, M.

The Third Party Annotation (TPA) project collects and presents high-quality annotation of nucleotide sequence. Annotation is submitted by researchers who have not themselves generated novel nucleotide sequence. In its first few years, the resource has proven to be popular with submitters from a range of biological research areas. Central to the project is the requirement for high-quality data, resulting from experimental and inferred analysis discussed in peer-reviewed publications. The data are divided into two tiers: those with experimental evidence and those with inferential evidence. Standards for TPA are detailed and illustrated with the aid of case studies. (Cochrane, G. et al. 2006)

(3) The concept of sampling in 'omics technology
Morrison, N., Cochrane, G., Faruque, N., Tatusova, T., Tateno, Y., Hancock, D., and Field, D.

Fundamental biological processes can now be studied by applying the full range of OMICS technologies (genomics, transcriptomics, proteomics, metabolomics, and beyond) to the same biological sample. Clearly, it would be desirable if the concept of sample were shared among these technologies, especially as up until the time a biological sample is prepared for use in a specific OMICS assay, its description is inherently technology independent. Sharing a common informatic representation would encourage data sharing (rather than data replication), thereby reducing redundant data capture and the potential for error. This would result in a significant degree of harmonization across different OMICS data standardization activities, a task that is critical if we are to integrate data from these different data sources. Here, we review the current concept of sample in OMICS technologies as it is being dealt with by different OMICS standardization initiatives and discuss the special role that the newly formed Genomic Standards Consortium (GSC) might have to play in this domain. (Morrison, N. et al. 2006)

(4) Exploration and grading of possible genes in 183 bacterial strains by a common fine protocol lead to new genes: Gene Trek in Prokaryote Space (GTPS).
Kosuge, T., Abe, T., Okido, T., Tanaka, N., Hirahata, M., Maruyama, Y., Mashima, J., Tomiki, A., Kurokawa, M., Himeno, R., Miyazaki, M., Gojobori, T., Tateno, Y., and Sugawara,, H.

A large number of the complete genomes for microorganisms have been sequenced and submitted to the public database, and then incorporated in our complete genome database, Genome Information Broker (GIB, http://gib.genes.nig.ac.jp/). When researchers carry out research in comparative genomics or others, however, they must be aware that there are protein coding genes not confirmed by homology or motif search, and that reliable protein coding genes are missing. Therefore, we have developed a protocol (Gene Trek in Prokaryote Space, GTPS) for finding possible protein coding genes in bacterial genomes. GTPS is equipped with a protocol for assigning a degree of reliability to predicted protein coding genes. We then systematically applied it to all complete genomes of 123 bacterial species and strains that were publicly available as of July 2003 first, and then again those of 183 species and strains available as of September 2004. As a result, we found a number of wrong genes and several new ones in the genome data in question with respect to the criteria of GTPS. We also showed a way of estimating the total number of orthologous genes in the bacterial world. (Kosuge T. et al., 2006)

(5) Molecular characterization of developmental gene in eyes: Through data-mining on integrated transcriptome databases
Choy, K.W., Wang, C. C., Ogura, A., Lau, T. K., Rogers M. S., Ikeo, K., Gojobori, T., Tang, L. Y., Lam, D. S., Chun, T. K. and Pang, C. P.

Our aim was to utilize publicly available and proprietary sources to discover candidate genes important for ocular development. DESIGN AND METHODS: The collated information on our 5092 non-redundant clusters was grouped and functional annotation was conducted using gene ontology (FatiGO) for categorizing them with respect to molecular function. The web-based viewer technological platform (H-InvDB) was employed for transcription analyses of in-house high quality fetal eye Expressed Sequence Tags (ESTs). Eye-specific ESTs were also analyzed across species by using EMBEST. RESULTS: According to adult eye cDNA libraries, nucleic acid binding and cell structure/cytoskeletal protein genes were the most abundant among the ESTs of fetal eyes. Using cDNA assembly in H-InvDB, 20 (80%) of the 25 most commonly expressed genes in the human eye are also expressed in extraocular tissues. The crystalline gamma S gene is highly

expressed in the eye, but not in other tissues. We used EMBEST to compare human fetal eye and octopus eye ESTs and the expression similarity was low (1.6%). This indicated that our fetal eye library contains genes necessary for the developmental process and biological function of the eye, which may not be expressed in the fully developed octopus eyes. The human fetal eye cDNA library also contained highly abundant eye tissue genes, including alphaA-crystallin, eukaryotic translation elongation factor 1 alpha 1 (EEF1A1), bestrophin (VMD2), cystatin C, and transforming growth factor, beta-induced (BIGH3). CONCLUSIONS: Our annotated EST set provides a valuable resource for gene discovery and functional genomic analysis. This display will help to appreciate the strengths and weaknesses of the different technological platforms, so that in future studies the maximum amount of beneficial information can be derived from the appropriate use of each method. (Choy, K. W. et al., 2006)

(6) Development of a method for constructing a phylogenetic tree by using many different orthologs
Tokumasa Horiike, Daisuke Miyata, Kazuo Hamada, Satoshi Saruhashi, Takao Shinozawa, Yoshio Tateno

To compare the topologies between a pair of phylogenetic trees, we developed a method that can accommodate the difference in the number of OTUs between the pair in question. This method enables us to extract a common set of phylogenetic relationships that are consistent among a group of the constructed trees irrespective of the number of OTUs. Since the one including the largest common set trees among the group is considered to show the closest phylogenetic relationships to the true ones, we also developed a statistical method to single it out. We are now constructing a dataset of orthologs for bacterial species to apply the method for elucidating bacterial phylogeny.

(7) We were in collaboration with Prof. Tadao Saito of Tohoku University and his laboratory on the function and evolution of glucosidase and galactosidase genes in Lactobcillus.
Saito, T, Yamazaki Y and Tateno Y

(8) We were in collaboration with Dr. Kaoru Fukami-Kobayashi of RIKEN on evolutionary analysis of MHC genes in primates.
Fukami-Kobayashi K and Tateno Y

(9) We were in collaboration with Prof. Naoko Takezaki of Kagawa Medical College on the evolution of genes expressed in brains.
Takezaki N and Tateno Y

(10) We are in collaboration with the Japan Biological Information Research Center (JBIRC) in the all human genes annotation (AHG).
Barrero, R., Mashima, J., Tateno, Y., Imanishi, T., Gojobori, T. et al.

Databases
1. DDBJ is operated by DNA Data Analysis, Gene Function Research, Gene-Product Informatics, Research and Development of Biological Databases and Gene Expression Laboratories, and Division of Population Genetics. DDBJ collects, annotates and publishes DNA sequence data, and exchanges the data with EMBL Bank and GenBank on a daily basis. In addition, DDBJ edits the data published by DDBJ, EMBL Bank and GenBank together four times a year and publishes as a release. In 2005 DDBJ published the following four releases.

Release 65 March, 06 55,890,995 entries, 60,564,721,635 bases
Release 66 June, 06 58,176,628 entries, 62,945,843,881 bases

Release 67 Sept., 06 61,144,621 entries, 65,443,024,193 bases
Release 68 Dec., 06 64,267,978 entries, 68,259,314,742 bases

2. The international public gene expression database, CIBEX, is operated by Gene Function Research and DNA Data Analysis Laboratories. We have collected gene expression data and released to the public.

3. Dr. Tateno visited UniProt to discuss with Director Amos Bairoch about collaboration between DDBJ and UniProt, SwissProt, Geneva, Switzerland, April, 2006.

4. Dr. Tateno attended the 19th International Nucleotide Sequence Databases Collaborative Meeting , and the 17th International Nucleotide Sequence Databases Advisory Meeting, National Center for Biotechnology Information, Bethesda, USA, May, 2006

5. Dr. Tateno attended Human Variome Meeting as an invited observer, Park Hyatt Hotel, Melbourne, Australia, June, 2006.

6. Dr. Tateno attended the 9th Microarray Gene Expression Society Meeting as a board member, University of Washington, Seattle, USA, September, 2006

EDUCATION
1. Dr. Y. Tateno co-organized and gave a lecture and practice at the 5th Japan-Korea Bioinformatics Training Course at NIG, March, 2006

2. Dr. Tateno gave a lecture on ✗genomic evolution of MHC class I region in primates〒 at Soongsil University in Seoul in Korea in September, 2006

3. Dr. Tateno gave a lecture on ✗the evolution of MHC genes viewed from LINEs〒 at Heinrich-Heine University in Dusseldorf, Germany, in October, 2006

SOCIAL CONTRIBUTIONS AND OTHERS

Dr. Y. Tateno served the Society of Molecular Biology and Evolution as a member on the Editorial Advisory Board.

Dr. Y. Tateno served the Microarray Gene Expression Data Society as an Advisory Board Member,

Dr. Y. Tateno served the Genetics Society of Japan as a Member of Editorial Board

Dr. Y. Tateno served the Genetics Society of Japan as Representative member of the Union of Academic Societies for Natural History

PUBLICATIONS
Papers

1 . Takeda, J., Suzuki, Y., Nakao, M., Barrero, R. A. et al. (2006) Large-scale identification and characterization of alternative splicing variants of human gene transcripts using 56,419 completely sequenced and manually annotated full-length cDNAs , **Nucleic Acids Res** , 34 , 3917 - 3928
2 . Okubo, K., Sugawara, H., Gojobori, T. and Tateno, Y. (2005) DDBJ in preparation for

overview of research activities behind data submissions. , **Nucleic Acids Res** , 34 , 6 - 9
3 . Cochrane, G., Bates, K., Apweiler, R., Tateno, Y., Mashima, J., Kosuge, T., Mizrachi, I., Schafer, S. and Fetchko, M （2006） Evidence standards in experimental and inferential INSDC Third Party Annotation data. , **OMICS** , 10 , 105 - 113
4 . Morrison, N., Cochrane, G., Faruque, N., Tatusova, T., Tateno, Y., Hancock, D., and Field, D （2006） The concept of sampling in 'omics technology , **OMICS** , 10 , 127 - 137
5 . Kosuge, T., Abe, T., Okido, T., Tanaka, N., Hirahata, M., Maruyama, Y., Mashima, J., Tomiki, A., Kurokawa, M., Himeno, R., Miyazaki, M., Gojobori, T., Tateno, Y., and Sugawara,, H. （2006） Exploration and grading of possible genes in 183 bacterial strains by a common fine protocol lead to new genes: Gene Trek in Prokaryote Space (GTPS). , **DNA Res** , 13 , 245 - 254

ORAL PRESENTATION

1 . 舘野義男、小見山智義　分子系統学、講義ならびに実習　JSTゲノムリテラシー、JST、東京　11/13
2 . 舘野義男　発現解析データベースCIBEXについて　ぬまづ産業振興プラザ　2/4
3 . Tateno, Y.　Genomic evolution of MHC class I region in primates　Heinrich Heine University, Dessuldorf, Germany　10/31
4 . Tateno, Y.　Genomic evolution of MHC class I region in primates　Soongsil University, Seoul　9/22

POSTER PRESENTATIONS

1 . Ogura A. and Daniel L. Hartl「 Targets of sex-ratio suppressors in Drosophila revealed by microarray and genome analyses 」, Society for Molecular Biology and Evolution Conference , Arizona , May
2 . Ogura A. Choy KW. Wang CC. Ikeo K. Pang CP. Gojobori T 「 Evolution of gene regulatory system for camera eye 」, Marine Genomics , , Oct
3 . Takaku, Y., Hayakawa, S., Wolf, A., Svensson, L., David, C., Fujisawa, T., Ikeo, K., Tateno, Y., Gojoboroi, T.「 Search for the evolution of gap junction 」, Marine Genomics , Sorrento, Italy , 10/27 - 11/1
4 . Komiyama, T., Otake, A., Ikeo, K., Tateno, Y., Inoko, H., Gojobori, T.「 An evolutionary origin and the selction process of goldfish by the mtDNA analysis 」, Marine Genonics , Sorrento, Italy , 10/27 - 11/1
5 . Tateno, Y.「 Evolution of LINEs and its implication about MHC and primate divergences 」, SMBE2006 , Tempi, Arizona , 5/24-5/28
6 . Tateno, Y.「 DDBJ activities of genome databases and evaluation of bacterial gene in INSDC 」, eGenomics , Cambridge , 9/11-9/13
7 . Tateno, Y. 「 Evaluation and Classification of Bacterial Genes 」, The 15th Korea Genome Organization Meeting , Seoul , 9/21-9/22

EDUCATION

1 . CIB/DDBJ, KRIBB (Korea), SCBIT (China)　The 5th JKC Bioinformatics Training Course　Mishima, Japan　3/14-3/17
2 . 遺伝研　2006日本進化学会大会　東京　8/29-8/31

BOOK

1 . 新村芳人、Roberto Barrero、五條掘孝 （2006） 真核生物におけるmRNA翻訳制御のインフォマティクス:開始コドン周辺の塩基パターン解析とマイクロRNAの標的遺伝子予測　機能性**Non-coding RNA**　189 - 202

OTHERS

1 . Tateno, Y. , 1 , Dr. Y. Tateno served the Microarray Gene Expression Data Society as an Advisory Board Member

2 . Tateno, Y. , 1 , Dr. Y. Tateno served the Society of Evolutionary Studies as a Member of the Committee of Genetics under the Science Council of Japan
3 . Tateno, Y. , 1 , Dr. Y. Tateno served the Genetics Society of Japan as a Member of Editorial Board
4 . Tateno, Y. , 1 , Dr. Y. Tateno served the Genetics Society of Japan as Representative member of the Union of Academic Societies for Natural History

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I. CENTER FOR INFORMATION BIOLOGY AND DNA DATA BANK OF JAPAN
I-d. Laboratory for Research and Development of Biological Databases

Hideaki Sugawara

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1 . Okubo K, Sugawara H, Gojobori T, Tateno Y. (2006) DDBJ in preparation for overview of research activities behind data submissions. , **Nucleic Acids Research (Database)** , 1 , 6 - 9

2 . Tanaka, N., Abe, T., Miyazaki, S. Sugawara, H. (2006) “G-InforBIO: Integrated system for microbial genomics” , **BMC Bioinformatics** , 7 , 368 - 368

3 . Tanaka, N., Abe, T., Miyazaki, S. Sugawara, H. (2006) “A useful bioinformatics suite for retrieving and analyzing microbial genome data (G-InforBIO)” , **Journal of Computer Aided Chemistry** , 7 , 87 - 93

4 . Riley, M., Abe, T., Arnaud, B.M., Berlyn, M., Blattner, R.F., Chaudhuri, R.R., Glasner, D.J., Horiuchi, T., Keseler, M.I., Kosuge, T., Mori, H., Perna, T.N., Plunkett, G., Rudd, E.K., Serres, H.M., Thomas, H.G., Thomson, R.H., Wishart, D., and Wanner, L.B. (2006) Escherichia coli K-12: a cooperatively developed annotation snapshot窶鏐2005 , **Nucleic Acids Research** , 34 , 1 - 9

5 . Abe, T., Sugawara, H., Kanaya, K., Kinouchi, M., Ikemura, T. (2006) “A large-scale Self-Organizing Map (SOM) unveils sequence characteristics of a wide range of eukaryote genomes” , **Gene** , 365 , 27 - 34

6 . Abe, T., Sugawara, H., Kanaya, S., Ikemura, T. (2006) “Sequences from almost all prokaryotic, eukaryotic, and viral genomes available could be classified according to genomes on a large-scale Self-Organizing Map constructed with the Earth Simulator” , **Journal of the earth simulator** , 6 , 17 - 23

7 . Abe, T., Sugawara, H., Kanaya, S., Ikemura, T. (2006) “A novel bioinformatics tool for phylogenetic classification of genomic sequence fragments derived from mixed genomes of uncultured environmental microbes” , **Polar Bioscience(in press)** , , 0 - 0

8 . Kosuge T, Abe T, Okido T, Tanaka N, Hirahata M, Maruyama Y, Mashima J, Tomiki A, Kurokawa M, Himeno R, Fukuchi S, Miyazaki S, Gojobori T, Tateno Y, Sugawara H. (2006) “Exploration and grading of possible genes from 183 bacterial strains by a common protocol to identification of new genes: Gene Trek in Prokaryote Space (GTPS)” , **DNA Research** , 31;13(6) , 245 - 254

ORAL PRESENTATION

1 . 菅原秀明 バイオインフォマティクス-すぐに役立つ実践講座-「公共データベースにおけるQoS」 ぬまづ産業振興プラザ 1/21

POSTER PRESENTATIONS

1．阿部貴志「 “微生物ゲノムの共通プロトコルによる遺伝子配列情報の提供”, RSCCにおける研究事例紹介と次世代スーパーコンピュータの開発 」, RSCCシンポジウム , 和光市 , 3/23
2．菅原秀明「 地球規模生物多様性情報機構 」, NBRPパネル展示 , つくば , 9/27
3．Sugawara,H,.「 Scientific Data and Knowledge within the Information Society From the World Directory of Collections of Cultures of Microorganisms towards Mash-up of Biodiversity and Sequence Databases Quality of Services of the Primary Nucleotide Sequence Databases 」, The 20th CODATA International Conference , 北京 , 10/23-25
4．菅原秀明「 21世紀の生物多様性　生物多様性インフォマティクスを創出する。」, 生命情報資源の相互運用性 , 東京 , 10/30

EDUCATION

1．菅原秀明　21世紀の生物多様性　生物多様性インフォマティクスを創出する。　国立遺伝学研究所研究会　東京　10/30
2．菅原秀明　21世紀の生物多様性　生物多様性インフォマティクスを創出する。　国立遺伝学研究所研究会　東京　10/30
3．菅原秀明　　International Workshop on the Interoperability of Biological Information Resouces　新宿パークタワー　3/17
4．菅原秀明　生物情報資源の相互運用性　国立遺伝学研究所共同研究会　三島　3/6

DB SOFT

1．菅原秀明、, Japanese Bio-portal site (Jabion)
http://www.bioportal.jp/
2．菅原秀明、, Genome Information Broker
http://gib.genes.nig.ac.jp/
3．菅原秀明 , WFCC-MIRCEN World Data Centre for Microorganisms (WDCM)
http://www.wdcm.org/
4．菅原秀明 , The portal site for pathogenic microorganisms
http://www.wdcm.org/byogen/
5．菅原秀明 , e-Workbench for Biological Classification and Identification
http://lilium.genes.nig.ac.jp/index_e.html
6．菅原秀明 , H-Invitational Database
http://www.h-invitational.jp/
7．菅原秀明 , タンパク･情報プラットフォーム
http://www.tanpaku.org
8．菅原秀明、宮崎智 , Backbone Databases for Genomics
http://www.jst-bird.nig.ac.jp/

OTHERS

1．, 3 , Global Biodiversity Information Facility（GBIF）副議長
2．, 1 , 財団法人バイオインダストリー協会　評議員
3．, 3 , (財）遺伝学普及会　評議員

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I. CENTER FOR INFORMATION BIOLOGY AND DNA DATA BANK OF JAPAN
I-e. Laboratory for Gene-Expression Analysis

Kousaku Okubo

RESEARCH ACTIVITIES

1) BodyMap-Xs: Anatomical breakdown of 17 million animal ESTs for cross-species comparison of gene expression (Ogasawara O, Watanabe K, Imamura H, Iizuka T, Okubo K)

BodyMap-Xs (http://bodymap.jp) is a database for cross-species gene expression comparison (Ogasawara, O., et.al., 2006) ; it was created by the anatomical breakdown of 17 million animal EST records in DDBJ by using a sorting program tailored for this purpose. In BodyMap-Xs, users are allowed to compare the expression patterns of orthologous and paralogous genes in a coherent manner; this will provide valuable insights for the evolutionary study of gene expression and identification of a responsive motif for a particular expression pattern. In addition, starting from a concise overview of the taxonomical and anatomical breakdown of all animal ESTs, users can navigate to obtain gene expression ranking of a particular tissue in a particular animal; this method may lead to the understanding of the similarities and differences between the homologous tissues across animal species. BodyMap-Xs will be automatically updated in synchronization with the major update in DDBJ, which occurs periodically.

2) Comparison of human gene expression profiles measured with EST, GeneChip, SAGE and iAFLP (Ogasawara O, Arikawa K, Watanabe K, Iizuka T, Okubo K) :

The practical definition of a transcriptome is a entire population of mRNA in a defined source, i.e. a cell, cells, tissue, or an organism.
The composition , which gene and how abundant, is central to the transcriptome data.
As an expansion of the world-first gene expression database BodyMap(http://bodymap.jp), we are collecting gene expression data for human and mouse with newly developed technique iAFLP (http://okubolab.genes.nig.ac.jp/bodymap_i).
In order to estimate performance (sensitivity, specificity and so on) of the iAFLP and the BodyMap gene expression profiles and to construct a reference gene expression profile, we compared these data to the other publicly available gene expression profiles obtained with CGAP-SAGE and GeneChip.

3)Machine interpretation of genome-wide measurement data (Okubo K):
Construction of a system for automatic recruitment of biomedical knowledge and machine interpretation of genome-wide measurement data.

PUBLICATIONS
Papers

1．Okubo K,Sugawara H, Gojobori T, Tateno Y.（2006）DDBJ in preparation for overview of research activities behind data submissions.，**Nucleic Acids Res.**，34，6 - 9
2．Ogasawara O, Otsuji M, Watanabe K, Iizuka T, Tamura T, Hishiki T, Kawamoto S,Okubo K（2006）BodyMap-Xs: anatomical breakdown of 17 million animal ESTs for cross-species comparison of gene expression.，**Nucleic Acids Res.**，34，628 - 631

POSTER PRESENTATIONS

1．大久保公策「「バイオインフォマティクス講座　計算機によるテキストデータの利用法」」，ぬまづ産業振興プラザ，沼津，2/18
2．大久保公策「DDBJの展望「生命情報データベースの動向と課題」」，第15回DDBjing 講演会 in 三島，三島，6/15
3．大久保公策「ばらばらな情報を「まとめ」る機械」，第841回遺伝研内部交流セミナー，三島，4/7
4．大久保公策「ライフサイエンスDBの現状と課題」，大阪大学臨床医工学融合研究教育センターシンポジウム，大阪，10/8
5．大久保公策「ライフサイエンスにおけるゲノム情報の高度利用に向けた生命知識の構造化ー構造情報の構造化から機能情報の構造化へー」，東京大学　知の構造化ワークショップ，東京，12/4
6．大久保公策「プロジェクト型研究時代の生命科学の課題」，日本分子生物学会2006フォーラム，名古屋，12/8

BOOK

1．小笠原理（2006）BodyMap-Xsとは --- それが目指すもの ---　生体の科学　第**57**巻第５号　364 - 365

DB SOFT

1．Okubo, K.,Ogasawara, O.，BodyMap-Xs
http://bodymap.jp

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J. CENTER FOR FRONTIER RESEARCH
J-a. Laboratory for Cell Lineage

J. CENTER FOR FRONTIER RESEARCH
J-a. Laboratory for Cell Lineage
Takako Isshiki

RESEARCH ACTIVITIES

Entry of neural stem cells to the quiescent state.

Takuya Tsuji, Takako Isshiki

We have been studying how Drosophila neural progenitors generate diverse cell types in a stereotyped order, changing their characteristics over time. It is known that Drosophila neural progenitors, called neuroblasts, sequentially express a set of transcription factors, some of which specify temporal identity. However, many parts of the mechanisms regulating temporal specification in the CNS remain unknown. In the past few years, we have focused on investigating temporal change of neuroblasts at the late stages of embryogenesis, as well as during the larval period. Before our study, very little was known about temporal change of neuroblasts at these late developmental stages, although the change deals with fundamental aspects of neurogenesis: (1) temporal specification of the late-born neurons occupying half of the CNS, (2) the quiescence and the reactivation of neuroblast proliferation, and (3) the size of the CNS. We have been investigating these aspects genetically by using a model neuroblast lineage. This year, we focused on the timing and the mechanism of entering to the quiescent state. We found that a few temporal specific transcription factors are involved in regulating the entry. In addition, we observed that the model neuroblast changes its morphology dramatically upon the entry, although it retain many feature of mitotic neuroblast, such as expression of neuroblast specific genes and cyclinE. This may suggest unknown fundamental aspects of the quiescence.

Asymmetric cell division and temporal change of neuroblasts

Eri Hasegawa, Takako Isshiki

Neuroblasts can change their characteristics over time, in contract, cell fate of ganglion mother cells, daughters of neuroblast, is largely fixed upon their birth. The asymmetry of temporal fate specification is the fundamental mechanism to generate diverse cell types via stem cells, and asymmetric cell division of neuroblast regulated by cortical polarity have been extensively investigated. However, how the asymmetry of temporal fate specification occurs is still unclear. We have been trying to elucidate the problem by studying the mechanisms controling asymmetirc pattern of expression of temporal specific transcription factors.

PUBLICATIONS

Papers

1．岡村勝友, 一色孝子 （0） small RNAによる発生過程の制御， 実験医学， 24， 814 -

819

ORAL PRESENTATION

1．一色孝子　基盤生命学特論Ⅱ　東京大学大学院理学系研究科　7/4

POSTER PRESENTATIONS

1．辻拓也「 ショウジョウバエ神経幹細胞の時間変化と休眠 」，神経発生討論会，愛知県岡崎市，12/22
2．一色孝子「 神経系における時間的な発生メカニズム 」，特定領域研究発生システムのダイナミクス研究終了シンポジウム，静岡県掛川市，9/4-9/6
3．Isshiki, T., Okamura, K., Kusano, A.「 Temporal change of *Drosophila* neural progenitors 」，Keystone Symposia Stem Cells，Whistler，3/29

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J. CENTER FOR FRONTIER RESEARCH
J-b. Neural Morphogenesis Laboratory

J. CENTER FOR FRONTIER RESEARCH
J-b. Neural Morphogenesis Laboratory
Emoto Kazuo

RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1．Emoto, K., Parrish, J.Z., Jan, L.Y., Jan, Y.N.（2007）The tumour suppressor Hippo acts with the NDR kinases in dendritic tiling and maintenance.，**Nature**，443，210 - 213

POSTER PRESENTATIONS

1．榎本和生「How do neurons shape their dendritic fields?」，日本分子生物学会フォーラム，名古屋，12/8

BOOK

1．榎本和生（2006）癌抑制遺伝子群の新たな神経機能の発見:ニューロンの受容領域を維持･管理する分子メカニズム　実験医学　2985 - 2988

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J. CENTER FOR FRONTIER RESEARCH
J-c. Cell Architecture Laboratory
Kimura Akatsuki

RESEARCH ACTIVITIES

Mechanics and dynamics of cell architecture: focusing on the cell nucleus and chromosomes

Akatsuki Kimura

The cell architecture laboratory was founded in June of 2006. The lab aims at understanding the mechanics and dynamics of cell architecture. A cell can be seen as a sophisticated architecture. The spatial organization of cell architecture is critical for the functions of the cell. The mechanical analysis of cell architecture is a frontier in basic biology and will contribute to understanding division, differentiation, metabolism, and morphology of the cell. Mathematical modeling and quantitative measurement are the two major approaches emphasized in the lab. Mathematical modeling is used to increase the accuracy of hypothesis-testing by computing the consequences of hypotheses. Quantitative measurement is crucial for mechanical understanding of cell architecture. The lab is developing various image-processing algorithms to quantitatively measure the position and morphology of cellular components. Our research will provide a novel strategy to analyze cell architecture and thus the mechanisms of cellular functions.
The ongoing research projects in the lab involves (i) construction of mathematical models on dynamic positioning of chromosomes during the mitotic phase, (ii) quantitative measurements of subcellular components in the nematode *Caenorhabditis elegans* embryos, and (iii) reconstitution of centrosome positioning *in vivo*, *in silico*, and *in vitro*. All research projects are in progress.

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RESEARCH ACTIVITIES

PUBLICATIONS

Papers

1．Shiraishi, K., Imai, Y., Yoshizaki, S., Tadaki, T., Ogata, Y., Ikeda, H. (2006) The role of UvrD in RecET-mediated illegitimate recombination in Escherichia coli., **Genes Genet. Syst.**, 81, 291 - 297

ORAL PRESENTATION

1．小方康至　南極同行報告会於駐・ノの遺伝子の獲得於鈩 (伊東地区ボーイスカウト集会)　伊東市ひぐらし会館　12/27
2．小方康至　南極同行報告会於駐・ノの遺伝子の獲得於鈩 (東京都台東区立上野中学校第一学年総合学習)　東京都台東区立上野中学校　11/16
3．小方康至　環境遺伝学於駐・ノの極限環境遺伝子の獲得於鈩 (平成18年度三島市民環境大学第3回講義)　日本大学国際関係学部　8/25
4．小方康至　南極同行報告会於駐・ノ遺伝子資源の無菌的な獲得於鈩　国立沼津高等工業専門学校　7/11
5．小方康至　南極同行報告「南極遺伝子資源の無菌的な獲得於註V領域融合研究センター専任にあたって於秩v (統計数理研究所・研究交流キャラバン・融合育成プロジェクト「離島・隔離集団の生態系フィールドデータの時空間モデリング」月例会)　統計数理研究所　7/15
6．小方康至　南極同行報告「南極遺伝子資源の無菌的な獲得於柱苴a場営業所との共同研究於秩v (鍋林フジサイエンス甲府支店勉強会)　鍋林フジサイエンス甲府支店　6/16
7．小方康至　南極同行報告「南極遺伝子資源の無菌的な獲得於駐・ノ地衣類に関する共同研究於秩v (秋田県立大学生物資源科学部セミナー)　秋田県立大学・生物資源科学部　6/21
8．小方康至　南極同行報告於駐・ノ遺伝子資源の無菌的な獲得於鈩　東京都台東区立上野中学校　6/14
9．小方康至　南極同行報告於駐・ノ遺伝子資源の採取於鈩　情報・システム研究機構本部　4/19
10．小方康至　南極同行報告於駐・ノ遺伝子資源の採取於鈩　G & Gサイエンス横浜研究所　4/26
11．小方康至　南極同行報告於駐・ノ遺伝子資源の無菌的な獲得於鈩 (微生物セミナー)　東京大学薬学部微生物薬品化学教室　5/13
12．小方康至　南極同行報告於駐・ノ遺伝子資源の採取於鈩　国立遺伝学研究所　4/21, 28

POSTER PRESENTATIONS

1．Ogata, Y., Narita, T., Abe, T., Kohara, Y., Niki, H., Kanda, H.「Metagenome analysis for

unveiling microbial diversity of Antarctic ice core.」, XXIX Symposium on Polar Biology , 東京 , 11/21

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RESEARCH ACTIVITIES

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Papers

1． Ito, Y. and Kurata, N. （2006） Identification and characterization of cytokinin-signalling gene families in rice , **Gene** , 382 , 57 - 65
2． Mizuta, Y., Harushima, Y. and Kurata, N. （2006） Mapping of a pair of reproductive barriers observed in the cross of Nipponbare and Kasalath , **Rice Genet. Newslet.** , 23 , 33 - 35
3． kurata, N. and Yamazaki, Y. （0） Oryzabase. An integrated biological and genome information database for rice , **Plant Physiol.** , 140 , 12 - 17
4． Ammiraju, J. S. S., Luo, M., Goicoechea, J. L., Wang, W., Kudrna, D., Muller C., Talag, J., Kim, H., Sisneros, N. B., Blackmon, B., Fang, E., Tomkins, J. B., Brar, D., MacKill, D., McCouch, S., Kurata, N., Lambert, G., Galbraith, D. W., Arumuganathan, K., Rao, K., Walling, J. G., Gill, N., Yu, Y., SanMiguel, P., Soderlund, C., Jackson S. and Wing, R. A. （0） The Oryza bacterial artificial chromosome library resource: Construction and analysis of 12 deep-coverage large-insert BAC libraries that represent the 10 genome types of the genus Oryza , **Genome Res.** , 16 , 140 - 147
5． Nonomura, K.I. Nakano, M., Eiguchi, M., Suzuki, T. and Kurata, N. （0） PAIR2 is essential for homologous chromosome synapsis in rice meiosis Ⅰ , **J. Cell Sci.** , 119 , 217 - 225
6． Kawakatsu, T., Itoh, J-I., Miyoshi, K., Kurata, N. Alvarez, N., Veit, B. and Nagato, Y. （0） PLASTOCHRON2 regulates leaf initiation and maturation in rice , **Plant Cell** , 18 , 612 - 625

ORAL PRESENTATION

1．倉田のり 植物ゲノムの進化、多様性、生殖隔離 東京大学大学院講義 東京大学・農学生命科学研究科 10/27

POSTER PRESENTATIONS

1． 野々村賢一,倉田のり,上田健治,豊澤恵子,宮尾安藝雄,廣近洋彦,井上正保 「 イネ花粉形成突然変異体の選抜と解析 」, 日本植物学会第70回大会 , 熊本 , 9/14-16
2． Ito, Y., and kurata, N.「 *KNOX LEAF EXPRESSION1* (*KLE1*), a rice gene required for *KNOX* gene suppression in leaf 」, 4th International Rice Functional Genomics Symposium , Montpellier, France , 10/9-11
3． Kurata, N., Suzuki, T., Eiguchi, M., Kumamaru, T.,Moriguchi K., Nagato Y., and Satoh H.「 A Simple TILLING and High Frequency Mutations Suitable for Approaching All Gene

Function in Rice」, 4th International Rice Functional Genomics Symposium , Montpellier, France , 10/9-11
4．野々村賢一「 イネの生殖細胞形成と減数分裂に関わる遺伝子の解析 」, 大阪大学蛋白質研究所セミナー , 大阪 , 11/21, 22
5．Nonomura, K.I.「 Rice meiotic genes; functional analyses and comparative genomics 」, 4th International Rice Functional Genomics Symposium , Montpellier, France , 10/9-11
6．大坪久子, 土本卓, 程朝陽, 徐健紅, 田村浩一郎, 倉田のり, 大坪榮一「 レトロエレメントを通してイネゲノムを見る 」, 第78回日本遺伝学会 , つくば , 9/25-27
7．野々村賢一「 イネバイオリソースプロジェクトの成果と今後の展望 」, 第78回日本遺伝学会 , つくば , 9/25-27
8．伊藤幸博 ,倉田のり「 KNOX遺伝子が葉で異所的に発現するイネ突然変異体の解析 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
9．春島嘉章,栗木哲,水多陽子,藤澤洋徳,倉田のり「 配偶体内または接合体内の異なる遺伝子座間の相互作用による生殖的隔離障壁の検出 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
10．水多陽子,春島嘉章,倉田のり「 イネ「日本晴」と「Kasalath」の雑種花粉で相互作用する2遺伝子座に起因する生殖的隔離 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
11．野々村賢一,諸星亜加子,倉田のり「 イネ属野生種における減数分裂遺伝子PAIR1の比較ゲノム解析 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
12．宮林登志江,野々村賢一,森島啓子,倉田のり「 遺伝研が保有するイネ属野生イネ系統のゲノムサイズ評価 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
13． 倉田のり「 イネ多様性研究と育種機能解析を支えるイネリソース 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
14． 佐野幸恵,金森裕之,並木信和,山崎由紀子,宮林登志江,倉田のり 「 野生イネOryza punctataおよびOryza officinalis由来ESTの比較解析 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
15． 堀内陽子,春島嘉章,川喜田雅則,望月孝子,江口真透,,倉田のり 「 Affymetrix Rice Genome arrayを用いたイネ遺伝子発現量検出における塩基配列差の補正と適用 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
16． 山中愼介,江花薫子,倉田のり,呉健忠,松本隆,D.A.Vaughan,廣近洋彦,奥野員敏,福田修一,河瀬眞琴「 イネAゲノム近縁野生種のdiversity research set作成に向けた多様性解析 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
17．倉田のり「 平成18年度特定領域研究発足案内 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
18．Ito, Y., Kurata, N.「 Complex regulation of KNOX gene suppression in rice leaf 」, 8th International Congress of Plant Molecular Biology , Adelaide , 8/20-25
19．野々村賢一,諸星亜加子,倉田のり「 イネ属野生種における減数分裂遺伝子PAIR1の比較ゲノム解析 」, 日本育種学会第110回講演会 , 松山 , 9/22-23
20．鈴木温, 永口貢, 佐藤光, 熊丸敏博, 長戸康郎, 倉田のり「 TILLING法によるイネの化学誘導変異系統群の逆遺伝学への利用 」, イネ遺伝学・分子生物学ワークショップ2006 , 東京 , 7/7
21．鈴木温, 永口貢, 佐藤光, 熊丸敏博, 長戸康郎, 倉田のり「 イネ全遺伝子の突然変異検索法奸注up度変異系統群と簡易TILLING法の確立 」, 日本育種学会第110回講演会 , 松山 , 9/22窶鑰23
22．野々村賢一・諸星亜加子・永口貢・宮尾安藝雄・広近洋彦・倉田のり「 生殖細胞の分裂と減数分裂染色体の凝縮が異常になるmeal突然変異体 」, イネ遺伝学・分子生物学ワークショップ2006 , 東京 , 7/7
23．野々村賢一, 諸星亜加子, 永口貢, 宮尾安藝雄, 広近洋彦, 倉田のり「 イネの生殖細胞発生が異常になるmeal突然変異体の細胞学的解析 」, 日本育種学会第109回講演会 , 東京 , 3/28-30
24．野々村賢一「 減数分裂遺伝子からイネ属の種分化を考える 」, イネゲノム解読記念シンポジウム -イネゲノム解読で何ができるのか , つくば , 3/22
25．川勝泰二, 伊藤純一, 三好一丸, 倉田のり, 長戸康郎「 イネの葉間期と葉の発生成熟速度を変更するPlastochron2変異体の解析 」, 日本育種学会第109回講演会 , 東京 , 3/28-30
26．大坪久子, 徐建紅, Marcia Yuri Kondo, 程朝陽, 土本卓, 倉田のり, 宮林登志江, 大坪榮一「 レトロポゾンp-SINE1によるイネの系統分類 」, 日本育種学会第109回講演会 , 東京 , 3/28-30

27．呉健忠, 江花薫子, 片桐敏, 細川聡美, 吉原里枝, 唐澤歩, 程朝陽, 徐健紅, 土本卓, 大坪久子, 大坪榮一, 宮林登志江, 倉田のり, 河瀬真琴, 井澤毅, 門脇光一, Duncan D. Vaughan, 奥野員敏, 並木信和, 佐々木卓治, 松本隆 「 p-SINEマーカーを用いた栽培及び野生種イネコレクションにおける詳細な系統解析 」, 日本育種学会第109回講演会 , 東京 , 3/28-30
28．倉田のり, 佐藤光, 吉村淳, 佐藤洋一郎, 北野英巳, 長戸康郎 「 イネバイオリソーストピックス:進化・多様性研究と機能ゲノム研究を支えるイネ遺伝資源 」, 第47回植物生理学会年会 , つくば , 3/19-21
29．川勝泰二, 伊藤純一, 三好一丸, 倉田のり, 長戸康郎 「 イネの葉間期と葉の発生成熟速度を変更するPlastochron2変異体の解析 」, 第47回植物生理学会年会 , つくば , 3/19-21
30．倉田のり, 佐藤光, 吉村淳, 佐藤洋一郎, 北野英巳, 長戸康郎 「 機能ゲノム研究および進化・多様性・遺伝・育種研究に不可欠なイネ遺伝資源 」, 第47回植物生理学会年会 , つくば , 3/19-21
31．伊藤幸博、倉田のり 「 KNOX遺伝子が葉で異所的に発現するイネ新奇突然変異体の同定 」, 第47回日本植物生理学会年会 , つくば , 3/19-21
32． Kurata, N.,Suzuki, T., Kumamaru, T., Nagato, Y., Satoh, H. 「 Systematic survey of mutants for all rice genes. 」, International Symposium on Rice Functional Genomics 2006. , Daegu, Korea , 4/20-21

EDUCATION

1．倉田のり・渡辺正夫・松岡信　高等植物の生殖形質におけるゲノム障壁制御遺伝子の分子遺伝学的解析　国立遺伝学研究所研究集会（共催） 三島　11/8-9
2．倉田のり・渡辺正夫・松岡信　植物の生殖過程におけるゲノム障壁　特定領域研究ワークショップ　三島　11/8-9
3．倉田のり　「植物ゲノム障壁」シンポジウム　特定領域研究公開シンポジウム　東京　10/21

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1．倉田のり（2006）生殖期染色体標本作製法:パキテン期染色体（ギムザ染色） クロモソーム・植物染色体研究の方法　32 - 33
2．倉田のり（2006）まるごと生き物大集合ーバイオリソースプロジェクトーイネ　遺伝　36 - 37

OTHERS

1．野々村賢一，1，日本育種学会幹事
2．倉田のり，3，生物遺伝資源イネ小委員会委員長
3．倉田のり，3，Rice Genetics Newsletter Editor
4． Nori Kurata， 3， NSF project advisory committee member and project proposal reviewer
5．倉田のり，1，日本学術会議　育種学分科会幹事
6．倉田のり，1，日本学術会議　植物科学分科会員

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N. TECHNICAL SECTION
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RESEARCH ACTIVITIES

The Technical section supports the research activity of NIG in many fields. For example, we support the Radioisotope center and Experimental farm, and the Genetic strain research center where genetic and transgenic strains of mice, rice, flies, and fish are produced, maintained, and distributed to other institutions. Members of the staff additionally support many types of experiments in various laboratories, such as developmental, cell, and molecular genetics. We continually update our technical services through attending the training and annual meetings for the technological staffs.

PUBLICATIONS
Papers

1．Tsuda M., Kiso M., Saga Y.（2006）Implication of nanos2-3'UTR in the expression and function of nanos2.，**Mech Dev.**，123，440 - 449
2．Morimoto M., Kiso M., Sasaki N., Saga Y.（2006）Cooperative Mesp activity is required for normal somitogenesis along the anterior-posterior axis.，**Dev Biol.**，300，687 - 698
3．Tambe Y., Yoshioka-Yamashita A., Mukaisho K., Haraguchi S., Chano T., Isono T., Kawai T., Suzuki Y., Kushima R., Hattori T., Goto M., Yamada S., Kiso M., Saga Y., Inoue H.（2007）Tumor prone phenotype of mice deficient in a novel apoptosis-inducing gene, drs.，**Carcinogenesis**，28，777 - 784
4．Nonomura, K., Nakano, M., Eiguchi, M., Suzuki, T., and Kurata N.（2006）PAIR2 is essential for homologous chromosome synapsis in rice meiosis I，**J Cell Sci**，119，217 - 225
5．Ito, H., Miura, A., Takashima, K., Kakutani T.（2007）Ecotype-specific and chromosome-specific expansion of variant centromeric satellites in *Arabidopsis thaliana*，**Mol Gen Genomics**，277，23 - 30

POSTER PRESENTATIONS

1．宮林登志江, 野々村賢一, 森島啓子, 倉田のり「遺伝研が保有するイネ属野生イネ系統のゲノムサイズ評価」, 第110回日本育種学会講演会 秋季大会，愛媛県松山市，
2．谷田 勝教「分裂酵母Schizosaccharomyces japonicus var. japonicus のrDNAの解析」, 第17回生物学技術研究会，愛知県岡崎市，2/16
3．鈴木智広, 古海弘康, 幸田尚, 岩舩浩孝, 京野志保, 金田秀貴, 若菜茂晴, 佐々木裕之, 石野史敏, 城石俊彦「ENU Mutagenesisによる生殖細胞ゲノムインプリンティング確立異常変異体の探索」, 第53回日本実験動物学会，神戸，5/11-13
4．Furuumi, H., Iwafune, H., Suzuki, T., Kohda, T., Kyono, S., Kaneda, H., Wakana, S., Shiroishi, T., Ishino, F., Sasaki H「Recent results of a screening system for mutants

affected in genomic imprinting in the RIKEN ENU-Mutagenesis project 」, International Genomic Imprinting Workshop 2006 , 東京 , 11/30-12/1
5 . 野々村賢一, 諸星亜加子, 中野睦子, 永口貢, 宮尾安藝雄, 廣近洋彦, 倉田のり「 生殖細胞の分裂と減数分裂染色体の凝縮が異常になるmeal突然変異体 」, イネ遺伝学・分子生物学ワークショップ , ,
6 . 鈴木温, 永口貢,佐藤光, 熊丸敏博, 長戸康郎, 倉田のり「 TILLING法によるイネの化学誘導変異系統群の逆遺伝学への利用 」, イネ遺伝学・分子生物学ワークショップ , ,
7 . 鈴木温, 永口貢, 佐藤光, 熊丸敏博, 長戸康郎, 倉田のり「 イネ全遺伝子の突然変異検索法-高頻度変異系統と簡易TILLING法の確立 」, 日本育種学会 , ,
8 . 永口　貢「 Embyo rescue法を用いたイネゲノム間雑種の作出について 」, 第17回生物技術研究会 , 愛知県岡崎市 ,
9 . 三浦　明日香「 トランスポゾン*CACTA*の転移と脱メチル化 」, 日本遺伝学会第78回大会 , , 9/25-27

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Abe, T.	G-b Genome biology Laboratory E-a Division of Human Genetics I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research I-d Laboratory for Research and Development of Biological Databases K RADIOISOTOPE CENTER
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Amano, T.	F-a Mammalian Genetics Laboratory
Amano,K.	H-d Biomolecular Structure Laboratory
Ammiraju, J. S. S.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Ana Hadiana	H-b Molecular Biomechanism Laboratory
Ando, M.	F-g Invertebrate Genetics Laboratory
Ando,M.	H-e Gene Network Laboratory
Antonio, B.	I-a Laboratory for DNA Data Analysis

Anzai, T.	I-a Laboratory for DNA Data Analysis
Aoki, K.	E-b Division of Agricultural Genetics
Aoto, T.	F-a Mammalian Genetics Laboratory
Apweiler, R.	I-c Laboratory for Gene Function Research
Arai,K.	F-g Invertebrate Genetics Laboratory
Araki, M.	G-a Genetic Informatics Laboratory
Araki, T.	E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Araki,H.	B-b Division of Microbial Genetics
Arima, T.	E-a Division of Human Genetics
Arnaud, B.M.	I-d Laboratory for Research and Development of Biological Databases
Arnaud, P.	E-a Division of Human Genetics
Aruga, J.	D-a Division of Population Genetics
Arumuganathan, K.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Asakawa, K.	C-c Division of Molecular and Developmental Biology
Asaoka, M.	C-a Division of Developmental Genetics
Aussie Suzuki	A-a Division of Molecular Genetics
Austen R.D. Ganley	B-a Division of Cytogenetics
Awasaki, T.	F-g Invertebrate Genetics Laboratory
Bahram, S.	I-a Laboratory for DNA Data Analysis
Bannai M	D-a Division of Population Genetics
Bannai, M.	D-a Division of Population Genetics
Banno, Y.	G-a Genetic Informatics Laboratory
Barbee, S. A.	F-g Invertebrate Genetics Laboratory
Barman, H.	E-b Division of Agricultural Genetics
Barman, H. K.	A-a Division of Molecular Genetics
Barman, H.K.	E-b Division of Agricultural Genetics
Barrero, RA.	I-a Laboratory for DNA Data Analysis
Bates, K.	I-c Laboratory for Gene Function Research
Beermann, F.	C-c Division of Molecular and Developmental Biology
Benno,Y.	G-a Genetic Informatics Laboratory
Berger, F.	E-b Division of Agricultural Genetics
Berlyn, M.	I-d Laboratory for Research and Development of Biological Databases
Berman, HK	E-b Division of Agricultural Genetics
Bessling, S.L.	C-c Division of Molecular and Developmental Biology
Billadeau DD	H-a Biological Macromolecules Laboratory
Blackmon, B.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Blanot D	F-g Invertebrate Genetics Laboratory
Blaser, H.	C-c Division of Molecular and Developmental Biology
Blattner, R.F.	I-d Laboratory for Research and Development of Biological Databases
Brar, D.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Brock, H. W.	C-b Division of Gene Expression

Brun S	F-g Invertebrate Genetics Laboratory
Carrero-Martinez,F.	H-e Gene Network Laboratory
Castanon, I.	C-c Division of Molecular and Developmental Biology
Chano T.	N Technical Section
Chantawannakul. P.	H-d Biomolecular Structure Laboratory
Chaudhuri, R.R.	I-d Laboratory for Research and Development of Biological Databases
Cheeseman, I. M.	A-a Division of Molecular Genetics
Cheeseman, M. I.	A-a Division of Molecular Genetics
Chen, P.	C-c Division of Molecular and Developmental Biology
Chen, Z.-X.	E-a Division of Human Genetics
Chiba, H.	E-a Division of Human Genetics
Chien, C.-T.	C-b Division of Gene Expression
Chien, HC.	I-a Laboratory for DNA Data Analysis
Chou, CK.	I-a Laboratory for DNA Data Analysis
Choy, KW.	I-a Laboratory for DNA Data Analysis
Chuma, S.	F-a Mammalian Genetics Laboratory
Chung, TK.	I-a Laboratory for DNA Data Analysis
Cochrane, G.	I-c Laboratory for Gene Function Research
Coller, J. M.	F-g Invertebrate Genetics Laboratory
Cziko, A-M.	F-g Invertebrate Genetics Laboratory
Daisuke Shibata	G-a Genetic Informatics Laboratory
Daniel L. Hartl	I-c Laboratory for Gene Function Research
Daniel S. Rokhsar	G-b Genome biology Laboratory
Dashnyam, B.	D-a Division of Population Genetics
David, C.	I-c Laboratory for Gene Function Research
del Rio	E-c Division of Brain Function
Desai, A.	A-a Division of Molecular Genetics
Ding, J.-P.	E-a Division of Human Genetics
Dong, W.	C-c Division of Molecular and Developmental Biology
Du, J.	C-c Division of Molecular and Developmental Biology
Dumstrei, K.	C-c Division of Molecular and Developmental Biology
Dushay MS	F-g Invertebrate Genetics Laboratory
Eguchi, T.	I-a Laboratory for DNA Data Analysis
Eiguchi, M.	N Technical Section F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Eiichi Shoguchi	G-b Genome biology Laboratory
Emoto, K.	J-b Neural Morphogenesis Laboratory
Endo, C.	E-a Division of Human Genetics
Endo, M.	E-b Division of Agricultural Genetics F-b Mammalian Development Laboratory
Endo, T.	G-a Genetic Informatics Laboratory
Eri Hasegawa	J-a Laboratory for Cell Lineage
Estes, P. S.	F-g Invertebrate Genetics Laboratory
Ezaki, T.	G-a Genetic Informatics Laboratory
Ezawa, K.	D-a Division of Population Genetics

F.Yamao	A-b Division of Mutagenesis
Fang, E.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Faruque, N.	I-c Laboratory for Gene Function Research
Feil, R.	E-a Division of Human Genetics
Ferrer, I.	E-c Division of Brain Function
Fetchko, M	I-c Laboratory for Gene Function Research
Fisher, S.	C-c Division of Molecular and Developmental Biology
Fujii, Y.	I-a Laboratory for DNA Data Analysis
Fujimi, T.	D-a Division of Population Genetics
Fujimura, K.	I-a Laboratory for DNA Data Analysis
Fujisawa T.	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis
Fujisawa, C.	C-a Division of Developmental Genetics
Fujisawa, T.	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Fujisawa,T.	C-a Division of Developmental Genetics
Fujita, M.	G-a Genetic Informatics Laboratory
Fujitani, K.	G-a Genetic Informatics Laboratory
Fujiwara, S.	I-a Laboratory for DNA Data Analysis
Fukagawa A.	H-a Biological Macromolecules Laboratory
Fukagawa T	A-a Division of Molecular Genetics
Fukagawa, T	A-a Division of Molecular Genetics
Fukagawa, T.	A-a Division of Molecular Genetics E-b Division of Agricultural Genetics
Fukasawa, M.	E-a Division of Human Genetics
Fuke, S.	F-b Mammalian Development Laboratory
Fukuchi S	I-d Laboratory for Research and Development of Biological Databases
Fukuchi, S.	I-a Laboratory for DNA Data Analysis I-b Laboratory for Gene-Product Informatics
Fumikazu Suto	C-a Division of Developmental Genetics
Furrer,M.	H-e Gene Network Laboratory
Furuhashi, H.	C-b Division of Gene Expression
Furutani-Seiki, M.	C-c Division of Molecular and Developmental Biology
Furuumi, H.	N Technical Section E-a Division of Human Genetics
Fuse, N.	C-b Division of Gene Expression
G.-L.	E-a Division of Human Genetics
Galbraith, D. W.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Ganley, A.R.	B-a Division of Cytogenetics
Gao, W.	C-c Division of Molecular and Developmental Biology
Gao, YG.	H-d Biomolecular Structure Laboratory
Garidkhuu A	D-a Division of Population Genetics
Garidkhuu, A.	D-a Division of Population Genetics
Gehring, W.	I-a Laboratory for DNA Data Analysis

Gehring, W. J.	F-g Invertebrate Genetics Laboratory
Gehring,WJ.	H-e Gene Network Laboratory
Geng, C.	F-g Invertebrate Genetics Laboratory
Ghadami M	D-a Division of Population Genetics
Ghadami, M.	D-a Division of Population Genetics
Ghangrekar, I.	F-g Invertebrate Genetics Laboratory
Ghangrekar,I.	H-e Gene Network Laboratory
Gil, V.	E-c Division of Brain Function
Gill, N.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Glasner, D.J.	I-d Laboratory for Research and Development of Biological Databases
Go, M.	I-a Laboratory for DNA Data Analysis
Goda, E.	F-g Invertebrate Genetics Laboratory
Goicoechea, J. L.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Gojobori T	I-d Laboratory for Research and Development of Biological Databases I-e Laboratory for Gene-Expression Analysis
Gojobori T.	I-a Laboratory for DNA Data Analysis
Gojobori, T	I-a Laboratory for DNA Data Analysis
Gojobori, T.	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Gojobori,T.	I-a Laboratory for DNA Data Analysis
Gojoboroi, T.	I-c Laboratory for Gene Function Research
Gomez TS	H-a Biological Macromolecules Laboratory
Gondo, Y.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Goto M.	N Technical Section
Gowher, H.	E-a Division of Human Genetics
Grice, E.A.	C-c Division of Molecular and Developmental Biology
H. Iwasaki	A-b Division of Mutagenesis
H.Iwasaki	A-b Division of Mutagenesis
H.Shinagawa	A-b Division of Mutagenesis
Habara, T.	I-a Laboratory for DNA Data Analysis
Habuchi, H.	F-g Invertebrate Genetics Laboratory
Hagino, K.	I-a Laboratory for DNA Data Analysis
Hagiwara, M.	A-a Division of Molecular Genetics
Hamann MJ	H-a Biological Macromolecules Laboratory
Hamlet, M. R.	C-c Division of Molecular and Developmental Biology
Hamlet, M.R.J.	C-c Division of Molecular and Developmental Biology
Hanada, K.	I-a Laboratory for DNA Data Analysis
Hanai, K.	C-b Division of Gene Expression
Hancock, D.	I-c Laboratory for Gene Function Research
Harada, H.	G-a Genetic Informatics Laboratory
Haraguchi S.	N Technical Section
Haraguchi, S.	F-b Mammalian Development Laboratory

Harashima, S.	G-a Genetic Informatics Laboratory
Harihara, S.	D-a Division of Population Genetics
Haruki, M.	I-b Laboratory for Gene-Product Informatics
Harushima, Y.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Haruta, N.	A-b Division of Mutagenesis
Hasegawa, K.	F-a Mammalian Genetics Laboratory
Hashiguchi, Abe	G-a Genetic Informatics Laboratory
Hashiguchi, M.	F-d Model Fish Genomics Resource
Hashimoto, K.	I-a Laboratory for DNA Data Analysis
Hashimoto, N.	I-a Laboratory for DNA Data Analysis
Hashiyama, K.	C-b Division of Gene Expression
Hata K.	E-a Division of Human Genetics
Hata, H.	I-a Laboratory for DNA Data Analysis
Hata, K.	E-a Division of Human Genetics
Hatada, I.	E-a Division of Human Genetics
Hatano, T.	F-f Microbial Genetics Laboratory
Hattori T.	N Technical Section
Hayakawa S.	I-a Laboratory for DNA Data Analysis
Hayakawa, E.	C-a Division of Developmental Genetics
Hayakawa, S.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Hayashi, E.	C-c Division of Molecular and Developmental Biology
Hayashi, S.	F-g Invertebrate Genetics Laboratory
Hayashi, T.	H-d Biomolecular Structure Laboratory
Hayashi,S.	H-e Gene Network Laboratory
Hayato, Yokoi.	F-b Mammalian Development Laboratory
Heisenberg, C.P.	C-c Division of Molecular and Developmental Biology
Henke, L.	D-a Division of Population Genetics
Herve M	F-g Invertebrate Genetics Laboratory
Hibi, M.	C-c Division of Molecular and Developmental Biology
Hideki NAKAYAMA	H-b Molecular Biomechanism Laboratory
Hijikata, A.	I-a Laboratory for DNA Data Analysis
Hillebr,	F-g Invertebrate Genetics Laboratory
Himeno R	I-d Laboratory for Research and Development of Biological Databases
Himeno, R.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Hirahata M	I-d Laboratory for Research and Development of Biological Databases
Hirahata, M.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Hirai, H.	D-a Division of Population Genetics
Hirai,K.	B-b Division of Microbial Genetics
Hiramoto, M.	C-a Division of Developmental Genetics
Hirasawa, R.	E-a Division of Human Genetics
Hirashima,Y.	I-a Laboratory for DNA Data Analysis

Hirata, T.	E-c Division of Brain Function
Hirayama K	D-a Division of Population Genetics
Hirayama, K.	D-a Division of Population Genetics
Hiroki Kokubo	F-b Mammalian Development Laboratory
Hiromi, Y.	C-a Division of Developmental Genetics
Hirose, M.	C-a Division of Developmental Genetics
Hirose, S.	C-b Division of Gene Expression
Hiroshi Ezura	G-a Genetic Informatics Laboratory
Hiroshi ICHIJO	H-c Multicellular Organization Laboratory
Hiroshi, Hori.	F-b Mammalian Development Laboratory
Hiroshi, Mitani.	F-b Mammalian Development Laboratory
Hiroshima M	H-a Biological Macromolecules Laboratory
Hiroshima M.	H-a Biological Macromolecules Laboratory
Hiroshima, M.	H-a Biological Macromolecules Laboratory
Hiroyuki Araki	B-b Division of Microbial Genetics
Hisano, M.	E-a Division of Human Genetics
Hishiki T	I-e Laboratory for Gene-Expression Analysis
Hitoshi Mori	G-a Genetic Informatics Laboratory
Hitoshi Ueda	I-a Laboratory for DNA Data Analysis
Hodgson, J.	C-b Division of Gene Expression
Hohn, B.	E-b Division of Agricultural Genetics
Hoki, Y.	E-a Division of Human Genetics
Homjo,K.	H-e Gene Network Laboratory
Homma, K.	I-a Laboratory for DNA Data Analysis I-b Laboratory for Gene-Product Informatics
Honjo, K.	F-g Invertebrate Genetics Laboratory
Hori, T.	A-a Division of Molecular Genetics
Horiguchi, T.	I-a Laboratory for DNA Data Analysis
Horii, A.	E-a Division of Human Genetics
Horikawa, K.	C-c Division of Molecular and Developmental Biology
Horiuchi, T.	B-a Division of Cytogenetics I-d Laboratory for Research and Development of Biological Databases
Hosomichi, K.	I-a Laboratory for DNA Data Analysis
Hosoya, M.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Hosoya,T.	H-e Gene Network Laboratory
Howlett, I. C.	F-g Invertebrate Genetics Laboratory
Huang, H.	C-c Division of Molecular and Developmental Biology
Huang, P.	C-c Division of Molecular and Developmental Biology
Huang, Y.-N.	E-a Division of Human Genetics
Huh, J. W.	D-a Division of Population Genetics
Hwang J. S.	I-a Laboratory for DNA Data Analysis
Hwang, J.S.	C-a Division of Developmental Genetics
Hyun, B. H.	D-a Division of Population Genetics
Iborra, J. F.	A-a Division of Molecular Genetics
Ichijo, H.	H-c Multicellular Organization Laboratory

Ichikawa, H.	E-b Division of Agricultural Genetics
Ichiro TORAYAMA	H-c Multicellular Organization Laboratory
Igarashi, K.	F-b Mammalian Development Laboratory
Ihara M	D-a Division of Population Genetics
Ihara, M.	D-a Division of Population Genetics
Iizumi, S.	E-b Division of Agricultural Genetics
Iino, Y.	H-c Multicellular Organization Laboratory
Iizuka T	I-e Laboratory for Gene-Expression Analysis
Ikeda, H.	K RADIOISOTOPE CENTER
Ikemura, T.	E-a Division of Human Genetics I-d Laboratory for Research and Development of Biological Databases
Ikeo K.	I-a Laboratory for DNA Data Analysis
Ikeo, K.	C-a Division of Developmental Genetics C-b Division of Gene Expression I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Ikeo,K.	I-a Laboratory for DNA Data Analysis
Ikuo Suzuki	I-a Laboratory for DNA Data Analysis
Imai, H.	E-a Division of Human Genetics
Imai, Y.	K RADIOISOTOPE CENTER
Imamizu, Y.	I-a Laboratory for DNA Data Analysis
Imamoto, N.	H-a Biological Macromolecules Laboratory
Imanishi, T.	I-a Laboratory for DNA Data Analysis
Imanishi,T.	I-a Laboratory for DNA Data Analysis
Ino, A.	F-g Invertebrate Genetics Laboratory
Ino,A.	H-e Gene Network Laboratory
Inoko, H.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Inomata, N.	D-a Division of Population Genetics
Inoue H.	N Technical Section
Inoue, F.	C-c Division of Molecular and Developmental Biology
Inoue, T.	F-b Mammalian Development Laboratory
Isao KATSURA	H-c Multicellular Organization Laboratory
Ishibashi M	D-a Division of Population Genetics
Ishibashi, M.	D-a Division of Population Genetics
Ishida T	D-a Division of Population Genetics
Ishida, C.	E-a Division of Human Genetics
Ishida, T.	D-a Division of Population Genetics
Ishihara, T.	H-c Multicellular Organization Laboratory
Ishikawa T	D-a Division of Population Genetics
Ishikawa, E.	H-a Biological Macromolecules Laboratory
Ishikawa, R.	G-a Genetic Informatics Laboratory
Ishikawa, T.	D-a Division of Population Genetics
Ishikawa, Y.	E-b Division of Agricultural Genetics
Ishino, F.	N Technical Section E-a Division of Human Genetics

Ishioka, Akiyama	G-a Genetic Informatics Laboratory
Islam, M.E.	C-c Division of Molecular and Developmental Biology
Isogai, T.	I-a Laboratory for DNA Data Analysis
Isono T.	N Technical Section
Isshiki, T.	J-a Laboratory for Cell Lineage
Ito, H.	N Technical Section
Ito, K.	E-c Division of Brain Function
Ito, T.	I-a Laboratory for DNA Data Analysis
Ito, Y.	E-b Division of Agricultural Genetics F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Ito,K.	H-b Molecular Biomechanism Laboratory
Itoh, J-I.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Itoh, M.	D-a Division of Population Genetics
Itoh, T.	I-a Laboratory for DNA Data Analysis
Itou, H.	H-d Biomolecular Structure Laboratory
Iwafune, H.	N Technical Section E-a Division of Human Genetics
Iwamoto, C.	I-a Laboratory for DNA Data Analysis
Iwasaki, H.	A-b Division of Mutagenesis
Iwata, J.	F-a Mammalian Genetics Laboratory
Iyama, S.	G-a Genetic Informatics Laboratory
J. R.	A-a Division of Molecular Genetics
J.A.	E-c Division of Brain Function
Jackson S.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Jaenisch, R.	E-a Division of Human Genetics
Jan, L.Y.	J-b Neural Morphogenesis Laboratory
Jan, Y.N.	J-b Neural Morphogenesis Laboratory
Jang IH	F-g Invertebrate Genetics Laboratory
Jang, S. B.	D-a Division of Population Genetics
Jaynes, J. B.	C-b Division of Gene Expression
Jeltsch, A.	E-a Division of Human Genetics
Jeong, S. B.	D-a Division of Population Genetics
Jin, F.	D-a Division of Population Genetics
Jin, L.	I-a Laboratory for DNA Data Analysis
Johnson, N.	F-g Invertebrate Genetics Laboratory
Jullien, P.	E-b Division of Agricultural Genetics
Jung Shan	I-a Laboratory for DNA Data Analysis
K-i. Shibahara	E-b Division of Agricultural Genetics
K.L.	C-c Division of Molecular and Developmental Biology
Kakutani T	E-b Division of Agricultural Genetics
Kakutani T.	N Technical Section
Kakutani, T.	E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Kambris Z	F-g Invertebrate Genetics Laboratory

Kamimura, K.	F-g Invertebrate Genetics Laboratory
Kamimura,Y.	B-b Division of Microbial Genetics
Kamiya, A.	D-a Division of Population Genetics
Kamiyama, S.	F-g Invertebrate Genetics Laboratory
Kanagawa O	H-a Biological Macromolecules Laboratory
Kanai, M.	C-a Division of Developmental Genetics
Kaname T	D-a Division of Population Genetics
Kaname, T.	D-a Division of Population Genetics
Kanaya, K.	I-d Laboratory for Research and Development of Biological Databases
Kanaya, S.	I-b Laboratory for Gene-Product Informatics I-d Laboratory for Research and Development of Biological Databases
Kanbara,K.	G-a Genetic Informatics Laboratory
Kaneda, H.	N Technical Section D-a Division of Population Genetics E-a Division of Human Genetics F-a Mammalian Genetics Laboratory
Kaneda, M.	E-a Division of Human Genetics
Kaneko A	D-a Division of Population Genetics
Kaneko, A.	D-a Division of Population Genetics
Kaneko, S.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Kaneko, Y.	G-a Genetic Informatics Laboratory
Kanesaki, T.	C-b Division of Gene Expression
Kannno, J.	F-b Mammalian Development Laboratory
Kanno, J.	F-b Mammalian Development Laboratory
Kanuka,H.	H-e Gene Network Laboratory
Kasai, T.	C-c Division of Molecular and Developmental Biology
Kato M	E-b Division of Agricultural Genetics
Kato, H.	G-a Genetic Informatics Laboratory
Kato, J.	G-a Genetic Informatics Laboratory
Kato, K.	E-a Division of Human Genetics F-a Mammalian Genetics Laboratory F-c Mouse Genomics Resource Laboratory
Kato, M.	E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Kato, Y.	E-a Division of Human Genetics
Katsumata, Y.	D-a Division of Population Genetics
Katsura, I.	H-c Multicellular Organization Laboratory
Katsuyama, Y.	I-a Laboratory for DNA Data Analysis
Kawabata, T.	I-b Laboratory for Gene-Product Informatics
Kawachi, Kasai	G-a Genetic Informatics Laboratory
Kawahara, T.	G-a Genetic Informatics Laboratory
Kawai T.	N Technical Section
Kawai, F.	I-b Laboratory for Gene-Product Informatics
Kawakami, A.	C-c Division of Molecular and Developmental Biology
Kawakami, K.	C-c Division of Molecular and Developmental Biology

Kawakami, N.	G-a Genetic Informatics Laboratory
Kawakatsu, T.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Kawamoto S	I-e Laboratory for Gene-Expression Analysis
Kawamura, A.	C-c Division of Molecular and Developmental Biology
Kawamura, Y.	G-a Genetic Informatics Laboratory
Kawasaki, T.	E-c Division of Brain Function
Kawashima, H.	I-a Laboratory for DNA Data Analysis
Kawaura,K.	G-a Genetic Informatics Laboratory
Kaya, H.	E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Kazuho Ikeo	I-a Laboratory for DNA Data Analysis
Kazuko Suzuki	A-a Division of Molecular Genetics
Kazuo, Araki.	F-b Mammalian Development Laboratory
Kazuyuki Hirai	B-b Division of Microbial Genetics
Keseler, M.I.	I-d Laboratory for Research and Development of Biological Databases
Kido, A.	D-a Division of Population Genetics
Kijimoto, T.	I-a Laboratory for DNA Data Analysis
Kikkawa, E.	I-a Laboratory for DNA Data Analysis
Kikuchi M	D-a Division of Population Genetics
Kikuchi, M.	D-a Division of Population Genetics
Kim DK	D-a Division of Population Genetics
Kim MS	F-g Invertebrate Genetics Laboratory
Kim, C. G.	D-a Division of Population Genetics
Kim, D.-K.	D-a Division of Population Genetics
Kim, H.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Kim, H.S.	D-a Division of Population Genetics
Kimata, K.	F-g Invertebrate Genetics Laboratory
Kimbara, K.	I-b Laboratory for Gene-Product Informatics
Kimura, G.	G-a Genetic Informatics Laboratory
Kimura, H.	A-a Division of Molecular Genetics
Kimura, K.	H-c Multicellular Organization Laboratory
Kimura, K. D.	H-c Multicellular Organization Laboratory
Kimura, M.	E-a Division of Human Genetics
Kimura, N.	I-a Laboratory for DNA Data Analysis
Kinjo, A.R.	I-b Laboratory for Gene-Product Informatics
Kinjo, S.	I-a Laboratory for DNA Data Analysis
Kinoshita A	D-a Division of Population Genetics
Kinoshita T	E-b Division of Agricultural Genetics
Kinoshita Y	E-b Division of Agricultural Genetics
Kinoshita, A.	D-a Division of Population Genetics
Kinoshita, T.	E-b Division of Agricultural Genetics
Kinouchi, M.	I-d Laboratory for Research and Development of Biological Databases
Kishimoto, Y.	C-c Division of Molecular and Developmental Biology

Kiso M	F-b Mammalian Development Laboratory
Kiso M.	N Technical Section
Kiso, M.	F-b Mammalian Development Laboratory
Kitadate, Y.	C-a Division of Developmental Genetics
Kitajima ,S.	F-b Mammalian Development Laboratory
Kitajima, S.	F-b Mammalian Development Laboratory
Kitano, T.	D-a Division of Population Genetics
Kiyoshi, Naruse.	F-b Mammalian Development Laboratory
Klarsfeld, A.	F-g Invertebrate Genetics Laboratory
Kline, S.	A-a Division of Molecular Genetics
Kloeppel T	H-a Biological Macromolecules Laboratory
Kobayashi, H.	G-b Genome biology Laboratory E-a Division of Human Genetics
Kobayashi, K.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Kobayashi, M.	C-c Division of Molecular and Developmental Biology F-g Invertebrate Genetics Laboratory
Kobayashi, N.	I-a Laboratory for DNA Data Analysis
Kobayashi, S	C-a Division of Developmental Genetics
Kobayashi, T	B-a Division of Cytogenetics
Kobayashi, T.	B-a Division of Cytogenetics
Kobayashi, Y.	H-c Multicellular Organization Laboratory
Kobayashi,M.	H-e Gene Network Laboratory
Kodama, E.	H-c Multicellular Organization Laboratory
Kohara, S.	I-a Laboratory for DNA Data Analysis
Kohara, Y.	G-b Genome biology Laboratory E-a Division of Human Genetics G-a Genetic Informatics Laboratory I-a Laboratory for DNA Data Analysis K RADIOISOTOPE CENTER
Kohda, T.	N Technical Section E-a Division of Human Genetics
Kohda,D.	H-d Biomolecular Structure Laboratory
Koide, T.	F-a Mammalian Genetics Laboratory F-c Mouse Genomics Resource Laboratory
Koji Arizono	G-b Genome biology Laboratory
Kokubo, H.	F-b Mammalian Development Laboratory
Kokubo,H.	F-b Mammalian Development Laboratory
Komaki R	D-a Division of Population Genetics
Komaki, R.	D-a Division of Population Genetics
Komatsu K	D-a Division of Population Genetics
Komatsu, K.	D-a Division of Population Genetics
Komiyama, T.	I-c Laboratory for Gene Function Research
Komori,A.	H-e Gene Network Laboratory
Komori,A.Manabe	H-e Gene Network Laboratory
Kondo, A.	F-a Mammalian Genetics Laboratory
Kondo, S.	C-a Division of Developmental Genetics C-c Division of Molecular and Developmental Biology

Kondo, T.	E-a Division of Human Genetics
Kondoh, H.	C-c Division of Molecular and Developmental Biology
Koriyama, H.	E-a Division of Human Genetics
Koseki, K.	F-b Mammalian Development Laboratory
Koshida, S.	C-c Division of Molecular and Developmental Biology
Kosuge T	I-d Laboratory for Research and Development of Biological Databases
Kosuge, T.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research I-d Laboratory for Research and Development of Biological Databases
Kotani, T.	C-c Division of Molecular and Developmental Biology
Kotaro KIMURA	H-c Multicellular Organization Laboratory
Kouichi ITO	H-b Molecular Biomechanism Laboratory
Koyama, T.	F-g Invertebrate Genetics Laboratory
Koyanagi, KO.	I-a Laboratory for DNA Data Analysis
Krainer, R. A.	A-a Division of Molecular Genetics
Krzyzanowska, A.	C-a Division of Developmental Genetics
Kubori, T.	H-b Molecular Biomechanism Laboratory
Kudo, A.	G-a Genetic Informatics Laboratory
Kudrna, D.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Kuhara, A.	H-c Multicellular Organization Laboratory
Kuliyev, E.	C-c Division of Molecular and Developmental Biology
Kulski, J.	I-a Laboratory for DNA Data Analysis
Kumagai,I.	H-d Biomolecular Structure Laboratory
Kumaki, K.	E-a Division of Human Genetics
Kumamaru, T.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Kuranaga, E.	F-g Invertebrate Genetics Laboratory
Kuranaga,E.	H-e Gene Network Laboratory
Kurata, N.	F-e Plant Genetics Laboratory G-a Genetic Informatics Laboratory L EXPERIMENTAL FARM
kurata, N.	L EXPERIMENTAL FARM
Kurata, N. Alvarez	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Kuriki, S.	F-a Mammalian Genetics Laboratory
Kurimoto, Y.	D-a Division of Population Genetics
Kuroda, T.	I-a Laboratory for DNA Data Analysis
Kurokawa M	I-d Laboratory for Research and Development of Biological Databases
Kurokawa, M.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Kurokawa, Y.	A-b Division of Mutagenesis
Kuroki,K.	H-d Biomolecular Structure Laboratory
Kurusu,M.	H-e Gene Network Laboratory
Kuryshev, V.	I-a Laboratory for DNA Data Analysis

Kusama, S.	F-g Invertebrate Genetics Laboratory
Kusano, A.	E-b Division of Agricultural Genetics J-a Laboratory for Cell Lineage
Kushima R.	N Technical Section
Kusumi, M.	E-a Division of Human Genetics
Kuwajima, K.	H-a Biological Macromolecules Laboratory
Kyono, S.	N Technical Section E-a Division of Human Genetics
L.B.	I-d Laboratory for Research and Development of Biological Databases
Lam, DS.	I-a Laboratory for DNA Data Analysis
Lambert, G.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Lau, TK.	I-a Laboratory for DNA Data Analysis
Lee WJ	F-g Invertebrate Genetics Laboratory
Lemaitre B.	F-g Invertebrate Genetics Laboratory
Leulier, F.	F-g Invertebrate Genetics Laboratory
Levine, R. B.	F-g Invertebrate Genetics Laboratory
Li, E.	E-a Division of Human Genetics
Li, S.	C-c Division of Molecular and Developmental Biology
Li, S.L.	D-a Division of Population Genetics
Li,WH.	I-a Laboratory for DNA Data Analysis
Li,Y.	B-b Division of Microbial Genetics
Liang DS	D-a Division of Population Genetics
Liang, D.-S.	D-a Division of Population Genetics
Lin, S.	C-c Division of Molecular and Developmental Biology
Liu, Q.-X.	C-b Division of Gene Expression
Lucotte, G.	D-a Division of Population Genetics
Luedeman, R. A.	F-g Invertebrate Genetics Laboratory
Luo, M.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
MacKill, D.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Macquin, C.	I-a Laboratory for DNA Data Analysis
Maeda, M.	F-a Mammalian Genetics Laboratory
Maenaka,K.	H-d Biomolecular Structure Laboratory
Maeno, A.	F-a Mammalian Genetics Laboratory
Makiko, Tsutsumi.	F-b Mammalian Development Laboratory
Makino, J.	F-a Mammalian Genetics Laboratory F-c Mouse Genomics Resource Laboratory
Makino, T.	I-a Laboratory for DNA Data Analysis
Makoto Hamaguchi	G-b Genome biology Laboratory
Mapendano CK	D-a Division of Population Genetics
Mapendano, C. K.	D-a Division of Population Genetics
Marlow, F.L.	C-c Division of Molecular and Developmental Biology
Maruyama Y	I-d Laboratory for Research and Development of Biological Databases

Maruyama, Y.	F-g Invertebrate Genetics Laboratory I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Maruyama,Y.	H-e Gene Network Laboratory
Masahiro Okada	A-a Division of Molecular Genetics
Masai,I.	H-e Gene Network Laboratory
Masaki Hiramoto	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis
Masayuki Oginuma	F-b Mammalian Development Laboratory
Mashima J	I-d Laboratory for Research and Development of Biological Databases
Mashima, J.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Masu, M.	F-g Invertebrate Genetics Laboratory
Masuya, H.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Matsubara, K.	E-a Division of Human Genetics
Matsuda, M.	G-a Genetic Informatics Laboratory
Mayumi Takahashi	A-a Division of Molecular Genetics
McCallion, A.S.	C-c Division of Molecular and Developmental Biology
McCouch, S.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
McLeod, I. X.	A-a Division of Molecular Genetics
Mead, P.E.	C-c Division of Molecular and Developmental Biology
Mengin-Lecreulx D	F-g Invertebrate Genetics Laboratory
Meyer, A.	I-a Laboratory for DNA Data Analysis
Mi-Sun Kwon	A-a Division of Molecular Genetics
Michaut, L.	F-g Invertebrate Genetics Laboratory
Michaut,L.	H-e Gene Network Laboratory
Mikami, Y.	G-a Genetic Informatics Laboratory
Miki, T.	G-a Genetic Informatics Laboratory
Mikoshiba, K.	D-a Division of Population Genetics
Miletic AV	H-a Biological Macromolecules Laboratory
Mimuro, H.	G-a Genetic Informatics Laboratory
Minami ,N.	F-b Mammalian Development Laboratory
Minami, N.	E-a Division of Human Genetics
Minezaki, Y.	I-b Laboratory for Gene-Product Informatics
Mingorance, A.	E-c Division of Brain Function
Mise, K.	E-a Division of Human Genetics
Mita, A.	F-a Mammalian Genetics Laboratory
Mitani, S.	G-a Genetic Informatics Laboratory
Mittelsten Scheid	E-b Division of Agricultural Genetics
Miura A	E-b Division of Agricultural Genetics
Miura, A.	N Technical Section
Miura, I.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Miura, M.	C-a Division of Developmental Genetics F-g Invertebrate Genetics Laboratory

Miwa N	D-a Division of Population Genetics
Miwa, N.	D-a Division of Population Genetics
Miyabayashi, M.	G-a Genetic Informatics Laboratory
Miyagawa-Tomita, S.	F-b Mammalian Development Laboratory
Miyazaki S	I-d Laboratory for Research and Development of Biological Databases
Miyazaki, M.	I-c Laboratory for Gene Function Research
Miyazaki, S.	I-a Laboratory for DNA Data Analysis
Miyoshi, A.	D-a Division of Population Genetics
Miyoshi, K.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Mizokami, M.	I-a Laboratory for DNA Data Analysis
Mizrachi, I.	I-c Laboratory for Gene Function Research
Mizusawa, K.	C-c Division of Molecular and Developmental Biology
Mizuta, Y.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Mizutani, M.	D-a Division of Population Genetics
Mochida, K.	G-a Genetic Informatics Laboratory
Mochizuki, H.	F-g Invertebrate Genetics Laboratory
Mochizuki,H.	H-e Gene Network Laboratory
Mohri-Shiomi, A.	H-c Multicellular Organization Laboratory
Mori, H.	I-d Laboratory for Research and Development of Biological Databases
Mori, K.	F-a Mammalian Genetics Laboratory
Moriguchi K.	L EXPERIMENTAL FARM
Moriguchi, K.	F-e Plant Genetics Laboratory
Moriguchi,M.	H-d Biomolecular Structure Laboratory
Morimoto M	F-b Mammalian Development Laboratory
Morimoto M.	N Technical Section
Morimoto, M.	F-b Mammalian Development Laboratory
Morita, S.	E-a Division of Human Genetics
Moriwaki, K.	F-a Mammalian Genetics Laboratory
Morrison, N.	I-c Laboratory for Gene Function Research
Morvan, G.	C-c Division of Molecular and Developmental Biology
Motono, C.	I-a Laboratory for DNA Data Analysis
Mukaisho K.	N Technical Section
Muller C.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Murakami S.	H-d Biomolecular Structure Laboratory
Murakami, R.	G-b Genome biology Laboratory
Muraki, M.	A-a Division of Molecular Genetics
Murayama, Y.	A-b Division of Mutagenesis
Murphy, J.	C-c Division of Molecular and Developmental Biology
Murray JC	D-a Division of Population Genetics
Murray, J. C.	D-a Division of Population Genetics
Nagai S.	I-a Laboratory for DNA Data Analysis

Nagai, K.	I-a Laboratory for DNA Data Analysis
Nagai, S.	I-a Laboratory for DNA Data Analysis
Nagamura, Y.	I-a Laboratory for DNA Data Analysis
Nagano, J.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Nagata, K.	C-b Division of Gene Expression
Nagato Y.	L EXPERIMENTAL FARM
Nagato, Y.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Nagayoshi, S.	C-c Division of Molecular and Developmental Biology
Nakagata, N.	G-a Genetic Informatics Laboratory
Nakagawa, S.	C-c Division of Molecular and Developmental Biology
Nakahara, T.	I-a Laboratory for DNA Data Analysis
Nakajima, M.	C-b Division of Gene Expression
Nakajima, T.	F-g Invertebrate Genetics Laboratory
Nakajima,T.	H-e Gene Network Laboratory
Nakamura M	E-b Division of Agricultural Genetics
Nakamura Y	D-a Division of Population Genetics
Nakamura, A.	F-g Invertebrate Genetics Laboratory
Nakamura, Y.	D-a Division of Population Genetics I-a Laboratory for DNA Data Analysis
Nakanishi,Y.	F-g Invertebrate Genetics Laboratory
Nakano, M.	N Technical Section
Nakao, M.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Nakao, Y.	F-a Mammalian Genetics Laboratory
Nakashima ,Y.	F-b Mammalian Development Laboratory
Nakashima M	D-a Division of Population Genetics
Nakashima, M.	D-a Division of Population Genetics
Nakatsuji, N.	F-a Mammalian Genetics Laboratory
Nakayama, T.	C-b Division of Gene Expression E-b Division of Agricultural Genetics
Nakayama,H.	H-b Molecular Biomechanism Laboratory
Nakazawa, M.	I-a Laboratory for DNA Data Analysis
Nam HJ	F-g Invertebrate Genetics Laboratory
Narita, T.	K RADIOISOTOPE CENTER
Naruse, T.	I-a Laboratory for DNA Data Analysis
Natsume N	D-a Division of Population Genetics
Natsume, N.	D-a Division of Population Genetics
Newbury, S. F.	F-g Invertebrate Genetics Laboratory
Ni, R.	C-c Division of Molecular and Developmental Biology
Nicolas, O.	E-c Division of Brain Function
Niikawa N.	D-a Division of Population Genetics
Niimi, T.	I-a Laboratory for DNA Data Analysis
Nik Putnam	G-b Genome biology Laboratory
Niki, H.	F-f Microbial Genetics Laboratory G-a Genetic Informatics Laboratory

	K RADIOISOTOPE CENTER
Nimura, K.	E-a Division of Human Genetics
Ninokata A	D-a Division of Population Genetics
Ninokata, A.	D-a Division of Population Genetics
Nishi, A.	F-c Mouse Genomics Resource Laboratory
Nishihara, S.	F-g Invertebrate Genetics Laboratory
Nishijima, H.	E-b Division of Agricultural Genetics
Nishikawa, K.	I-a Laboratory for DNA Data Analysis I-b Laboratory for Gene-Product Informatics
Nishimoto, T.	E-b Division of Agricultural Genetics
Nishioka, K.	C-b Division of Gene Expression
Nishitani, H.	E-b Division of Agricultural Genetics
Nishiwaki,Y.	H-e Gene Network Laboratory
Nobuo SHIMAMOTO	H-b Molecular Biomechanism Laboratory
Nobuo Shimamoto	H-b Molecular Biomechanism Laboratory
Nobuyoshi, Shimizu.	F-b Mammalian Development Laboratory
Nobuyuki Tominaga	G-b Genome biology Laboratory
Noda, T.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Noguchi, H.	D-a Division of Population Genetics
Nomura M	D-a Division of Population Genetics
Nomura, M.	D-a Division of Population Genetics
Nomura, N.	I-a Laboratory for DNA Data Analysis
Nomura, Y.	E-b Division of Agricultural Genetics
Nonomura, K-I.	F-e Plant Genetics Laboratory
Nonomura, K.	N Technical Section
Nonomura, K.I.	L EXPERIMENTAL FARM
Nori Satoh	G-b Genome biology Laboratory
Norio SUZUKI	H-c Multicellular Organization Laboratory
Noro, Y.	C-a Division of Developmental Genetics
Nozaki, M.	E-a Division of Human Genetics
Nozaki, N.	A-a Division of Molecular Genetics
OOta, S.	D-a Division of Population Genetics
Ochiai, Kondoh	G-a Genetic Informatics Laboratory
Ogasawara O	I-e Laboratory for Gene-Expression Analysis
Ogasawara, O.	I-e Laboratory for Gene-Expression Analysis
Ogata, K.	H-a Biological Macromolecules Laboratory
Ogata, Y.	K RADIOISOTOPE CENTER
Ogawa, M.	I-a Laboratory for DNA Data Analysis
Ogawa, Y.	E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Ogihara, Y.	G-a Genetic Informatics Laboratory
Ogura A.	I-c Laboratory for Gene Function Research
Ogura, A.	I-a Laboratory for DNA Data Analysis
Oh BH	F-g Invertebrate Genetics Laboratory

Ohad, N.	E-b Division of Agricultural Genetics
Ohhata, T.	E-a Division of Human Genetics
Ohkawa, K.	D-a Division of Population Genetics
Ohta T	D-a Division of Population Genetics
Ohta, T.	D-a Division of Population Genetics I-b Laboratory for Gene-Product Informatics
Ohyanagi, H.	I-a Laboratory for DNA Data Analysis
Oka, A.	F-a Mammalian Genetics Laboratory
Okada, M.	A-a Division of Molecular Genetics
Okada, N.	I-a Laboratory for DNA Data Analysis
Okada, U.	H-d Biomolecular Structure Laboratory
Okagaki, Y.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Okamoto, H.	G-a Genetic Informatics Laboratory
Okamoto,H.	H-e Gene Network Laboratory
Okamura, K.	J-a Laboratory for Cell Lineage
Okano, M.	E-a Division of Human Genetics
Okawa, K.	A-a Division of Molecular Genetics
Okido T	I-d Laboratory for Research and Development of Biological Databases
Okido, T.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Okubo K	I-d Laboratory for Research and Development of Biological Databases I-e Laboratory for Gene-Expression Analysis
Okubo, K.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research I-e Laboratory for Gene-Expression Analysis
Okumura, M.	H-c Multicellular Organization Laboratory
Okuno, T.	E-a Division of Human Genetics
Okuwaki, M.	C-b Division of Gene Expression
Ono, T.	A-a Division of Molecular Genetics E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Osada, N.	I-a Laboratory for DNA Data Analysis
Osakabe, K.	E-b Division of Agricultural Genetics
Oshima, H.	I-a Laboratory for DNA Data Analysis
Oshima, K. Takeda	F-g Invertebrate Genetics Laboratory
Ota N	H-a Biological Macromolecules Laboratory
Ota, M.	I-a Laboratory for DNA Data Analysis I-b Laboratory for Gene-Product Informatics
Ota, S.	C-c Division of Molecular and Developmental Biology
Otake, A.	I-c Laboratory for Gene Function Research
Otsuji M	I-e Laboratory for Gene-Expression Analysis
Otsuki, T.	I-a Laboratory for DNA Data Analysis
P. E.	C-c Division of Molecular and Developmental Biology
Palmer, E.	F-g Invertebrate Genetics Laboratory
Pang, CP.	I-a Laboratory for DNA Data Analysis

Parker, R.	F-g Invertebrate Genetics Laboratory
Parrish, J.Z.	J-b Neural Morphogenesis Laboratory
Perna, T.N.	I-d Laboratory for Research and Development of Biological Databases
Petruck, S.	C-b Division of Gene Expression
Pichaud, F.	F-g Invertebrate Genetics Laboratory
Picot, M.	F-g Invertebrate Genetics Laboratory
Pili-Floury S	F-g Invertebrate Genetics Laboratory
Plunkett, G.	I-d Laboratory for Research and Development of Biological Databases
Poidevin M	F-g Invertebrate Genetics Laboratory
Postlethwait, J.H.	C-c Division of Molecular and Developmental Biology
Q-X. Liu	I-a Laboratory for DNA Data Analysis
Qazi MR	F-g Invertebrate Genetics Laboratory
Qi, F.	C-c Division of Molecular and Developmental Biology
Qing-Xin Liu	I-a Laboratory for DNA Data Analysis
Rao, K.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Rasubala,L.	H-d Biomolecular Structure Laboratory
Reichman-Fried, M.	C-c Division of Molecular and Developmental Biology
Reiss, J.	C-c Division of Molecular and Developmental Biology
Ren, J.	C-c Division of Molecular and Developmental Biology
Ren, X.	C-c Division of Molecular and Developmental Biology
Ribeiro, S P.	F-g Invertebrate Genetics Laboratory
Riggs, A.D.	E-a Division of Human Genetics
Riley, K. M.	C-b Division of Gene Expression
Riley, M.	I-d Laboratory for Research and Development of Biological Databases
Robertson, D.	F-g Invertebrate Genetics Laboratory
Rodriguez-Mari, A.	C-c Division of Molecular and Developmental Biology
Rogers, MS.	I-a Laboratory for DNA Data Analysis
Romeo Y	F-g Invertebrate Genetics Laboratory
Rudd, E.K.	I-d Laboratory for Research and Development of Biological Databases
Russom	D-a Division of Population Genetics
Russom,o	D-a Division of Population Genetics
Ryosuke Morita	C-a Division of Developmental Genetics
Ryusuke FUJITA	H-b Molecular Biomechanism Laboratory
S.-C.	C-b Division of Gene Expression
Sachiko Sakamoto	B-b Division of Microbial Genetics
Sachiko, Tsuda.	F-b Mammalian Development Laboratory
Sado, T.	E-a Division of Human Genetics
Saenko VA	D-a Division of Population Genetics
Saenko, V. A.	D-a Division of Population Genetics
Saez-Valero, J.	E-c Division of Brain Function
Saga Y	F-b Mammalian Development Laboratory
Saga Y.	N Technical Section

Saga, M.	G-a Genetic Informatics Laboratory
Saga, Y.	G-b Genome biology Laboratory
Saga,Y.	F-b Mammalian Development Laboratory
Sagai, T.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Sagara,H.	H-e Gene Network Laboratory
Sahara, K.	I-a Laboratory for DNA Data Analysis
Saigo, K.	F-g Invertebrate Genetics Laboratory
Saigo,K.	H-e Gene Network Laboratory
Saito S	D-a Division of Population Genetics
Saito T.	H-a Biological Macromolecules Laboratory
Saito, K.	F-d Model Fish Genomics Resource
Saito, S.	D-a Division of Population Genetics
Saito, T.	H-a Biological Macromolecules Laboratory
Saito, Y.	I-b Laboratory for Gene-Product Informatics
Saitou N	D-a Division of Population Genetics
Saitou N.	D-a Division of Population Genetics
Saitou Naruya	D-a Division of Population Genetics
Saitou, N.	D-a Division of Population Genetics D-a Division of Population Genetics
Sakabe, E.	I-a Laboratory for DNA Data Analysis
Sakai, H.	I-a Laboratory for DNA Data Analysis
Sakai, N.	F-d Model Fish Genomics Resource H-d Biomolecular Structure Laboratory
Sakaki, T.	I-a Laboratory for DNA Data Analysis
Sakamoto,S.	B-b Division of Microbial Genetics
Sakaniwa, S.	G-a Genetic Informatics Laboratory
Sakata-Sogawa K	H-a Biological Macromolecules Laboratory
Sakata-Sogawa K.	H-a Biological Macromolecules Laboratory
Sakata-Sogawa, K.	H-a Biological Macromolecules Laboratory
Sakuma, M.	H-a Biological Macromolecules Laboratory
Sakuraba, Y.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Sakurada, A.	E-a Division of Human Genetics
Sakurai, N.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Sakurai, T.	F-a Mammalian Genetics Laboratory
SanMiguel, P.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Sanematsu, F.	A-a Division of Molecular Genetics E-b Division of Agricultural Genetics
Sano, K.	I-a Laboratory for DNA Data Analysis
Sarhan, M.	C-b Division of Gene Expression
Sasagawa, T.	G-a Genetic Informatics Laboratory
Sasagawa,N.	F-b Mammalian Development Laboratory
Sasaki H	N Technical Section
Sasaki N	F-b Mammalian Development Laboratory

Sasaki N.	N Technical Section
Sasaki, H.	E-a Division of Human Genetics
Sasaki, Y.	D-a Division of Population Genetics
Sasaki,T.	H-d Biomolecular Structure Laboratory
Sato, K.	G-a Genetic Informatics Laboratory
Sato, M.	E-a Division of Human Genetics
Sato, S.	E-a Division of Human Genetics
Sato, Y.	C-c Division of Molecular and Developmental Biology
Satoh, H.	L EXPERIMENTAL FARM
Saze H	E-b Division of Agricultural Genetics
Schafer, S.	I-c Laboratory for Gene Function Research
Scheid, O.M.	E-b Division of Agricultural Genetics
Scherfer C	F-g Invertebrate Genetics Laboratory
Schwarz, G.	C-c Division of Molecular and Developmental Biology
Schweisguth, F.	C-b Division of Gene Expression
Sedkov, Y.	C-b Division of Gene Expression
Seiji Tanaka	B-b Division of Microbial Genetics
Sekine I	D-a Division of Population Genetics
Sekine, I.	D-a Division of Population Genetics
Senoo-Matsuda, N.	C-a Division of Developmental Genetics
Serikawa, Obata	G-a Genetic Informatics Laboratory
Serizawa, N.	B-a Division of Cytogenetics
Serres, H.M.	I-d Laboratory for Research and Development of Biological Databases
Sezutsu, H.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Shan, H.J.	I-a Laboratory for DNA Data Analysis
Sharoh, Y.	G-a Genetic Informatics Laboratory
Shen CK.	I-a Laboratory for DNA Data Analysis
Shibahara, K-I.	E-b Division of Agricultural Genetics
Shibahara, K-i.	E-b Division of Agricultural Genetics
Shibahara, K.	A-a Division of Molecular Genetics E-b Division of Agricultural Genetics
Shibano, T.	C-c Division of Molecular and Developmental Biology
Shigemoto, Y.	I-a Laboratory for DNA Data Analysis
Shigenobu, S.	C-a Division of Developmental Genetics
Shigeo, Takashima.	F-b Mammalian Development Laboratory
Shiina N.	H-a Biological Macromolecules Laboratory
Shiina, T.	I-a Laboratory for DNA Data Analysis
Shimamoto, N.	H-b Molecular Biomechanism Laboratory
Shimamoto,N.	H-b Molecular Biomechanism Laboratory
Shimizu, A.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Shimizu, S.	I-a Laboratory for DNA Data Analysis
Shimizu, T.	D-a Division of Population Genetics

Shimizu, Y.	D-a Division of Population Genetics
Shimoda, T.	G-a Genetic Informatics Laboratory
Shimojima, T.	C-b Division of Gene Expression H-d Biomolecular Structure Laboratory
Shimosaka, E.	G-a Genetic Informatics Laboratory
Shimozono, N.	I-a Laboratory for DNA Data Analysis
Shin Watanabe	G-a Genetic Informatics Laboratory
Shin-I, T.	G-a Genetic Informatics Laboratory
Shin-i, T.	G-b Genome biology Laboratory
Shinkura K.	H-a Biological Macromolecules Laboratory
Shinkura, K.	H-a Biological Macromolecules Laboratory
Shinoda, K.	I-a Laboratory for DNA Data Analysis
Shinya, M.	F-d Model Fish Genomics Resource
Shionyu, M.	I-a Laboratory for DNA Data Analysis
Shiota, K.	E-a Division of Human Genetics
Shiraishi, K.	K RADIOISOTOPE CENTER
Shirakihara, Y.	H-d Biomolecular Structure Laboratory
Shirakihara,Y.	H-d Biomolecular Structure Laboratory
Shiratori A.	H-d Biomolecular Structure Laboratory
Shiratori, A.	H-d Biomolecular Structure Laboratory
Shiroishi, T.	N Technical Section E-a Division of Human Genetics F-a Mammalian Genetics Laboratory F-c Mouse Genomics Resource Laboratory G-a Genetic Informatics Laboratory
Shiroishi,M.	H-d Biomolecular Structure Laboratory
Shuichi, Asakawa.	F-b Mammalian Development Laboratory
Shunsuke Imanishi	G-a Genetic Informatics Laboratory
Sisneros, N. B.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
So, S.	E-b Division of Agricultural Genetics
Soderlund, C.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Solnica-Krezel, L.	C-c Division of Molecular and Developmental Biology
Song, H.	C-c Division of Molecular and Developmental Biology
Sonoda S	D-a Division of Population Genetics
Sonoda, S.	D-a Division of Population Genetics
Soriano, E.	E-c Division of Brain Function
Sosonkina N	D-a Division of Population Genetics
Sosonkina, N.	D-a Division of Population Genetics
Spellman P	F-g Invertebrate Genetics Laboratory
Starks, A.M.	C-c Division of Molecular and Developmental Biology
Suda, C.	G-b Genome biology Laboratory E-a Division of Human Genetics
Suda, T.	F-g Invertebrate Genetics Laboratory
Suemori, H.	F-a Mammalian Genetics Laboratory
Suetake, I.	C-c Division of Molecular and Developmental Biology

Suga, H.	I-a Laboratory for DNA Data Analysis
Sugano, S.	I-a Laboratory for DNA Data Analysis
Sugawara H	I-d Laboratory for Research and Development of Biological Databases I-e Laboratory for Gene-Expression Analysis
Sugawara H.	I-d Laboratory for Research and Development of Biological Databases
Sugawara, H.	G-a Genetic Informatics Laboratory I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research I-d Laboratory for Research and Development of Biological Databases
Sugawara,H	I-d Laboratory for Research and Development of Biological Databases
Sumiyama, K.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Susa, M.	H-b Molecular Biomechanism Laboratory
Susumu Hirose	I-a Laboratory for DNA Data Analysis
Suzuki T.	H-d Biomolecular Structure Laboratory
Suzuki Y.	N Technical Section
Suzuki, H.	H-d Biomolecular Structure Laboratory
Suzuki, T.	N Technical Section E-a Division of Human Genetics F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Suzuki, Y.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Suzuki,E.	H-e Gene Network Laboratory
Suzuki,E.Chiba	H-e Gene Network Laboratory
Svensson, L.	I-c Laboratory for Gene Function Research
Swat W	H-a Biological Macromolecules Laboratory
T. Gojobori1	I-a Laboratory for DNA Data Analysis
T. Natsume	A-b Division of Mutagenesis
T.Morishita	A-b Division of Mutagenesis
TOKUNAGA, M.	H-a Biological Macromolecules Laboratory
Tada, T.	F-a Mammalian Genetics Laboratory
Tadaki, T.	K RADIOISOTOPE CENTER
Tadasu Sin-I	G-b Genome biology Laboratory
Taira, M.	C-c Division of Molecular and Developmental Biology
Taisen Iguchi	G-b Genome biology Laboratory
Tajima, S.	C-c Division of Molecular and Developmental Biology
Takada, T.	F-a Mammalian Genetics Laboratory
Takagi, N.	F-a Mammalian Genetics Laboratory
Takagi, Y.	C-c Division of Molecular and Developmental Biology
Takahashi A	D-a Division of Population Genetics
Takahashi H	D-a Division of Population Genetics
Takahashi K	F-g Invertebrate Genetics Laboratory
Takahashi, A.	D-a Division of Population Genetics

	F-a Mammalian Genetics Laboratory F-c Mouse Genomics Resource Laboratory
Takahashi, H.	D-a Division of Population Genetics D-a Division of Population Genetics
Takahashi, K.	F-g Invertebrate Genetics Laboratory I-a Laboratory for DNA Data Analysis
Takahashi, R.	F-a Mammalian Genetics Laboratory
Takahashi, T.	C-a Division of Developmental Genetics
Takahashi, Y.	C-c Division of Molecular and Developmental Biology F-b Mammalian Development Laboratory
Takahashi,K	H-e Gene Network Laboratory
Takahashi,K.	F-g Invertebrate Genetics Laboratory H-e Gene Network Laboratory
Takai, M.	C-b Division of Gene Expression
Takako Isshiki	J-a Laboratory for Cell Lineage
Takaku, Y.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Takami, Y.	A-a Division of Molecular Genetics E-b Division of Agricultural Genetics
Takano-Shimizu T.	D-a Division of Population Genetics
Takano-Shimizu,T.	D-a Division of Population Genetics
Takanori ,Narita.	F-b Mammalian Development Laboratory
Takashi Gojobor	I-a Laboratory for DNA Data Analysis
Takashi Gojobori	I-a Laboratory for DNA Data Analysis
Takashima K	E-b Division of Agricultural Genetics
Takashima, K.	N Technical Section
Takashima, M.	G-a Genetic Informatics Laboratory
Takasu, M.	I-a Laboratory for DNA Data Analysis
Takeda, A.	E-a Division of Human Genetics
Takeda, H.	C-c Division of Molecular and Developmental Biology
Takeda, J.	I-c Laboratory for Gene Function Research
Takeda, JI.	I-a Laboratory for DNA Data Analysis
Takeda, K. Yamazaki	G-a Genetic Informatics Laboratory
Takeda, M.	C-c Division of Molecular and Developmental Biology
Takeda, S.	C-c Division of Molecular and Developmental Biology E-b Division of Agricultural Genetics E-b Division of Agricultural Genetics
Takeda.	F-b Mammalian Development Laboratory
Takehiko Kobayashi	B-a Division of Cytogenetics
Takeichi, M.	C-c Division of Molecular and Developmental Biology
Takemoto,K.	H-e Gene Network Laboratory
Takeo Katsuki	C-a Division of Developmental Genetics
Takeshi ISHIHARA	H-c Multicellular Organization Laboratory
Takeshi Kawashima	G-b Genome biology Laboratory
Takeuchi T.	D-a Division of Population Genetics

Takizawa, N.	A-a Division of Molecular Genetics
Takuya Tsuji	J-a Laboratory for Cell Lineage
Talag, J.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Tambe Y.	N Technical Section
Tamon Tanaka	B-b Division of Microbial Genetics
Tamura T	I-e Laboratory for Gene-Expression Analysis
Tamura, M.	F-a Mammalian Genetics Laboratory
Tamura, T.	H-d Biomolecular Structure Laboratory
Tan, B. C.-M.	C-b Division of Gene Expression
Tanabe, H.	F-a Mammalian Genetics Laboratory
Tanabe, K.	C-c Division of Molecular and Developmental Biology
Tanaka N	I-d Laboratory for Research and Development of Biological Databases
Tanaka, I.	H-d Biomolecular Structure Laboratory
Tanaka, N.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research I-d Laboratory for Research and Development of Biological Databases
Tanaka, S.	E-a Division of Human Genetics
Tanaka, T.	I-a Laboratory for DNA Data Analysis
Tanaka, Y.	I-a Laboratory for DNA Data Analysis
Tanaka,S.	B-b Division of Microbial Genetics
Tanaka,T.	B-b Division of Microbial Genetics
Tang, B.L.	E-c Division of Brain Function
Tang, LY.	I-a Laboratory for DNA Data Analysis
Tani, A.	I-b Laboratory for Gene-Product Informatics
Tanino, M.	I-a Laboratory for DNA Data Analysis
Tao Zhang	H-b Molecular Biomechanism Laboratory
Tate, S.	C-b Division of Gene Expression
Tateno Y	I-d Laboratory for Research and Development of Biological Databases
Tateno Y.	I-d Laboratory for Research and Development of Biological Databases I-e Laboratory for Gene-Expression Analysis
Tateno, Y.	I-a Laboratory for DNA Data Analysis I-c Laboratory for Gene Function Research
Tatsumi Hirata	I-a Laboratory for DNA Data Analysis
Tatsumi, R.	F-g Invertebrate Genetics Laboratory
Tatsuo Fukagawa	A-a Division of Molecular Genetics
Tatsuta, T.	D-a Division of Population Genetics
Tatusova, T.	I-c Laboratory for Gene Function Research
Tenev, T.	F-g Invertebrate Genetics Laboratory
Terasaki, H.	G-b Genome biology Laboratory
Tetsuya Hori	A-a Division of Molecular Genetics
Tetsuya Matsuno	G-b Genome biology Laboratory
Theopold U	F-g Invertebrate Genetics Laboratory
Thierry-Mieg, D.	I-a Laboratory for DNA Data Analysis

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Thomas, H.G.	I-d Laboratory for Research and Development of Biological Databases
Thomson, R.H.	I-d Laboratory for Research and Development of Biological Databases
Tian, W.	D-a Division of Population Genetics
Titus, T.A.	C-c Division of Molecular and Developmental Biology
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Toda,H.	H-e Gene Network Laboratory
Todokoro, F.	I-a Laboratory for DNA Data Analysis
Toki, S.	E-b Division of Agricultural Genetics
Tokunaga K	D-a Division of Population Genetics
Tokunaga M	H-a Biological Macromolecules Laboratory
Tokunaga M.	H-a Biological Macromolecules Laboratory
Tokunaga, M.	H-a Biological Macromolecules Laboratory
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Tomaru, M.	G-a Genetic Informatics Laboratory
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Tomioka, Y.	H-c Multicellular Organization Laboratory
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Tomizawa, J.	H-b Molecular Biomechanism Laboratory
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Tomoko Motohashi	A-a Division of Molecular Genetics
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Toyoda, H.	F-g Invertebrate Genetics Laboratory
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Tsuchiya, R.	G-a Genetic Informatics Laboratory
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Tsudzuki, M.	E-a Division of Human Genetics
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Tsutsui, Y.	A-b Division of Mutagenesis
Tsuyoshi Mizoguchi	G-a Genetic Informatics Laboratory
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Ueda, R. Aigaki	F-g Invertebrate Genetics Laboratory
Ueda,R.	F-g Invertebrate Genetics Laboratory H-e Gene Network Laboratory
Uegaki, K.	E-b Division of Agricultural Genetics
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Ueyama, M.	F-g Invertebrate Genetics Laboratory
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Urasaki, A.	C-c Division of Molecular and Developmental Biology
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Vinton, R.M.	C-c Division of Molecular and Developmental Biology
W. H.	D-a Division of Population Genetics
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Wakamatsu, Y.	G-a Genetic Informatics Laboratory
Wakana, S.	N Technical Section D-a Division of Population Genetics E-a Division of Human Genetics F-a Mammalian Genetics Laboratory
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Walter, J. C.	B-b Division of Microbial Genetics

Wang, CC.	I-a Laboratory for DNA Data Analysis
Wang, HY.	I-a Laboratory for DNA Data Analysis
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Wei, W.	C-c Division of Molecular and Developmental Biology
Wen, L.	C-c Division of Molecular and Developmental Biology
Wiemann, S.	I-a Laboratory for DNA Data Analysis
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Y. Tsutsui	A-b Division of Mutagenesis
Y.Tsutsui	A-b Division of Mutagenesis
Yamada S.	N Technical Section
Yamada, K.	E-a Division of Human Genetics
Yamaguchi, A.	I-a Laboratory for DNA Data Analysis
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Yamaichi, Y.	F-f Microbial Genetics Laboratory
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Yamamoto. T.	F-a Mammalian Genetics Laboratory

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Yamanaka, S.	E-a Division of Human Genetics
Yamasaki S.	H-a Biological Macromolecules Laboratory
Yamasaki, C.	I-a Laboratory for DNA Data Analysis
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Yamazaki, Y.	F-e Plant Genetics Laboratory G-a Genetic Informatics Laboratory L EXPERIMENTAL FARM
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Yanagi, T.	G-a Genetic Informatics Laboratory
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Yanagiya, K.	I-a Laboratory for DNA Data Analysis
Yao, M.	H-d Biomolecular Structure Laboratory
Yaoita,Y.	G-a Genetic Informatics Laboratory
Yasuhiko, Y.	G-b Genome biology Laboratory F-b Mammalian Development Laboratory
Yasukochi, Y.	I-a Laboratory for DNA Data Analysis
Yasumatsu,H.	F-b Mammalian Development Laboratory
Yasushi HIROMI	C-a Division of Developmental Genetics
Yasushi Hiromi	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis
Yasutaka Kubo	G-a Genetic Informatics Laboratory
Yates III	A-a Division of Molecular Genetics
Yazawa, S.	D-a Division of Population Genetics
Ydao, Kitagawa.	F-b Mammalian Development Laboratory
Yergeau, D. A.	C-c Division of Molecular and Developmental Biology
Yergeau, D.A.	C-c Division of Molecular and Developmental Biology
Yi, J.M.	D-a Division of Population Genetics
Yo, M.	G-a Genetic Informatics Laboratory
Yoichiro Kamimura	B-b Division of Microbial Genetics
Yokomine, T.	E-a Division of Human Genetics
Yokosuka T.	H-a Biological Macromolecules Laboratory
Yokosuka, T.	H-a Biological Macromolecules Laboratory
Yokota,A.	H-d Biomolecular Structure Laboratory
Yokoyama, H.	D-a Division of Population Genetics F-a Mammalian Genetics Laboratory
Yonekawa, H.	F-a Mammalian Genetics Laboratory
Yoshida M.	H-d Biomolecular Structure Laboratory
Yoshida, H.	F-g Invertebrate Genetics Laboratory
Yoshida, K.	C-a Division of Developmental Genetics I-a Laboratory for DNA Data Analysis
Yoshihiro YUASA	C-a Division of Developmental Genetics
Yoshikawa, T.	E-a Division of Human Genetics
Yoshikawa,A.	F-b Mammalian Development Laboratory
Yoshimoto, T.	D-a Division of Population Genetics
Yoshimune,K.	H-d Biomolecular Structure Laboratory

Yoshioka, M.	G-a Genetic Informatics Laboratory
Yoshiura K	D-a Division of Population Genetics
Yoshiura, K.	D-a Division of Population Genetics
Yoshiyuki Suzuki	I-a Laboratory for DNA Data Analysis
Yoshizaki, S.	K RADIOISOTOPE CENTER
Yosuke Amemiya	H-b Molecular Biomechanism Laboratory
Yu, Y.	F-e Plant Genetics Laboratory L EXPERIMENTAL FARM
Yuasa, I.	D-a Division of Population Genetics
Yuji Kohara	G-b Genome biology Laboratory
Yuji, Ishikawa.	F-b Mammalian Development Laboratory
Yukiko Yamazaki	G-a Genetic Informatics Laboratory
Yumiko Saga	F-b Mammalian Development Laboratory
Yumiko, Saga.	F-b Mammalian Development Laboratory
Yura, K.	I-a Laboratory for DNA Data Analysis
Yuri KOBAYASHI	H-c Multicellular Organization Laboratory
Yutaka Satou	G-b Genome biology Laboratory
Zachariou, A.	F-g Invertebrate Genetics Laboratory
Zaidman-Remy A	F-g Invertebrate Genetics Laboratory
Zhang, B.	C-c Division of Molecular and Developmental Biology
Zheng, N.	C-c Division of Molecular and Developmental Biology
Zhu, Z.	C-c Division of Molecular and Developmental Biology
Zinn,K.	H-e Gene Network Laboratory
Zou, J.	C-c Division of Molecular and Developmental Biology

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Apr, 13 2006	脊索動物カタユウレイボヤにおける発生遺伝学の進展(Yasunori Sasakura)
Apr, 13 2006	Increased Susceptibility to Retinoic Acid Teratogenicity in Diabetic Pregnancy(Alisa SW Shum)
Apr, 20 2006	A Periodic Table for protein structure（タンパク質立体構造の「周期律表」）(William R.Taylor)
May, 15 2006	代謝型グルタミン酸受容体の遺伝子操作による小脳機能の解析(Atu Aiba)
Jun, 5 2006	マウスにおける細胞内ヘッジホグシグナル伝達機構の解析(Shigeru Makino)
Jun, 7 2006	Autonomously emerging asymmetry in early mammalian development(Takashi Hiiragi)
Jun, 27 2006	ClosedからOpenへ:クロマチン構造変化によるIL-2遺伝子の転写誘導(Satoru Ishihara)
Jul, 10 2006	Midline radial glia translocation and cortical astrocyte migration require Fgf signaling(Yasushi Ohkubo)
Jul, 26 2006	減数分裂特異的mRNAを体細胞分裂期の細胞から選択的に排除する分子機構(Masayuki Yamamoto)
Jul, 27 2006	メダカのリバースジェネティクス：ENUミュータジェネシスによるp53欠損メダカの作製(Yoshihito Taniguchi)
Aug, 7 2006	NF-κB抑制効果を指標とした成人T細胞白血病(ATL)の予防的治療法開発の試み-ATL克服のKey molecule:分子標的がん治療剤 ?(Hidekatsu Iha)
Aug, 17	分裂酵母の相同組換えの中間体形成とその解消-分子機構と生理的役割-(Hiroshi

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Aug, 17 2006	rDNA、核小体から探る細胞の機能(Takehiko Kobayashi)
Aug, 24 2006	Microevolution of microRNAs(Chung-I Wu)
Aug, 28 2006	ナノスケール感覚神経プロセス内分子カスケードの定量化(Takashi Kurahashi)
Aug, 28 2006	Genetics of transcription regulation and speciation in Drosophila(Chung-I wu)
Aug, 31 2006	電気活動非依存的・依存的な神経回路形成の制御機構(Nobuhiko Yamamoto)
Sep, 5 2006	Mechanisms of microtubule-dependent kinetochore transport(Kozo Tanaka)
Sep, 11 2006	Transposon tools for transgenesis and insertional mutagenesis in Xenopus tropicalis(Paul E. Mead)
Sep, 22 2006	シロイヌナズナ近縁種の動原体領域の進化(Akira Kawabe)
Sep, 28 2006	人工進化によりボディプランの発生進化を研究する(Koichi Fujimoto)
Sep, 28 2006	ネットワークモチーフによる形態形成(Shuji Ishihara)
Oct, 18 2006	ポストゲノム時代の分子進化系統解析法の開発と応用(Koichiro Tamura)
Oct, 20 2006	Roberts症候群原因遺伝子の同定(Itaru Yanagihara)
Oct, 23 2006	神経上皮細胞はミステリーの宝庫（Noriko Ohsumi
Oct, 24 2006	分裂酵母の減数分裂期の微少管構造を制御するHrs1/Mcp6(Kayoko Tanaka)
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Nov, 8 2006	Theory of Directional Mutation and Germ line-to-Somatic Switches of Directional Mutation rates. (Noboru Sueoka)
Nov, 21 2006	In vivo neuroimaging analysis of chemotaxis neuronal circuit in C.elegans - Toward elucidation of the computational logic in a biological neuronal circuit - (Hiroshi Suzuki)
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Dec, 11 2006	The Basal Chordate Amphioxus: an Emerging Model for the Prototypical Vertebrate(Linda Z. Holland)
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Jan, 13 2007	高等植物におけるエンドサイトーシス　～分子機構から高次現象に果たす役割へ～（Takashi Ueda）
Jan, 15 2007	細胞周期DNAチェックポイント機構のDNA複製時のゲノム安定維持における役割（Kanji Furuya）
Jan, 23 2007	Common diseaseの疾患遺伝子解析から集団遺伝学の展開（Itsuro Inoue）
Jan, 23 2007	Mechanisms for the amplification of retrotransposons in Bacteria and Eucarya (Kenji Ichiyanagi)
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Feb, 27 2007	Modeling of Fragile X mental retardation in fruitflies (Yong Q.Zhang)
Feb, 27 2007	Probing intracellular choresterol trafficking:lessons from Drosophila models of Niemann Pick type C disease (Xun Huang)
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Mar, 10 2007	DNAマーカーによるマメ科植物の分子遺伝解析（Satoshi Tabata）
Mar, 13 2007	魚類生殖幹細胞の可塑性とその発生工学的利用（Goro Yoshizaki）

Mar, 15 2007	神経細胞の個性決定化プログラムが制御する軸索ガイダンス (Ryuichi Shirasaki)
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Mar, 22 2007	Animal models of alcohol-related behavior:genetics and environment (David A.Blizard)
Mar, 24 2007	形態進化と分子進化の架け橋，脊椎動物の進化とシスエレメントの進化・遺伝子コーディング領域の進化（Hiroshi Wada）
Mar, 27 2007	New insights into the regulation of mammalian origins of DNA replication: Structure and Function （Aloys Schepers）
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Mar, 31 2007	細胞は膜電位情報をどのように細胞内へ伝えるか？（Yasushi Okamura，Mari Sasaki，Thomas Mc Cormack）

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Foreign Visitors

Apr, 3 2006	Hsueh-Wen Chang	National Sun Yat-Sen University, Taiwan, Republic of China
Apr, 13 2006	Alisa SW Shum	Department of Anatomy The Chinese University of Hong Kong
Apr, 20 2006	William R. taylor	National Institute for Medical Research(MRC), Mill Hill, London, UK
Jun, 5 2006	Shigeru Makino	The Hospital for Sick Children University of Toronto
Jun, 7 2006	Takashi Hiiragi	Max-Planck Institute of Immunobiology, Feribrug
Jun, 27 2006	Satoru Ishihara	HIN/HIAID Bethesda, MD, USA
Jul, 10 2006	Yasushi Ohkubo	Yale School of Medicine, Child Study Center
Aug, 24 2006	Chung-I Wu	University of Chicago
Sep, 5 2006	Kozo Tanaka	School of Life Sciences, University of Dundee, UK
Sep, 11 2006	Paul E. Mead	St Jude Chidren's Research Hospital, Memphis
Sep, 22 2006	Akira Kawabe	University of Edinburgh Institute of Evolutionary Biology
Oct, 27 2006	Masato Yonezawa	Research Institute of Molecular Pathology (IMP) The Vienna Biocenter, Austria
Oct, 30 2006	Nancy Hopkins	Massachusetts Institute of Technology

Nov, 8 2006	Noboru Sueoka	Department of Ecology and Evolutionary Biology, University of California at Irvine
Nov, 21 2006	Hiroshi Suzuki	Division of Biological Sciences University of California, San Diego
Dec, 11 2006	Artur Kania	Director, Neural Circuit Development Laboratory, Institut de Recherches Cliniques de Monter'al (IRCM), Canada
Dec, 11 2006	Linda Z. Holland	Scripps Institution of Oceanography, University of California San Diego
Dec, 11 2006	Hiroko Sano	Developmental Genetics Skirball Institute, NYU Medical Center
Dec, 13 2006	Hiroyuki Matsumoto	Department of Biochemistry & Molecular Biology University of Oklahoma Health Sciences Center
Dec, 19 2006	Oliver Hobert	Investigator, Howard Hughes Medical Institute Columbia University Medical Center, Department of Biochemistry & Molecular Biophysics
Feb, 2 2007	Masahiro Kaneda	The Wellcome Trust/Cancer Research UK Gurdon Institute University of Cambridhe
Feb, 27 2007	Yong Q. Zhang	Institute of Genetics and Developmental Biology, Chinese Academy of Science
Feb, 27 2007	Xun Huang	Institute of Genetics and Developmental Biology, Chinese Academy of Science
Mar, 9 2007	Tadahiro Iimura	Stowers Institute for Medical Research, Kansas City, Missouri U.S.A
Mar, 9 2007	Jianzhi George Zhang	University of Michigan
Mar, 19 2007	Wolfang Stephan	Biocenter, University of Munich
Mar, 20 2007	Andrew Holmes	Secion on Behavioral Science and Genetics Laboratory for Integrative Neuroscience National Institute on Alcohol Abuse and Alcoholism National Institutes of Health
Mar, 22 2007	David A. Blizard	Center for Developmental and Health Genetics, Pennsylvania State University
Mar, 27 2007	Aloys Schepers	GSF-National Research Center for Environment and Heath Department of Gene Vectors, Munich, Germany

Mar, 29 2007 Geraldine Seydoux Dept. of Molecular Biology and Genetics

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