Psychological and Neural Bases of Social Interaction:
Are Facial Expressions and Gazes the Windows to the Soul?

Professor Sakiko Yoshikawa - Kokoro Research Center

Prof. Sakiko Yoshikawa and her colleagues are conducting research on how people recognize social signals from a face, such as facial expression and gaze. They are interested in elucidating human social competence, which makes it possible to perceive the emotions and intentions of others, to understand the relations between oneself and others, and to modulate our behavior flexibly in face-to-face communication. Her current research topics focus on perceptual processes and recognition of emotion from dynamic facial expressions, gaze effects on attentional shift, and spontaneous facial mimicry in face-to-face interaction. She utilizes both behavior experiment and neuro-scientific methods such as brain-imaging when conducting the research. Recent neuroscience literature offers an accumulation of convincing evidence indicating that the same face-responsive brain areas in the occipito-temporal region (superior temporal sulcus) and in the amygdala are involved in processing both facial expression and gaze direction. This implies that facial expression and gaze direction processing interact in the early stages of visual perception. Focusing on "the threatening face advantage" in the perception of facial expression, her research group investigated whether gaze direction modulates this effect by using a perceptual matching task. The threatening face advantage is a phenomenon whereby angry, threatening faces are more quickly and accurately detected than are other emotional faces. They found that face/gaze direction affected the early visual stages of facial expression processing; a threatening face looking toward the perceiver was processed more accurately than the same face looking away. Their results showed that humans have an ecologically valid mechanism for detecting a threatening signal and efficiently avoiding imminent potential danger.

kokoro.kyoto-u.ac.jp/en/staff-en/2011/02/sakiko_yoshikawa.html

Visualization of the Molecular Mechanism of Memory Using New Experimental Methods

Professor Tomoo Hirano - Graduate School of Science [left]
Postdoctoral Fellow Hiromitsu Tanaka - Graduate School of Science [right]

When we learn and remember something, the efficacy of information transmission at synapses in the brain changes. At a synapse, a presynaptic neuron secretes a transmitter molecule such as glutamate, and receptors on the postsynaptic membrane capture the transmitter and respond. Repeated use of a synapse increases the long term transmission efficacy. This phenomenon is called long-term potentiation (LTP), and contributes to memory formation. The increase in the number of glutamate receptors is one of the main molecular mechanisms for LTP. However, when and how different types of glutamate receptor increase in the postsynaptic membrane had been unclear. Prof. Tomoo Hirano and Dr. Hiromitsu Tanaka addressed this issue by developing new experimental methods to visualize the changes and movements of glutamate receptors around the postsynaptic membrane.

Direct formation of postsynaptic membrane on a glass surface coated with neurexin molecule and the application of total internal reflection microscopy enabled them to observe glutamate receptors tagged with a fluorescent molecule with a high resolution. LTP induction in cultured neurons revealed changes in the number of receptors and in their exocytosis during LTP. The results of the experiment indicated that different types of glutamate receptor increase in the postsynaptic membrane through distinct pathways during LTP induction. This study contributes to a deeper understanding of the LTP mechanism, and the methods developed here are applicable to studies focusing on the movements and functions of molecules bound to cell-membrane in general.

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2011/120323_1.htm
www.cell.com/cell-reports/abstract/S2211-1247(12)00047-2

Involvement of the Circadian Clock of the Urinary Bladder in Diurnal Urination Rhythm

Professor Osamu Ogawa - Graduate School of Medicine

The research team led by Prof. Osamu Ogawa has been pioneering a molecular biological approach to unraveling unknown functional mechanisms of the urinary bladder. In place of a conventional physiological approach, they have introduced cell biology, bioinformatics, and genetically-modified animals to pursue new frontiers in this field.

With this approach, the team discovered that our biological clocks control bladder capacities, so that we don't have to wake up during the night to urinate. It is already known that people don't feel the need to go to the bathroom while asleep because bladder capacity increases at night. It has been unclear, however, what controls the change in capacity. Using a newly devised machine that constantly moves filter papers beneath a mouse cage to capture the mice's urine, Ogawa's team conducted experiments to find out whether there were differences in the mice's day and night urination patterns, even in a 24-hour period of darkness. They found that normal urination patterns were lost in mice with defective biological clocks, which shows that urination is an event controlled by an intrinsic genetic rhythm.

When the quantity of the protein connexin 43 produced in the bladder decreases, bladder capacity increases and urination becomes less frequent. The quantity of connexin 43 changes throughout a 24-hour cycle. During sleep, it decreases by 50% compared to the daytime. Ogawa's team found that the amount of connexin 43 was controlled by circadian clocks, even in bladder cells in a culture dish, without the control of a central nervous system.

These findings could help treat children's bedwetting and nocturia among the elderly. This discovery was recently published in the journal Nature Communications.

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2012/120502_1.htm

TRIM28: A Chromatin Regulatory Factor that Prevents T Cell Mediated Auto-Inflammatory Diseases

Assistant Professor Shunsuke Chikuma - Graduate School of Medicine

T-lymphocytes (T cells) provide powerful defense against pathogens and tumors. However, excessive activation of T cells is a cause of serious autoimmune diseases (i.e. type I diabetes, thyroiditis and rheumatoid arthritis.) If healthy , T cells remain "naïve" until they find enemies. Naïve T cells must frequently interact with self-tissues to acquire "weak" survival signals, thus there must be inhibitory mechanisms to avoid their activation against self-tissues. A dynamic change in gene expression is known to occur during the activation of T cells; however, little is known about gene regulation and the factor that prevents the activation of naïve T cells against self-tissues. TRIM28 is a chromatin regulatory factor which regulates transcription of many genes through its association with histone methyltransferases and heterochromatin proteins.

The research team led by Professor Tasuku Honjo and Assistant Prof. Shunsuke Chikuma found that Ser473 residue within TRIM28 protein, which is known to work as an on/off switch for gene regulation by TRIM28, is controlled by the T cell's survival signals at the level of phosphorylation. To understand the role of TRIM28 in T cells, the Team newly generated conditional knockout mice that lack TRIM28, specifically in T cells. These mice, when kept in pathogen free conditions, developed T cell-mediated inflammation against various organs and died younger than normal mice. Naïve T cells eventually lost their "naïveness" and differentiated into memory-like T cells that produced inflammatory cytokine IL-17 against self-tissues. At the mechanistic level, T cells without TRIM28 showed de-repression of immune-regulatory cytokines such as TGF beta, which altered systemic cytokine balance, and thus caused autoimmunity. The study demonstrated that an active gene silencing by an epigenetic factor is involved in T cell homeostasis and prevention of autoimmune diseases.

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2012/120430_1.htm

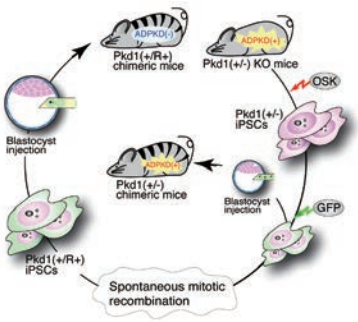
Toward Clinical Application of iPS Cells from Patients with Genetic Disorders

Genome Editing in Pluripotent Stem Cells

Associate Professor Takashi Tada - Institute for Frontier Medical Sciences

Induced pluripotent stem (iPS) cells, which are pluripotent stem cells reprogrammed from individual somatic cells, are anticipated to contribute to regenerative medicine as a cell source for generating replacement cells and tissues. In iPS cells, an epigenotype, but not a genotype, can be reprogrammed into a pluripotent cell type. Therefore, mutations that cause genetic disorders are not restored in iPS cells generated from patients. For therapeutic treatment of genetic disorders with iPS cells, development of a technique of genome editing in disease-specific iPS cells is required.

To demonstrate proof of principle for spontaneous genetic correction of disease-related mutation alleles through mitotic recombination, Associate Prof. Takashi Tada investigated a prevalent inherited disorder, autosomal dominant polycystic kidney disease (ADPKD), which is caused by genetic mutation of the PKD1 in 85% and PKD2 in 15% of cases clinically diagnosed by intrarenal cystogenesis. Large-scale screening for the PKD1 mutation in heterozygous iPS clones demonstrated that restoration of genetic mutation occurred spontaneously through mitotic cell divisions. Genetically restored iPS cells generated no intrarenal cysts, while parental (genetically mutated) iPS cells induced cystogenesis in chimeric mice. The mitotic recombination-mediated genetic correction approach will open a new path to clinical application for human iPS cells that is relevant to patient groups.



Dr. Tada believes that further development of the new technologies and understanding mechanisms involved in epigenetic reprogramming will advance the shift in iPS cell technology application from bench to bed.

www.frontier.kyoto-u.ac.jp/es03/index.html

Atomic Resolution Imaging of Organic Crystals

New Ways of Structural Analysis of Defects

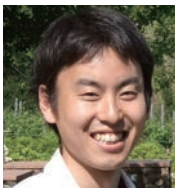
Professor Hiroki Kurata (left) and Dr. Mitsutaka Haruta (Right)- Institute for Chemical Research

The recent development of an electron microscope incorporating a spherical aberration corrector of the electron lens makes it possible to directly observe the arrangement of atomic columns in crystals. However, its use has been limited to inorganic materials because organic crystals are easily destroyed under electron irradiation. Although many researchers have tried to attain molecular images with atomic resolution, it has been difficult to visualize the atomic columns of light elements within organic molecular crystals.

Dr. Mitsutaka Haruta and Prof. Hiroki Kurata achieved the direct observation of molecular columns in organic crystals using an aberration-corrected scanning transmission electron microscope (STEM) equipped with a nano-tip field emission gun. They applied an ultra-fine electron probe with a size of less than 0.1 nm in diameter and a current of 1 pA to the observed images, and they succeeded in visualizing the contrast of light elements (C and N) together with the heavier elements (Cl and Cu) within copper hexachlorophthalocyanine ($C_{16}CuPc$) crystal. A new type of defective structure with an unexpected molecular orientation was found at the grain boundaries in the crystal after the researchers used a low-dose STEM technique. Such a structure in the grain boundary affects the properties of the thin organic films. This technology will open up new ways to analyze defective structures in organic molecular crystals. The direct observation of the grain boundary structure can also illuminate the relation between the overall properties of thin organic film transistors and the quality of the underlying crystal.

www.nature.com/srep/2012/120207/srep00252/full/srep00252.html

A New Coordination Chemistry Material for the Electrolytes of Fuel Cell Batteries



Assistant Professor Satoshi Horike - Graduate School of Engineering

Fuel cells are regarded as a new class of energy source which may contribute to the replacement of the current energy infrastructure based on fossil fuels. There are several types of fuel cell systems, and the core systems are basically composed of several materials such as electrodes and electrolytes. The discovery of new materials is necessary in order to develop fuel cells more broadly. Assistant Prof. Satoshi Horike is working on the synthesis of new solid electrolytes for fuel cells. An electrolyte is an ion conductor between two electrodes, and they require high conductivity and stability. Solid electrolytes, which show proton (H^+) conductivity at above 100°C under anhydrous (non-humid) conditions, are particularly necessary, because these materials make it possible to increase the efficiency of fuel cells, avoid the deactivation of catalysis on electrodes, and also have other advantages. There are limited numbers of anhydrous proton conductors because of the synthesis difficulties.

Assistant Prof. Horike is synthesizing the anhydrous proton conductors using coordination chemistry. Coordination bonded polymers consist of metal ions such as Zn^{2+} and Cu^{2+}, and organic ligands such as terephthalic acid and imidazole. Extended coordination bonds create crystalline polymers, and a fast proton conduction pathway can be constructed in the structures without humidity. The coordination polymers obtained have both organic and inorganic advantages: high stability, plasticity and structural diversity. Use of the coordination polymers for battery materials has not been explored, but the recent developments will encourage chemists to challenge synthesizing the ion conductive organic and inorganic hybrid materials for a new class of fuel cell system.

www.sbchem.kyoto-u.ac.jp/kitagawa-lab/research_details-e.html#3

Loss of Flight Promotes Beetle Diversification

A Novel Hypothesis for Beetle Diversification

Professor Teiji Sota - Graduate School of Science
Postdoctoral Fellow Hiroshi Ikeda - Graduate School of Science
(currently Forestry and Forest Product Research Institute)

Insects are an enormously species-rich group representing more than half of all described species. One of the most important events for insect diversification is the acquisition of flight, which facilitates the search and colonization of distant habitats, wide dispersal, and the ability to find mates and food. However, despite these advantages, many insect species of various lineages have lost their ability to fly by losing flight muscles and wings. As the maintenance of such flight apparatuses is energetically expensive, allocating that energy to survival and reproduction can be more adaptive under some conditions. The low dispersal ability of flightless species would lowers the rate of gene flow, eventually leading to differentiations among populations, and consequently resulting in higher rates of allopatric speciation. Thus, the loss of flight in various lineages could be an important factor contributing to current insect diversity.

Prof. Teiji Sota and Postdoctoral Fellow Hiroshi Ikeda tested this hypothesis in beetles (Coleoptera), which represent 40% of all insect species, using carrion beetles (Silphidae) as a model system. They demonstrated that flightless species retain higher genetic differentiation among populations and comprise a higher number of genetically distinct lineages than flight-capable species, indicating a high possibility for allopatric speciation. Furthermore, they elucidated that the speciation rate of the flightless state is higher than the flight-capable state. Moreover, a meta-analysis of 51 beetle species from 15 families revealed a higher genetic differentiation among populations in flightless compared to flight-capable species. Thus, a loss of flight may be a key event that contributes to the beetle diversification.

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2011/120201_1.htm

Individual Spider Mites Cooperate With Outsiders To Cope With Predators

Assistant Professor Shuichi Yano - Graduate School of Agriculture

Herbivorous and carnivorous mites on a leaf form deadly predator-prey interactions much like herbivorous and carnivorous mammals of the savanna. Spider mites are agricultural pests that are less than 0.5 mm in length. They live together in silk webs on leaf surfaces. Since individuals living in a group generally incur the costs of increased competition for resources among group members, group living does not pay unless it has a considerable benefit. Dr. Shuichi Yano has found that spider mites live in a group to cooperatively defend against predatory mites (e.g. Euseius sojaensis).

Spider mite webs act as refuges that most predators cannot access. However, spider mites have to build new webs every time they move to a new leaf, and are exposed to predators until the new webs are completed. During this period, the per capita predation on mites is diluted in larger groups, seemingly because webs are completed while the initial prey is eaten. An individual mite that has to build a web alone gets a free ride by joining webs established by others. On the other hand, the original inhabitant mite that has labored to build the web never kicks the newcomer mite out, but readily hosts it because it is advantageous for the hosting mite to cooperate with the newcomer against predators.

Surprisingly, this interaction is consistent even when it involves different mite species (see photo: Tetranychus urticae and Tetranychus kanzawai). Since the two species can discriminate mates for copulation, they may share webs to benefit from cooperation, while being aware that the residents are different species. It is difficult for humans to form alliances with very different people; however, it appears to be a common behavior for mites that are always faced with life-and-death decisions.

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2011/120221_3.htm

Genome Features of "Dark-fly"

Molecular Mechanisms Underlying Environmental Adaptation

Research Fellow Naoyuki Fuse - Graduate School of Science

Organisms are remarkably adapted to diverse environments by specialized metabolisms, morphologies or behaviors. How organisms come to possess adaptive traits is a fundamental question for evolutionary biology. Experimental evolution studies have provided insights into the molecular mechanisms underlying environmental adaptation, but were limited mostly to bacteria that carry a small genome. Recently, next-generation sequencing technology has enabled researchers to determine the whole genome sequences of sexual organisms and is beginning to be applied to experimental evolution studies. Research Fellow Naoyuki Fuse and his research team are studying the environmental adaptation using an unusual Drosophila melanogaster line, termed "Dark-fly," which has been maintained in constant dark conditions for 57 years (1400 generations). They have found high fecundity rates of Dark-fly in darkness, and determined the whole genome sequence of Dark-fly using a next-generation sequencer. They have identified many genomic alterations and obtained a list of the potential candidate genes involved in the Dark-fly's traits. These included genes related to detoxification and light perception. Although functional analysis of each mutation remains a future issue, they are able to present a framework for linking genomic alterations to environmental adaptation. This finding was published on the PLoS ONE Website.
(www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0033288).

www.kyoto-u.ac.jp/en/news_data/h/h1/news6/2011/120315_1.htm

Figure legend:
The Dark-fly [right] looks similar to normal fly [left], but they carry many mutations in their genome.