【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Informatics)

Title of Project : Large-Scale, Tempo-Spatial Information Gathering Mechanism over DTN-enabled Distributed Micro-modules

Teruo Higashino
(Osaka University, Graduate School of Information Science and Technology, Professor)

Research Project Number : 26220001　Researcher Number : 80173144
Research Area : Informatics
Keyword : Information Network

【Purpose and Background of the Research】

Earthquakes and disasters are unavoidable in Japan. Therefore, the information infrastructure should be robust to such emergency cases, and innovative technologies for constructing alternative infrastructure have been required. In this research project, we consider emergency situations with limited availability of cellular networks and Internet connections in urban areas, and develop a methodology to autonomously organize survived communicating nodes to realize a large-scale, tempo-spatial information gathering. One of the significant research goals is to support rescue teams' critical missions and disaster victims' evacuation planning. The mechanism employs ad-hoc collaboration between the survived infrastructure and a number of mobile nodes involving mobile base station, on-board units of vehicles and disaster victims' smartphones.

【Research Methods】

We design the following functions. (1) micro-sensing functions by available mobile nodes and stations (called micro-modules) for sensing and situation awareness, (2) DTN-based communication facilities over micro-modules (Figure 1), (3) micro-processing functions for smart understanding of situations on micro-modules and (4) autonomous tempo-spatial information gathering among micro-modules. Finally, we will prototype a platform that involves these functions (Figure 2).

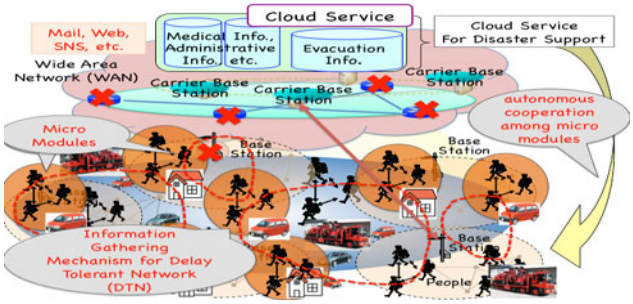

Figure 1 Information Gathering Mechanism over DTN

【Expected Research Achievements and Scientific Significance】

It is very necessary in well-populated urban areas to deploy resistant cellular network infrastructure with uninterruptible power supply (UPS). However, installation of such infrastructure is not often reasonable in rural areas. Meanwhile, recent smartphones and car navigation systems have sufficient capabilities to communicate and co-operate toward information gathering and sharing in disaster areas, but these mobile nodes are not always connected and designing self-organized computation mechanism is a primary research challenge. This motives us to realize information sharing over delay tolerant networks (DTNs).

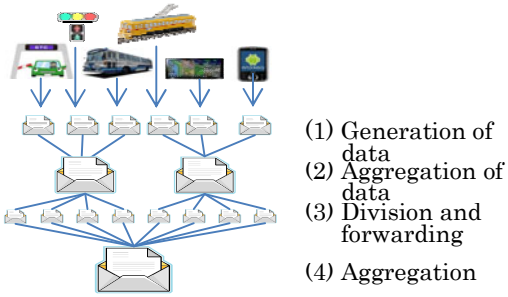

Figure 2 Tempo-Spatial Info. Gathering Mechanism

【Publications Relevant to the Project】

T. Higashino and A. Uchiyama: "A Study for Human Centric Cyber Physical System Based Sensing -Toward Safe and Secure Urban Life-", *Communications in Computer and Information Science*, vol.146, pp.61-70 (2013).
H. Yamaguchi, A. Hiromori, T. Higashino, et al.: "A Novel Scheduling Algorithm for Densely- Deployed Wireless Stations in Urban Areas", *Proc. of 16th ACM Int. Conf. on Modeling, Analysis and Simulation of Wireless and Mobile Systems (MSWiM 2013)*, pp.317-326 (2013).

【Term of Project】 FY2014-2018

【Budget Allocation】 140,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www-higashi.ist.osaka-u.ac.jp/kaken-s/

Title of Project: Advancement of CFD Applications for Manufacturing Technology to Exascale

Takayuki Aoki
(Tokyo Institute of Technology, Global Scientific Information and Computing Center, Professor)

Research Project Number : 26220002 Researcher Number : 00184036
Research Area: Informatics
Keywords: HPC, manufacturing, CFD

【Purpose and Background of the Research】

Innovative developments in CAE are necessary for Japan to become a leading manufacturing technology country in the world. To this end, it is essential to make use of large-scale simulations using ultra-high resolution computation with a leading-edge supercomputer. Due to the low memory access and node interconnection performance compared to the high performance of floating-point arithmetic computation, it is hard to achieve a high performance on current supercomputers, and this imbalance is predicted to become worse. We need to develop new numerical schemes, algorithms, and parallelization techniques suitable for next-generation exascale supercomputers to enable more efficient use of computer resources. The purpose of this project is to develop and demonstrate the efficient run of applications for exascale super computers to contribute to manufacturing. We do not focus on FLOPS performance or the computational efficiency of benchmark tests but rather attach importance to **time-to-solution**, which refers to the actual time it takes to acquire the simulation results.

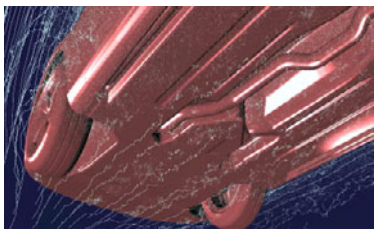

Fig.1 Aerodynamics around an automobile.

【Research Methods】

In order to improve the **time-to-solution** performance on exascale supercomputers, we are developing a novel performance model considering local memories, caches, and internode communication specifications and are exploring efficient numerical schemes and algorithms. We are also experimenting with combining various optimization techniques, such as overlapping of calculation and communication, minimizing the data transfer and have evaluated resulting application performances on a peta-scale supercomputer TSUBAME2.5/3.0

Essentially, we show the path to exascale simulation for manufacturing technology by developing prototype applications and evaluating their **time-to-solution** performances. The target applications include incompressible turbulent flow (Large-Eddy Simulation), multi-phase flow, fluid-structure interaction, phase-field simulation of material dendritic solidification in flow field, and particle-based simulation.

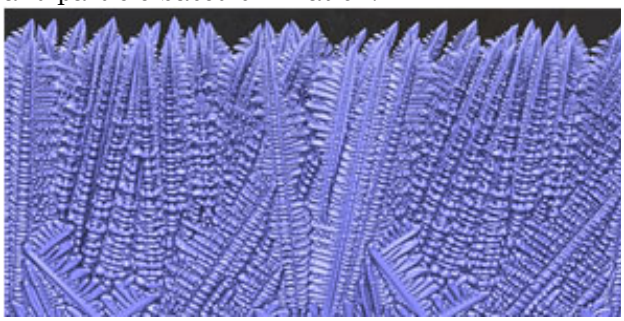

Fig.2 Phase field simulation for dendritic solidification of binary alloy on TSUBAME 2.0 (4,096 × 6,400 × 12,800 mesh, 2.0 PFLOPS in single precision).

【Expected Research Achievements and Scientific Significance】

We predict a more than 30 times reduction of the **time-to-solution** on exascale supercomputers. Another expected advantage is a reduced electronic power consumption due to shortening the **time-to-solution**. The project outcomes can be applied to other mesh/particle-based HPC applications for manufacturing technology.

【Publications Relevant to the Project】

T. Shimokawabe, T. Aoki, T. Takaki, A. Yamanaka, A. Nukada, T. Endo, N. Maruyama, S. Matsuoka: "Peta-scale Phase-Field Simulation for Dendritic Solidification on the TSUBAME2.0 Supercomputer", in Proceedings of the 2011 ACM/IEEE and Analysis, SC'11, IEEE Computer Society, Seattle, WA, USA, Nov. 15, 2011, SC'11 Technical Papers.

【Term of Project】 FY 2014-2018

【Budget Allocation】 144,900 Thousand Yen

【Homepage Address and Other Contact Information】

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【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Informatics)

Title of Project : Acquisition of Body Schema, Tool Usages and Behavioral Manner through Human Observation and Interactive Practice on Various Humanoid Series

Masayuki Inaba
(The University of Tokyo, Graduate School of Information Science and Technology, Professor)

Research Project Number : 26220003　Researcher Number : 50184726
Research Area : Informatics
Keyword : Intelligent robot

【Purpose and Background of the Research】

Considering anthropomorphic robots, i.e., humanoids, as a general form of intelligent robots, we have developed various types of humanoids ranging from small remote-brain robots to life-sized daily assistive humanoids, high-torque and high-speed humanoids and human mimetic musculoskeletal robots, while building up a common compatible intelligent robot kernel. Moreover, we have developed an observation-driven task-learning framework that enables humanoids to imitate not only motions but also intentions of humans. This framework includes an attention control system for observing people, their tools and the manipulated objects, as well as a variety of multi-level planners. Recently, we have integrated the software and hardware techniques developed so far to build a life-sized humanoid with whole-body passivity and attention inductivity.

The goal of our research is to incrementally discover a basic principle for various types of humanoid robots to obtain automatically the knowledge of how they should act, which, until now, has been given by humans manually. This process is composed of the following three stages: 1) action learning through observation of human demonstrations; 2) repeated practice with outcome evaluations provided by humans; 3) action modification through human intervention.

【Research Methods】

We have developed a system by manually constructing knowledge models of robots' bodies, environments, objects and tool usages for humanoid robots to perform various daily assistive tasks. Concurrently, we have also proposed a method for musculoskeletal robots to estimate both the intra-body space and the current state simultaneously – this is an extension of SLAM, Simultaneous Localization and Mapping, which calculates the map around a robot and its position on the map at the same time. In this research, we extend SLAM for learning tool usages and behavior patterns from human observations using iterative learning. This observation-driven method allows simultaneous estimation of tool manipulation method and target state, or human action and target reaction, using manually constructed models as a starting point. We implement this system on various humanoids and evaluate them in real environments. For the observation method, we consider the following three observer points of view: 1) first person – observer shares demonstrator's point of view; 2) second person – teacher demonstrates directly on observer; 3) third person – observer watches unconstrained movements of demonstrator.

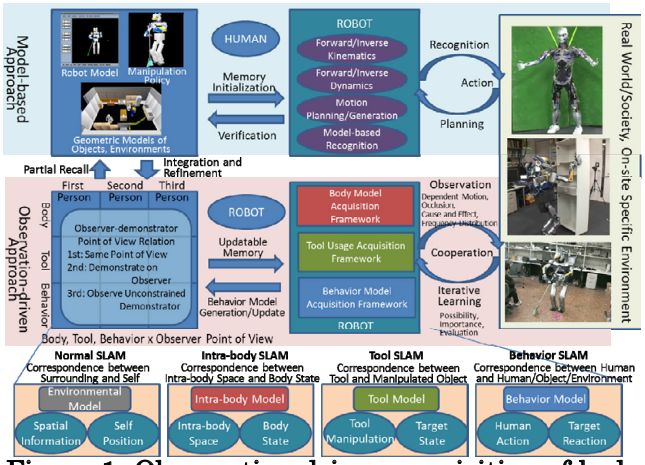

Figure 1. Observation-driven acquisition of body schema, tool usages and behavior pattern.

【Expected Research Achievements and Scientific Significance】

Our project aims to enable humanoids to acquire automatically the knowledge required for working with human tools and environments. The result establishes a robotic intelligence foundation allowing humanoids to work on behalf of humans at disaster sites, factories, farms, as well as daily environments with only on-site simple instructions given by general users.

【Publications Relevant to the Project】

Y. Nakanish, M. Inaba, et al.: "Joint Proprioception Acquisition Strategy Based on Joints-Muscles Topological Maps for Musculoskeletal Humanoids," in Proc. of ICRA2010, pp.1727--1732, 2010.

K. Okada, M. Inaba, et al.: "Task-Guided Attention Control and Visual Verification in Tea Serving by the Daily Assistive Humanoid HRP2JSK," in Proc. of IROS2008, pp.1551--1557, 2008.

【Term of Project】 FY2014-2018

【Budget Allocation】 172,000 Thousand Yen

【Homepage Address and Other Contact Information】

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Title of Project : Developmental Dynamics of Human Brain from Pattern Formation to Generation of Behaviors

Gentaro Taga
(The University of Tokyo, Graduate School of Education, Professor)

Research Project Number : 26220004　Researcher Number : 00272477
Research Area : Informatics
Keyword : Biological information, complex systems

【Purpose and Background of the Research】

Human brain imaging studies have shown the properties of the structural and functional network of the brain. However, limited information is available as to the ontogenetic mechanisms how the complex network of the human brain is constructed. The present study covers issues from the pattern formation in fetus to emergence of behavior in young infants. In particular, we focus on the interplay between spontaneous activity of the brain and the changes in structural network, and sleep state dependent mechanisms for processing external stimuli and learning. The purpose of the study is to empirically and theoretically elucidate the pattern formation of the brain in embryo, the generation of white matter tract and gyrus in fetus, the functional development of the brain in preterm-born infants, and learning-dependent changes in the functional network of the brain in young infants by means of neuroimaging techniques, behavioral measurement, and computer simulation.

【Research Methods】

(1) To reveal the mechanisms for genesis of white matter tract and folding of the cortex in embryo and fetus, magnetic resonance (MR) microscope imaging and diffusion tensor imaging (DTI) of specimens of embryos and fetuses are performed.
(2) To clarify the typical and atypical development of the functional network of the brain, near infrared spectroscopy (NIRS) is used for detecting the cerebral blood oxygenation of preterm-born infants in a neonatal intensive care unit.

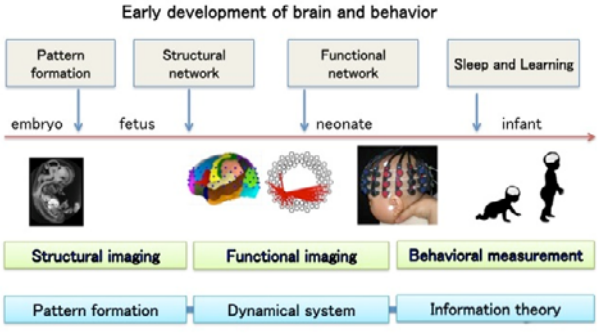

Fig1. Research strategy

(3) To understand the mechanisms underlying differentiation of sleep and awake states and functional roles of sleep for learning, spontaneous and stimulus-induced activity and learning-related changes in activity of the cortex in young infants are measured by using NIRS and EEG.
(4) Developmental processes of the brain from embryo to infant are modeled as dynamical systems and computer simulations are performed. We link the theory of pattern formation with information theory with neural networks.

【Expected Research Achievements and Scientific Significance】

The present study will provide profound insight into understanding dynamic principles for each of three different developmental processes regarding pattern formation of the brain, generation of functional networks, and transition of sleep states in relation to learning and how these processes over different time scales interact with each other. The present study will also establish a new framework for understanding pattern formation and information creation in the brain as complex systems.

【Publications Relevant to the Project】

・Taga G et al.: Phil. Trans. R. Soc. A. 369, 4495-4511, 2011
・Imai M et al.: Neuroimage 85, 272-278, 2014
・Watanabe H et al.: Human Brain Mapping 34, 543-565, 2013
・Yamada S & Takakuwa T eds.: The human embryo. InTech publisher, 2012
・Fujimoto K et al.: PLoS ONE, e2772, 2008

【Term of Project】 FY2014-2018

【Budget Allocation】 150,100 Thousand Yen

【Homepage Address and Other Contact Information】

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【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Environmental Science)

Title of Project : Synthesis of Dynamical and Chemical Descriptions on the Atmospheric Processes in the Tropical Tropopause Layer

Fumio Hasebe
(Hokkaido University, Faculty of Environmental Earth Science, Professor)

Research Project Number : 26220101　Researcher Number : 00261735
Research Area : Environmental science
Keyword : Atmospheric transport processes

【Purpose and Background of the Research】

Atmospheric minor constituents are transported into the stratosphere (ST) through the Tropical Tropopause Layer (TTL) and return to the troposphere in high latitudes. Chemistry climate models simulate gross features of the general circulation. The dehydration processes taking place in the cold TTL environment and the stratospheric age of air, however, are not well reproduced due to the lack of knowledge on underlying mechanisms.

The stratospheric processes are characterized by interactions among radiation, dynamics and chemistry. It is thus necessary to attain a synthetic view in order to understand stratospheric changes on a global scale. The purpose of this study is to synthesize views on atmospheric dynamics and chemistry by conducting comprehensive observations, analyses and numerical simulations.

【Research Methods】

Our dynamics group (SOWER) has been carrying out campaign observations focusing on the TTL dehydration. Chemistry (cryogenic air sampling) group has been working on the long-term changes in the age of air by detailed analyses of air samples collected in the ST. A field campaign is scheduled at Biak (1.17° S, 136.06° E) as collaborations of these groups together with LAPAN, Indonesia. Intensive observations are planed with launches of cryogenic samplers and aerosol samplers on board thin-film high-altitude balloons under continued operation of a ground-based Mie lidar. Special sondes such as CO_2, ozone, frostpoint hygrometers, cloud particles, and Optical Particle Counters (OPCs) with the inlet-tube heating capability are launched to get comprehensive data on TTL dehydration.

Air samples are analyzed to derive mixing ratio, isotopic ratio, and isotopomers of varieties of minor constituents to study chemical changes taking place in the air ascending in the ST. The results are compared with those observed by US-lead aircraft project (ATTREX) having been conducted in February-March 2014. The aerosol samples are analyzed by an environmental electron microscope to study the function of aerosols on ice formation.

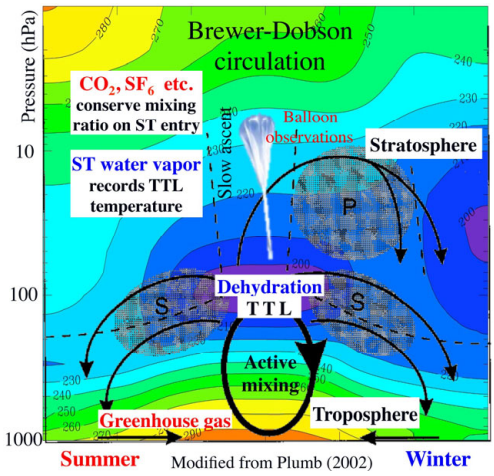

Figure 1　Scope of the study

【Expected Research Achievements and Scientific Significance】

Efficiencies of homogeneous and heterogeneous ice nucleation will be studied as a function of the degree of supersaturation and size distributions of aqueous and solid sulfate aerosols. Independent estimates of the age of air, one derived from CO_2 mixing ratio and the other from water vapor profile, will be compared to see mutual consistency and with diagnosis from chemistry climate models.

The results are brought into non-hydrostatic cloud-resolving models to improve knowledge of stratospheric change and the reliability of models.

【Publications Relevant to the Project】

Aoki *et al.*, 2003: *Tellus*, **55B**, 178-186.
Hasebe, 2012: *Tenki*, **59**(9), 788-796.
Shibata *et al.*, 2012: *J. Geophys. Res.*, **117**, D11209, doi:10.1029/2011JD017029.

【Term of Project】 FY2014-2018

【Budget Allocation】 138,400 Thousand Yen

【Homepage Address and Other Contact Information】

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Title of Project : Experimental Studies of Ocean Acidification Impact on Coastal Marine Organisms and Ecosystem

Yukihiro Nojiri
(National Institute for Environmental Studies, Center for Global Environmental Research, Principal Senior Researcher)

Research Project Number : 26220102 Researcher Number : 10150161
Research Area : Environmental science, Environmental analyses and evaluation, Environmental dynamic analysis
Keyword : Carbon dioxide, Ocean acidification, Marine calcifier, Manipulation experiment

【Purpose and Background of the Research】

The increasing atmospheric CO_2 causes ocean acidification (OA), in other words, increasing partial pressure of CO_2 (pCO_2) or decreasing of pH in surface seawater. The increasing pCO_2 in surface seawater makes decreasing of saturation state of $CaCO_3$, which in turn, decreasing easiness of calcification for marine calcifiers. In this project, impact of increasing pCO_2 in seawater on coastal marine organisms is experimentally studied in species level. Impact on ecosystem is also studied by recruitment experiment and by observation of interspecies interaction. The target is coastal marine biome around Japan.

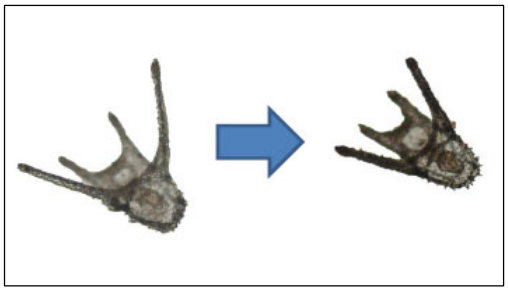

Figure 1 Seawater pCO_2 of 600 ppm (right) gives impact on arm length of sea urchin larvae, compared with pre-industrial seawater pCO_2 of 300 ppm (left).

Researches have been done mainly for marine calcifiers, such as corals, shellfishes, sea urchins and so on. Calcifiers are generally sensitive for pCO_2 change and their calcification rate decreases at high pCO_2. However, details for impacts on grows, reproduction, and abundance are not well understood even for these sensitive groups.

【Research Methods】

1. Impact of OA on various species will be done with indoor CO_2 manipulation system for small organism and larvae. The system can mimic the diurnal variation of pCO_2, which is useful for the understanding of effect of CO_2 variability.
2. Using outdoor CO_2 manipulation system, impact study of multiple species will be done simultaneously. The system will be applied for recruitment study, observing settlement of calcifiers and non-calcifiers in the overflowing seawater tanks with various pCO_2.
3. Reproduction experiment (spawning, fertilization, and hatching) of valuable fish species under various pCO_2 will be done using large volume seawater tanks.

【Expected Research Achievements and Scientific Significance】

Impact of OA on various marine organisms around Japan will be evaluated using state-of-art CO_2 manipulation systems. OA impact on coastal marine ecosystem will be evaluated under unified protocol within Japanese maritime laboratories. The experimental data will be submitted to international database. The project will contribute to collaboration with Asia-Pacific developing countries for OA research.

【Publications Relevant to the Project】

T.Onitsuka, R.Kimura, T.Ono, H.Takami, and Y.Nojiri, Effects of elevated pCO_2 on the early developmental stages of the horned turban, *Turbo cornutus*, *Marine Biology*, **161**, 1127-1138 (2014).

A.Kato, M.Hikami, N.H.Kumagai, A.Suzuki, Y.Nojiri, and K.Sakai, Negative effects of ocean acidification on two crustose coralline species using genetically homogenous samples, *Marine Environmental Research*, **94**, 1-6 (2013).

R.Suwa, Y.Nojiri, T.Ono, and Y.Shirayama, Effects of low pCO_2 conditions on sea urchin larval size, *Marine Ecology*, **34**, 443-450 (2013).

【Term of Project】 FY2014-2018

【Budget Allocation】 149,900 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.cger.nies.go.jp/ja/news/2014/140516
http://www.cger.nies.go.jp/ja/library/qa/6/6-1/qa_6-1-j

Title of Project : Multiple Omics Analysis to Understand the Species Difference in Chemical-intracellular Receptor Signaling Disruption

Hisato Iwata
(Ehime University, Center for Marine Environmental Studies, Professor)

Research Project Number : 26220103 Researcher Number : 10271652
Research Area : Environmental Science
Keyword : Toxicology, Endocrine Disrupting Substances

【Purpose and Background of the Research】

There are large interspecies differences in the sensitivity and response to chemicals. However, when extrapolating the differences in response and sensitivity of the experimental model animals to individual non-model species, we unwillingly apply the uncertainty factor with no scientific basis. Thus, to assess the risk of a variety of non-model species, it is necessary to directly measure the reactions in the species of interest. As intracellular receptors are mediators for converting chemical signals to biological signals in animal bodies, the species difference in the signaling pathway may be useful as one of the factors to account for the differential sensitivity and the diversity of responses to chemicals.

On the other hand, because of the difficulty of administration experiments and sample collection, measuring the reaction in non-model animals is not easy. As a result, the need for ecotoxicological testing has dramatically increased, but the evaluation of a majority of chemicals has remained untested. Translational science that bridges toxicology targeting model animals and environmental toxicology for wild and companion animals is lacking. Knowledge of the multiple functions of intracellular receptors is mostly gained from experiments on mice, but such findings cannot be generalized to diverse species such as birds and fish. In addition, as there is currently no tool to envisage an overview of the receptor signaling in environmental animals, this becomes a barrier to verify the diversity of effects of chemicals through the receptors.

This study intends to exhaustively explore the disruption of the system *via* the intracellular receptor signaling caused by chemical substances by constructing a platform to monitor the system in wild and companion animals. The aims are to assess the effect of chemicals on receptor-mediated signaling, and to determine the factors underlying the susceptibility that cause species differences in the receptor-mediated disruption.

【Research Methods】

We will focus on the disruption of intracellular receptor signaling by chemical exposure in environmental and experimental model animals including fish, birds, and mammals. Changes at multi-ome levels through intracellular receptors caused by chemical exposure will be measured. To identify factors underlying species differences in susceptibility at genome, gene and protein levels, we will address the following sub-themes (A-E).

A) Exposome analysis of chemical substances accumulated in wild and companion animals
B) Comprehensive analysis of the interaction of exposome and intracellular receptors
C) Multiple omics and pathway analyses of experimental model animals
D) Multiple omics and pathway analyses of environmental animals
E) Searching the factors underlying the susceptibility of intracellular receptor signaling

【Expected Research Achievements and Scientific Significance】

Putting multiple omics analysis in practice will lead to a systematic understanding of the effects of chemical exposure, and identification of biomarkers in a variety of species. In addition, advantages and limitations of the usefulness of model and environmental animals will become clear and the achievements will serve as a model for developing standardized and sophisticated ecotoxicological testing.

【Publications Relevant to the Project】

Thuruthippallil, L. M., Kubota, A., Kim, E. Y., Iwata, H. (2013): Alternative *in vitro* approach for assessing AHR-mediated CYP1A induction by dioxins in wild cormorant (*Phalacrocorax carbo*) population. *Environmental Science and Technology*, 47(12), 6656-6663.

Hirakawa, S., Imaeda, D., Nakayama, K., Udaka, M., Kim, E. Y., Kunisue, T., Ogawa, M., Matsuda, T., Matsui, S., Petrov, E. A., Batoev, V. B., Tanabe, S., Iwata, H. (2011): Integrative assessment of potential effects of dioxins and related compounds in wild Baikal seals (*Pusa sibirica*): Application of microarray and biochemical analyses. *Aquatic Toxicology*, 105(1-2), 89-99.

【Term of Project】

FY2014-2018

【Budget Allocation】

150, 000 Thousand Yen

【Homepage Address and Other Contact Information】

http://ecotoxiwata.jp/en/index.html

Title of Project : Development of a Low-energy Flat Plane-emission Panel Device Employing Single-walled Carbon Nanotubes

Kazuyuki Tohji
(Tohoku University, Graduate School of Environmental Studies, Professor)

Research Project Number : 26220104　Researcher Number : 10175474
Research Area : Environmental studies
Keyword : energy efficiency, carbon nanotubes, flat-pane emission

【Purpose and Background of the Research】

After the East Japan great earthquake disaster, we faced big challenges to save and use energy more effectively.

One means of reducing energy demand is to develop new technologies to reduce power consumption in daily life. In this study, we promote the development of a flat plane-emission lighting device employing highly purified and crystallized single-walled carbon nanotubes (SWCNTs) as a field emitter. The flat-plane lighting system is a new device with potential to contribute to low power consumption, and thus to reducing carbon dioxide emission. Furthermore, if we can use SWCNTs throughout the electrical industry, this may contribute towards a low carbon society.

【Research Methods】

We propose to develop a new device employing highly crystallized SWCNT according to the following:

(1) Construction of an electron source device as a field emitter with reduced energy consumption
(2) Construction of a flat-plane lighting device with high brightness efficiency to control ray wavelength, afterglow and phosphorescence.

Specifically for (1), we aim to construct a field electron emission source with a low driving field power below 0.5V/μm using highly purified and crystallized SWCNTs. The electron source will be fabricated with ITO application film dispersing the metallic conductive SWCNTs homogeniously by a wet coating process.

We have succeeded in making a mixture of dispersed SWCNTs by mixing metallic and semiconductor CNTs using a surfactant (Fig.1); this enabled us to fabricate a field emission cathode which showed homogenous lighting emission in a vacuum chamber (Fig. 2).

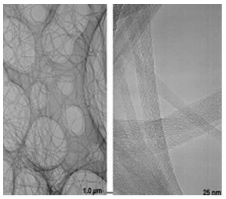

Fig. 1　TEM views of dispersed SWCNTs

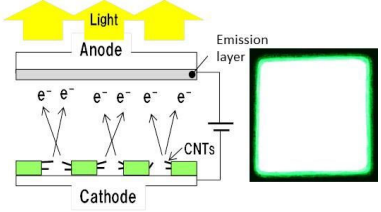

Fig. 2　Structure of cathode and emission homogeneity

In the case of (2), we aim to establish the principle of the flat plane-emission lighting device which can control wavelengths from ultraviolet to near infrared and afterglow characteristics without energy loss in electron-beam excitation.

【Expected Research Achievements and Scientific Significance】

The flat plane-emission panel device controlling phosphorescence characteristic of the lighting layer excited by electron-beam is shown in Fig. 3.

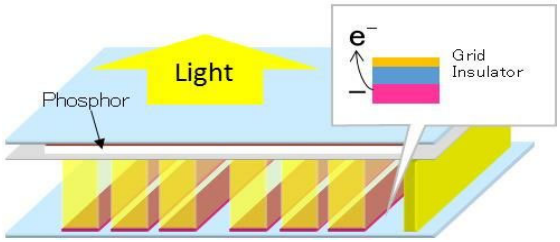

Fig. 3　Structure of a flat-plane-lighting

This lighting device is expected to reduce power consumption to 1/100 of an LED device with controlling an electron beam scan method in a plane. The carbon footprint is thus greatly reduced by our device through saving energy. In addition, the employment of highly crystallized SWCNTs is available to the establishment of assembly technologies for nanocarbon materials in electrical devices.

【Publications Relevant to the Project】

・K. Tohji et al. Nature, 383, 679 (1996).
・S. Iwata et al. J.Phys.Chem. 111, 14937-14941, (2007).
・N. Shimoi et al. Carbon, 65, 223-228(2013).

【Term of Project】 FY2014-2018

【Budget Allocation】 147,800 Thousand Yen

【Homepage Address and Other Contact Information】

http://bucky1.kankyo.tohoku.ac.jp/index.html
tohjik@mail.kankyo.tohoku.ac.jp

【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Complex Systems)

Title of Project : Basic and Applied Studies of Chrononutrition Based on Development of Functional Foods and Nutrients

Shigenobu Shibata
(Waseda University, Faculty of Science and Engineering, Professor)

Research Project Number : 26220201　Researcher Number : 10162629
Research Area : Eating habit, Food science
Keyword : Circadian, Clock gene, Nutrition, Functional food

【Purpose and Background of the Research】

Circadian 24 hr rhythm systems are important for maintaining the day/night rhythm of bodily functions, such as the sleep/wake cycle, the endocrine system, and the autonomic nervous system. Many studies have investigated the circadian clock system in mammals, which organizes physiological functions including metabolism, digestion, absorption of food, and energy expenditure. Food and/or nutrition can be a synchronizer for the circadian clock systems, and can be as potent as external light-dark signals. Recent studies have also investigated different kinds of food, frequency of consumption, and time of consumption for optimizing the body clock and ensuring healthy habits. In this study, we will try to discover new healthy foods and eating habits, based on the interaction of chronobiology and nutrition (so-called chrononutrition) (Fig.1). The development of chrononutrition based functional foods and nutrition will help us to develop health science in humans. We will prepare various types of food components; i.e. TOKUHO, Chinese traditional herbs (KAMPO), and anti-oxidant polyphenols, such as flavone derivatives.

【Research Methods】

We will investigate the effects of foods, their components, nutrition, and health promoting compounds (TOKUHO) on free-running period, phase, and amplitude of circadian rhythms using fibroblasts, peripheral organs, and PER2::LUC knock-in mice. In addition, we will apply these data to human circadian rhythms. As it is now known that feeding timing affects energy, metabolism, and obesity, a 2-3 meals-per-day schedule will be developed for PER2::LUC mice. When feeding mice functional foods is breakfast, lunch or supper most effective against obesity? Additionally, we will find the most effect functional foods for entraining circadian peripheral rhythm. In the next experiment, we want to test whether these functional food/components can normalize circadian rhythms using established rhythm disorder models such as Clock-/- and db/db-/- mice.

【Expected Research Achievements and Scientific Significance】

We will find new functional foods/components, which affect the period, amplitude or phase of circadian rhythms. Among these functional food/components, we will determine which food/components are most appropriate for breakfast, lunch, supper, and/or a nighttime snack in order to maintain a healthy body. The metabolic syndrome induced by a high fat diet, shift-work, and clock gene dysfunction will be prevented by considering the timing of food/components (chrononutrition). In addition, we will confirm these data in human experiments.

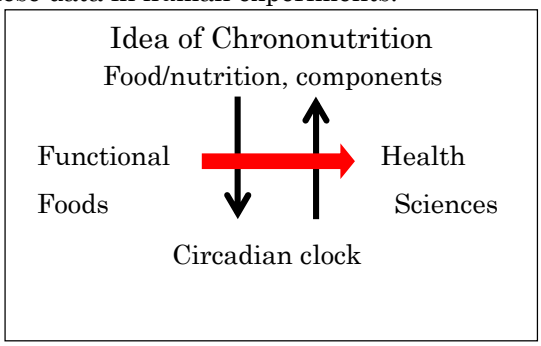

Figure 1

【Publications Relevant to the Project】

1) Tahara Y., Shibata S. Chronobiology and nutrition. Neuroscience 253,78-88, 2013
2) Tahara Y and Shibata S., et al. In vivo monitoring of peripheral circadian clocks in the mouse. In vivo monitoring of peripheral circadian clocks in the mouse. Current Biology 22(11):1029-1034, 2012.

【Term of Project】 FY2014-2018

【Budget Allocation】 89, 900 Thousand Yen

【Homepage Address and Other Contact Information】

http:// //www.waseda.jp/sem-shibatas/
shibatas@waseda.jp

Title of Project： Asian Monsoon Variability during the Past 120 Years

Jun Matsumoto
(Tokyo Metropolitan University, Graduate School of Urban Environmental Sciences, Professor)

Research Project Number：26220202　Researcher Number：80165894
Research Area： Geography
Keyword： Asian monsoon, climatic change, flood, extreme rainfall, data rescue

【Purpose and Background of the Research】

Recently, climate change issues such as global warming have become a vital societal concern. However, the climatic data utilised for climatic change studies are very limited prior to 1950 in the Asian monsoon region, except for in India, Korea, and Japan (Figure 1), and many data are stored in paper or image formats. More than 60% of world's population lives in the monsoon region of Asia. In particular, most of these people live in South and Southeast Asia and depend on agriculture, which is affected by climatic changes. To feed a growing population, the effects of climatic changes need to be minimised. Proper recognition of past climatic changes is also important for better climate prediction.

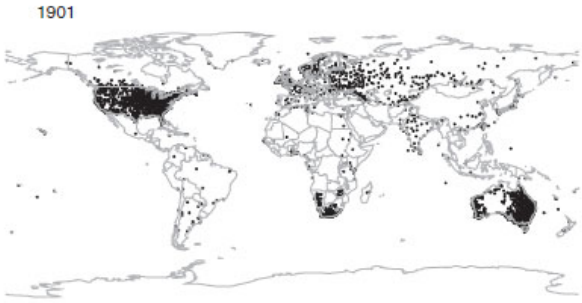

Figure 1　Distribution of stations where monthly rainfall data are available from the global GHCN-M data set for the year 1901

Our previous research found numerous climatic data stored in paper or image format. We intend to locate additional data from all over the world and digitise these as a data rescue activity. We then intend to utilise these data to reveal climatic changes in the Asian monsoon region through the past 120 years. The causes of these changes and the effects of global warming will also be analysed.

【Research Methods】

Most of the South and Southeast Asian countries became independent after World War II. Of these countries, we are planning to digitise the daily rainfall data of present-day Myanmar, Bangladesh, and Pakistan listed in "Rainfall of India" and "Daily Rainfall of India". We also plan to digitise data in China listed in the "Zi-Ka-Wei" and other data books published by Japan and data of the Spanish and American Philippines. Utilising these data, we will analyse long-term changes in rainfall intensity, onset and withdrawal dates of the rainy season, rainfall and its regional characteristics through the past 120 years. We will further discuss the causes and linkages with global warming of these variations by utilising various meteorological data, including typhoon track data.

【Expected Research Achievements and Scientific Significance】

In climate change research, past observation data are the most important first order material. Thus, we should be able to reveal long-term Asian monsoon activities by analysing the newly available data. Changes in the monsoon strongly affect Asian society, a society in which most people have primarily agricultural livelihoods. Our results will provide basic information useful for the prevention of flood disasters, water resource management, and minimising the effects of climate change on agriculture.

【Publications Relevant to the Project】

Villafuerte, M.Q.II, Matsumoto, J., et al. 2014. Long-term trends and variability of rainfall extremes in the Philippines, Atmos. Res. 137: 1–13.
Endo, N., Matsumoto, J., et al. 2009. Trends in precipitation extremes over Southeast Asia, SOLA, 5:168-171.

【Term of Project】 FY2014-2018

【Budget Allocation】 148,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.tmu.ac.jp/stafflist/data/ma/791.html

Title of Project : Mechanomedicine: Application of Mechanobiological Engineering to Regenerative and Reproductive Medicine

Keiji Naruse
(Okayama University, Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Professor)

Research Project Number : 26220203　Researcher Number : 40252233
Research Area : Complex systems
Keyword : Biological information, mechanobiology

【Purpose and Background of the Research】

Human body perceives mechanical stress. While adequate response to the mechanical stress leads to preservation of normal physiological function, inadequate response leads to pathological condition. Therefore, mechanomedicine plays important roles to unravel causes for diseases and to develop cures. In this project, we carry out translational researches on mechanobiology-based cardiac regenerative medicine and reproductive medicine, employing a theory of mechanobiology we have developed in molecular, cellular, tissue, and individual levels. We will develop innovative mechanomedical technologies, obtaining feedbacks from medical front.

【Research Methods】

This project consists of the following two components:

1. Mechanobiology-based cardiac regeneratie medicine (Figure 1)

We will develop a self-assembled vascularized cardiac tissue by applying stretch and shear stress. Effectiveness of this tissue will be examined in a preclinical study using a myocardial infarction model.

2. Mechanobiology-based reproductive medicine (Figure 2)

We will develop an artificial oviduct system replicating mechanical stress in vivo. Analysis of molecular mechanotransduction in fertilized eggs and a preclinical study will be performed at the same time.

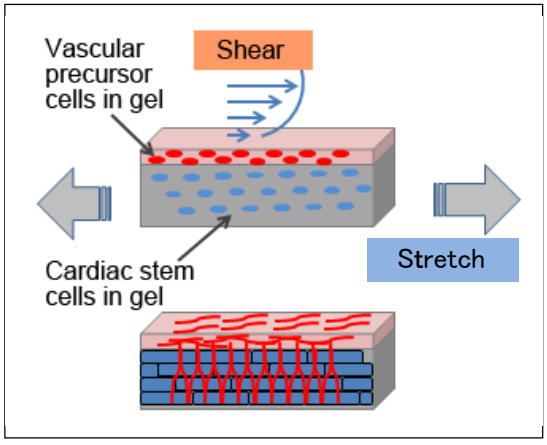

Fig. 1. Cardiac regenerative medicine

【Expected Research Achievements and Scientific Significance】

Our cardiac regenerative medicine project is feasible because it is an extension of the TICAP clinical study held in Okayama University. Development of a next-generation regenerative medicine is expected by executing the mechanobiology-based projects.

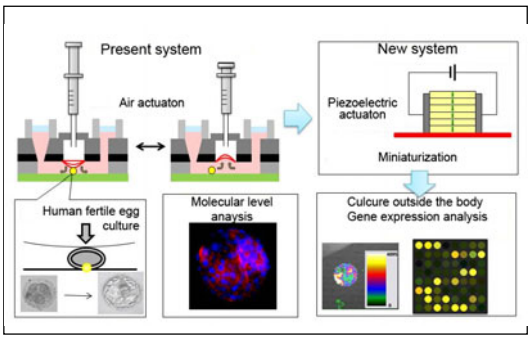

Fig. 2. Reproductive medicine

【Publications Relevant to the Project】

・TRPV2 is critical for the maintenance of cardiac structure and function in mice. Nat Commun., 29(5), 3932, 2014
・A tilting embryo culture system increases the number of high-grade human blastocysts with high-implantation competence. Reproductive BioMedicine Online., 26(3), 260-268, 2013
・Molecular identification of a eukaryotic, stretch-activated nonselective cation channel. Science 285(5429): 882-886 (1999)

【Term of Project】 FY2014-2018

【Budget Allocation】 155,200 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.okayama-u.ac.jp/user/med/phy2/
knaruse@md.okayama-u.ac.jp

Title of Project : **Generation of Minimal Peptide Catalysts Based on the Macrocyclic Scaffold**

Hiroaki Suga
(The University of Tokyo, Graduate School of Science, Professor)

Research Project Number : 26220204 Researcher Number : 00361668
Research Area : Molecular biological science
Keyword : Peptides, enzymes

【Purpose and Background of the Research】

Protein enzymes play the central role in catalyzing chemical reactions in cellular systems, and residues responsible for catalysis or/and binding to target molecules in any of enzymes are set in the three-dimensional space. However, we do not well understand how such complex proteins have evolved to the present forms. For instance, one of the shortest enzymes, 4-oxalocrotonate tautomerase yet has the length of 62 residues; therefore a chance to evolve such an enzyme is one out of 10^{80} possibility, which is extremely rare chance. On the other hand, RNA catalysts that are responsible for catalytic function before advent protein enzymes might have evolved a protein synthesis machinery, primitive ribosome. It is well known that the modern translation machinery requires many protein factors/enzymes for efficient translation. This indicates that the primitive ribosome would not be able to synthesize long peptide molecules, probably their length is limited to 20–30 residues at most.

There were many attempts to generate shorter enzymes using the secondary structural modules of alpha-helices or/and beta-sheets *in silico* or *in vitro*, so-called de novo protein design. Although there are some successes, their protein lengths are not less than 50 residues. Upon considering the elongation capability of the primitive ribosome, this would be difficult to achieve synthesis of such long peptides. Thus, the above successes do not necessarily reveal how the primitive protein enzymes evolved or what minimal length of proteins to be catalytic.

We here aim at generating libraries of short peptides with highly constrained scaffolds and seeking catalytically active molecules by the selection strategy. Each specific aims set in this program are follows:

① Construction of macrocyclic peptides that generate 3D space

② Selection of catalytically active species, pepzymes

③ Studies on the mechanisms of individual pepzymes and their structural engineering

【Research Methods】

To achieve the goals of ①–③, we will utilize our knowledge of the RaPID system devised in our laboratory to design the experiments of construction of macrocyclic libraries and selections. In the aim ①, we will construct the macrocyclic peptides constrained with a mono, bi, and tri-cyclic structures. In the aim ②, we will select *cis*-active species for four independent reactions. In the aim ③, the mechanistic studies on the individual clones for the reactions will be conducted and based on the knowledge we will engineer the *cis*-acting pepzymes to the trans-acting pepzymes.

【Expected Research Achievements and Scientific Significance】

We expect that the outcomes of this research program will provide a hint of "the origin of protein catalysts". Also, such pepzymes can be a new tool for chemical biology.

【Publications Relevant to the Project】

・K. Yamagata, Y. Goto, H. Nishimasu, J. Morimoto, R. Ishitani, N. Dohmae, N. Takeda, R. Nagai, I. Komuro, H. Suga, O. Nureki "Structural basis for potent inhibition of SIRT2 deacetylase by a macrocyclic peptide inducing dynamic structural change" **Structure** *22*, 345-352 (2014).

・Y. Tanaka, C.J. Hipolito, A.D. Maturana, K. Ito, T. Kuroda, T. Higuchi, T. Katoh, H.E. Kato, M. Hattori, K. Kumazaki, T. Tsukazaki, R. Ishitani, H. Suga*, O. Nureki "Structural basis for the drug extrusion mechanism by a MATE multidrug transporter" **Nature** *496*, 247-51 (2013).

【Term of Project】 FY2014-2018

【Budget Allocation】 140,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.chem.s.u-tokyo.ac.jp/users/bioorg/index.html
hsuga@chem.s.u-tokyo.ac.jp

【Grant-in-Aid for Scientific Research (S)】

Integrated Disciplines (Complex Systems)

Title of Project : RNA Modifications Associated with Biological Processes

Tsutomu Suzuki
(The University of Tokyo, Graduate School of Engineering, Professor)

Research Project Number : 26220205　Researcher Number : 20292782
Research Area : Complex systems
Keyword : RNA modification, RNA epigenetics, tRNA, mRNA, rRNA, ribosome

【Purpose and Background of the Research】

Higher order biological processes represented by development, differentiation, and complex metal activity are generated by sophisticated regulation of gene expression. Ill-regulated gene expression frequently results in pathological consequences. Thus, elucidating the regulatory mechanism of gene expression is required for deeper understanding of biological activities and processes, and contributes to medical and pharmaceutical applications. RNAs are decorated with various modifications introduced post-transcriptionally. Regulatory gene expression mediated by RNA modifications is also called as 'RNA epigenetics', because they are regulated spatiotemporally by expression level of RNA-modifying enzymes as well as cellular concentration of metabolites used as substrates for RNA modifications. Moreover, dysregulation of RNA modifications frequently cause human diseases, establishing a new concept of disease 'RNA modopathy'. In this project, we aim to elucidate biological processes mediated by RNA modifications and to understand molecular pathogenesis of RNA modopathies. This project comprises the following sub-projects; (1) Exploration of RNA epigenetic information and functional characterization, (2) Molecular pathogenesis of human diseases caused by aberrant RNA modifications, and (3) Crossroad between RNA epigenetics and DNA epigenetics.

【Research Methods】

Individual cellular RNAs can be isolated by our original method called 'reciprocal circulating chromatography (RCC)'. A species and site of each modification in the isolated RNA can be analyzed by a highly sensitive detection system for RNA molecules using mass spectrometry (RNA-MS). mRNA modifications will be analyzed by our new method based on RNA chemical biology. We also explore RNA-modifying enzymes, enabling us to study RNA modification biochemically as well as genetically.

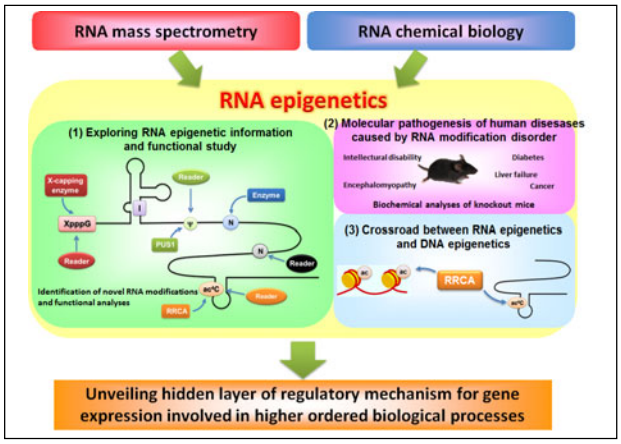

Figure 1　RNA epigenetics and biological processes

【Expected Research Achievements and Scientific Significance】

Discovery of novel RNA modifications and determination of RNA epigenetic information will reveal new regulatory mechanisms of gene expression. Identification of RNA-modifying enzymes and reader proteins that recognize RNA modifications will enable us to approach functional and physiological aspects of RNA modifications biochemically as well as genetically. Understanding of molecular pathogenesis of RNA modopathies will contribute to medical and pharmaceutical applications.

【Publications Relevant to the Project】

・Sakurai et al. A biochemical landscape of A-to-I RNA editing in the human brain transcriptome. ***Genome Res***, 24, 522-534 (2014)
・Miyauchi et al. A cyclic form of N^6-threonylcarba moyladenosine as a widely distributed tRNA hypermodification. ***Nature Chem Biol.***, 9, 105-111 (2013)
・Terasaka et al. Biogenesis of 2-agmatinylcytidine catalyzed by the dual protein and RNA kinase TiaS. ***Nature Struct Mol Biol.***, 18, 1268-1274 (2011)

【Term of Project】 FY2014-2018

【Budget Allocation】 150, 200 Thousand Yen

【Homepage Address and Other Contact Information】

http://rna.chem.t.u-tokyo.ac.jp/
ts@chembio.t.u-tokyo.ac.jp

Title of Project : Control and Analysis of Cells by Synthetic Small Molecules

Motonari Uesugi
(Kyoto University, Institute for Integrated Cell-Material Sciences, Professor)

Research Project Number : 26220206　Researcher Number : 10402926
Research Area : Complex Systems
Keyword : Chemical probes

【Purpose and Background of the Research】

This research project proposes a new way of using synthetic small molecules, in which small chemical compounds serve as tools for improving the efficacy and productivity of cell therapy by manipulating and detecting fundamental biological processes in human cells. The proposed research includes proof-of-concept experiments that develop and use small molecule tools for cell therapy. Specific goals are the discovery, understanding, and use of (i) small molecule anoikis inhibitors, (ii) small molecules that promote cardiomyogenesis, (iii) chemical probes that visualize human stem cells, (iv) small molecules that eliminate human pluripotent stem cells. Through the proposed research, we hope to open a new field of synthetic bioactive molecules.

【Research Methods】

Aim 1: Discovery, understanding, and use of small molecule anoikis inhibitors. One of the major problems encountered in cell transplantation is the low level of survival of transplanted cells due to detachment-induced apoptosis, called anoikis. The aim of this project is to design an anoikis inhibitor by mimicking fibronectin, a large 440KDa extracellular protein.

Aim 2: Discovery, understanding, and use of small molecules that promote cardiomyogenesis. Stem cell therapy requires differentiation of iPS or ES cells into specific, clinically useful cell types after expansion. The aim of this project is to understand molecular mechanism of KY02111, the most potent small molecule promoter of cardiomyogenesis that we previously discovered. We also plan to design even more potent small molecule inducers based on the molecular understanding.

Aim 3: Discovery, understanding, and use of chemical probes that visualize human stem cells. One of the current problems of stem cell therapy is the tumorigenic risk of residual undifferentiated cells. Fluorescent compounds that selectively labels residual pluripotent stem cells would permit convenient detection and purification of residual stem cells. Screening of fluorescent chemical libraries with human iPS cells, and subsequent evaluation of hit molecules, identified a fluorescent compound (Kyoto Probe 1; KP-1) that selectively labels human pluripotent stem cells. However, its selectivity is not perfect. The aim of this project is to improve its selectivity.

Aim 4: Discovery, understanding, and use of small molecules that eliminate human pluripotent stem cells. KP-1 is capable of detecting human pluripotent stem cells but not eliminating them. The aim of this project is to develop small molecules that eliminate residual pluripotent stem cells from cell mixtures for safer transplantation. We previously revealed the selectivity mechanism of KP-1. Based on its mechanism, we search for stem-cell-eliminating molecules.

【Expected Research Achievements and Scientific Significance】

Cell therapy will play an essential role in the future practice of medicine. One of the problems of cell therapy is high cost. Small molecules offer the advantage of cost-effective mass production. Success of the concept of the proposed research will eventually reduce the cost of therapy.

【Publications Relevant to the Project】

・Takemoto, N., 20 others, *Uesugi, M. Small Molecule-induced Clustering of Heparan Sulfate Promotes Cell Adhesion. ***J. Am. Chem. Soc.*** 135 (30), 11032-11039 (2013).
・Hirata, N., 23 others, *Uesugi, M. A Chemical Probe that Labels Human Pluripotent Stem Cells. ***Cell Reports*** 6(6), 1165-1174 (2014).

【Term of Project】 FY2014-2018

【Budget Allocation】 150,000 Thousand Yen

【Homepage Address and Other Contact Information】

http://www.scl.kyoto-u.ac.jp/~uesugi/

Title of Project : Elucidation of Sleep/Wakefulness Regulation through Novel Sleep-regulating Genes Identified by a Forward Genetic Approach

Masashi Yanagisawa
(University of Tsukuba, International Institute for Integrative Sleep Medicine, Director and Professor)

Research Project Number : 26220207　Researcher Number : 20202369
Research Area : Brain sciences
Keyword : Sleep

【Purpose and Background of the Research】

Although sleep is ubiquitously observed in mammalian species, the regulatory mechanism of sleep/wakefulness remains unknown. Through a large-scale forward genetic screen of randomly mutagenized mice, we have recently established 10 pedigrees showing heritable sleep abnormalities. We then have succeeded in identifying genetic mutations in two pedigrees termed *Sleepy* and *Dreamless*. In the present project, we are aiming to elucidate the neural networks regulating sleep/wakefulness behaviors through *Sleepy* gene- or *Dreamless* gene-modified mice. By examining the function of wild-type and mutant forms of the Sleepy and Dreamless proteins, we will dissect the intracellular mechanism regulating sleep. These efforts will enable us to make a paradigm-shifting breakthrough in the field of sleep research.

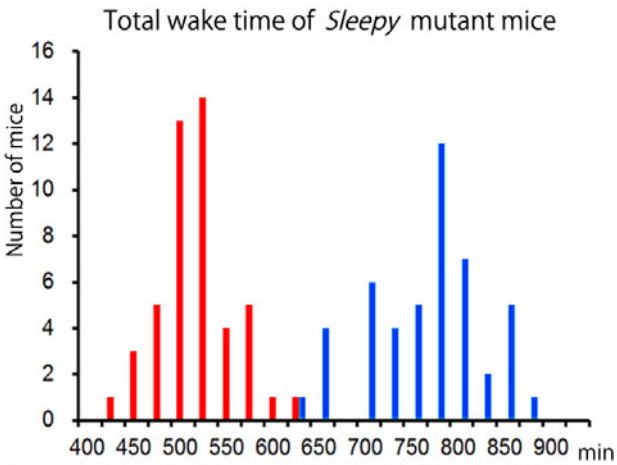

Figure 1 Histogram of total wake time of *Sleepy* mutant mice (red) and wild-type littermates (blue). *Sleepy* mutant mice show robust sleep phenotype.

【Research Methods】

To identify the brain regions or neuronal populations responsible to sleep/wakefulness abnormalities caused by the mutations in the *Sleepy* and *Dreamless* genes, we will produce gene-modified mice in which the mutant forms of genes can be activated in a Cre-dependent way. By crossing these mice with Cre driver mice or by stereotaxically injecting Cre viral vectors, we will identify neural circuits regulating sleep. Through quantitative mass spectrometry of proteins from mutant brains and electrophysiological assessment of mutant neurons, we will elucidate the intracellular signal pathway regulating sleep.

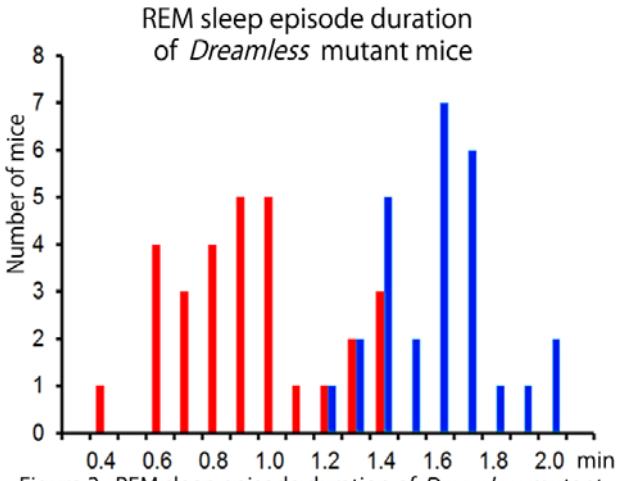

Figure 2 REM sleep episode duration of *Dreamless* mutant mice (red) were much shorter than that of wild-type littermates (blue).

【Expected Research Achievements and Scientific Significance】

By focusing on novel sleep-regulating genes, this project will elucidate the fundamental mechanism confining sleep amounts and the switching mechanism between NREM sleep and REM sleep. The project may also prove that the Sleepy and Dreamless proteins are attractive drug targets for sleep disorders.

【Publications Relevant to the Project】

・Chemelli, Yanagisawa et al. Narcolepsy in orexin knockout mice: molecular genetics of sleep regulation. Cell 98, 437-451, 1999.
・Takahashi JS, Shimomura K, Kumar V. Searching for genes underlying behavior: lessons from circadian rhythms. Science 322, 909-912, 2008.

【Term of Project】 FY2014-2018

【Budget Allocation】 150,100 Thousand Yen

【Homepage Address and Other Contact Information】 http://sleepymouse.tsukuba.ac.jp