FACULTY OF ADVANCED LIFE SCIENCE

HOKKAIDO UNIVERSITY

Education

Graduate School of Life Science

Division of Life Science

(Transdisciplinary Life Science Course) and

Division of Soft Matter

April 2022 – March 2023

Division of Life Science (Transdisciplinary Life Science Course)

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Division of Soft Matter

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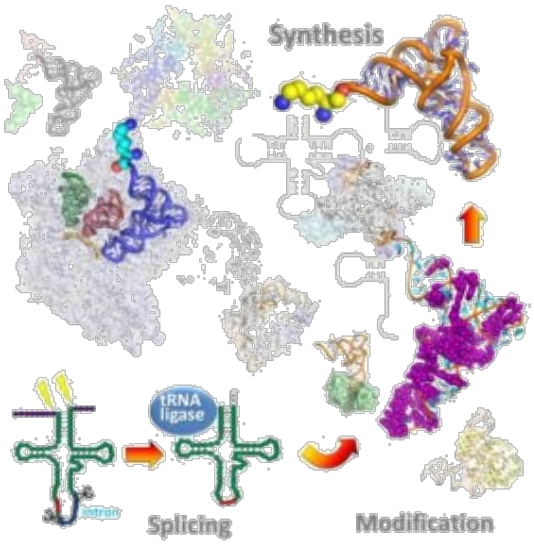
Overview

To decipher essence of biological phenomenon, we use multimodal structural methods including X-ray/neutron crystallography, cryo-EM, and NMR. Our targets are signal transduction pathways related to viral infection, cancer, and immunology. We are also interested in enzyme chemistry for natural product biosynthesis and RNA modification. We are required to study the basic knowledge of structural biology weekly such as Fourier-transform to apply for each project. The interests toward kinetics, thermodynamic analysis, and organic chemistry are also desired. To develop new methods for neutron crystallography is additionally underway.



RESEARCH THEME

Multimodal structural biological elucidation regarding proteins and nucleic acid / Structural and functional study on signal transduction pathway related to viral infection and cancer / Structural biology for enzyme chemistry / Method developments for protein crystallography

KEYWORDS

Protein, nucleic acid, enzyme, signal transduction, infection regulation, disease related factor, X-ray/neutron structural biology, cryo-EM, NMR, quantum biology, protein crystallography, computer science, protein science, biophysics

Laboratory of Structural & Biological Chemistry

Ose.toyoyuki@castor.sci.hokudai.ac.jp

Professor

OSE Toyoyuki

Selective Recent Publications

Yuma Nagano, Aoi Sugiyama, Madoka Kimoto, Takuya Wakahara, Yasuyo Noguchi, Xinxin Jiang, Shinya Saijo, Nobutaka Shimizu, Nana Yabuno, Min Yao, Paul Gooley, Gregory Moseley, Takashi Tadokoro, Katsumi Maenaka, Toyoyuki Ose, The measles virus V protein binding site to STAT2 overlaps that of IRF9, ***J. Virol.* 94**, e01169-20 (2020)

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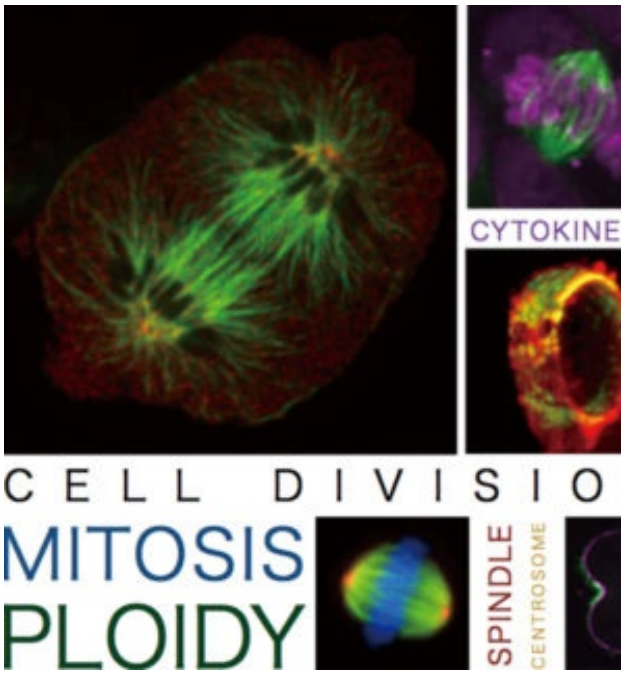
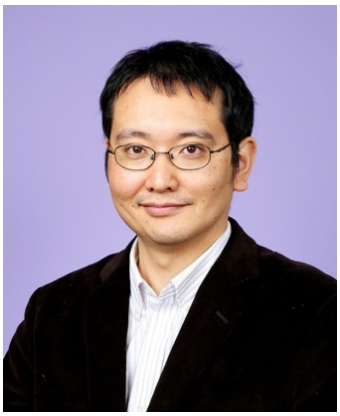
Toyoyuki Ose, Azusa Oikawa, Yukiko Nakamura, Katsumi Maenaka, Yuya Higuchi, Yuki Satoh, Shiho Fujiwara, Makoto Demura, Teruo Sone and Masakatsu Kamiya, Solution structure of an avirulence protein, AVR-Pia, from Magnaporthe oryzae, ***Biomol. NMR* 63**, 229-35 (2015)

Overview

Precisely controlled cell division is an essential process of heredity, development and homeostasis. However, it is not known how a cell equally distributes its contents, or generates force to divide itself. Using cutting-edge microscopes and cellular biological techniques, we are trying to elucidate structure and function of cellular machineries that govern elaborate regulation of cell division.





RESEARCH THEME

Cell biology

KEYWORDS

Cell division, ploidy, cytoskeleton, motor protein, self organization, cancer, aging, liver disease, microscopic analysis, biochemistry, molecular biology, cell culture, mouse model, transcriptome, mathematical modeling, compound screen

Laboratory of Cellular Machinery Science

ruehara@sci.hokudai.ac.jp

Associate Professor

UEHARA Ryota

Selective Recent Publications

Kan Yaguchi, Kimino Sato, Koya Yoshizawa, Daisuke Mikami, Kohei Yuyama, Yasuyuki Igarashi, Gabor Banhegyi, Eva Margittai, and Ryota Uehara*, Mevalonate pathway-mediated ER homeostasis is required for haploid stability in human somatic cells, ***Cell Structure and Function*** (2021) 46:1-9

Koya Yoshizawa, Kan Yaguchi, and Ryota Uehara*, Uncoupling of DNA replication and centrosome duplication cycles is a primary cause of haploid instability in mammalian somatic cells, ***Frontiers in Cell and Developmental Biology*** (2020) 8:721

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Yaguchi, K.#, Yamamoto, T.#, Shimada, M.#, Sugimoto, R.#, Nakamura, K., Ayabe, T., and Uehara, R.*, Ploidy-dependent change in cyclin D2 expression and sensitization to cdk4/6 inhibition in human somatic haploid cells, ***Biochemical and Biophysical Research Communications*** (2018)

Yaguchi, K., Yamamoto, T.#, Matsui, R.#, Tsukada, Y., Shibanuma, A., Kamimura, K., Koda, T., and Uehara, R.*, Uncoordinated centrosome cycle underlies the instability of non-diploid somatic cells in mammals, ***Journal of Cell Biology*** (2018) 217: 2463-2483

(*corresponding author; #equally contributed)

Overview

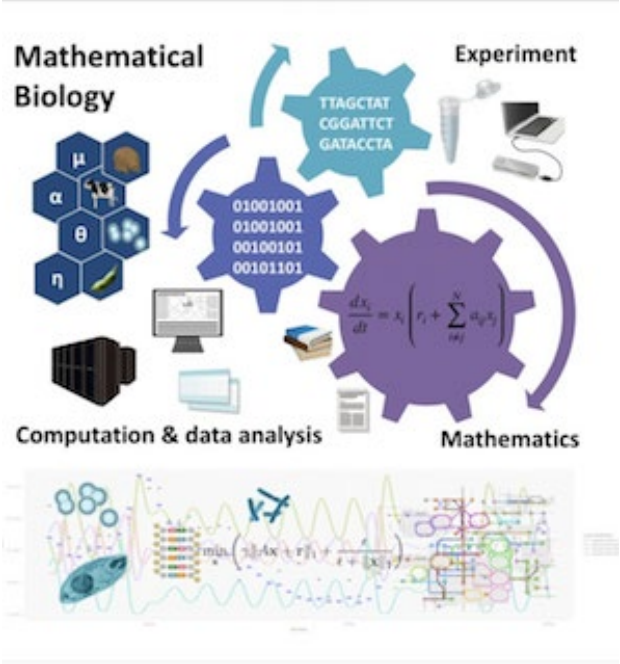
In our laboratory, mathematical and statistical models are employed to work with experimental or field biologists in order to understand biological phenomena of interest, or quantitatively characterize data. Primary research target of our laboratory is to develop ecomics and ecomimetics. The former represents a type of research to investigate a given microbial community by integrating omics data on the basis of community ecology theories and methodologies. While the latter is motivated by biomimetics to represent a type of study to extract the essence of community assembly rules from existing microbial ecosystem to construct a new artificial microbial community. Other related topics in our laboratory include omics data analysis in precision medicine or the development of novel mathematical tools for data analysis in life sciences.

RESEARCH THEME

mathematical modeling and data analysis in life science

KEYWORDS

mathematical biology, systems biology, bioinformatics, microbial ecology, precision medicine, multi-omics, mathematical modeling, machine learning, big data analysis



Laboratory of Mathematical Biology

snakaoka@sci.hokudai.ac.jp

Associate Professor

NAKAOKA Shinji

Selective Recent Publications

Shinji Nakaoka, Data-driven mathematical modeling of microbial community dynamics, ***Handbook of Statistics* Vol.39 Part A**, pp.93--130 (2018).

Yamaguchi, R., Yamanaka, T. and Liebhold, A. M. 2019. Consequences of hybridization during invasion on establishment success. ***Theoretical Ecology Springer*. 12**: 197-205.

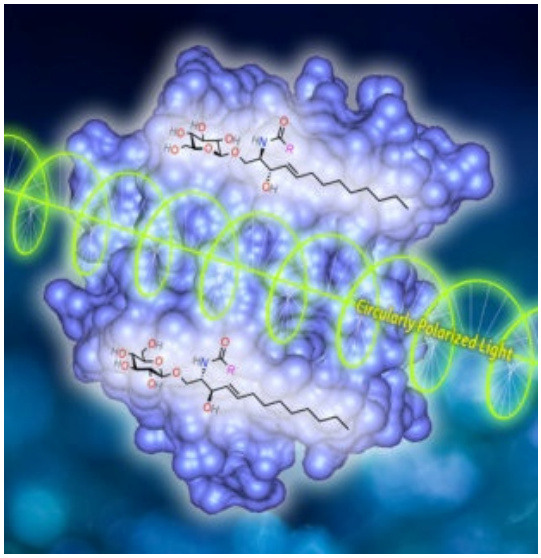
Akane Hara, Shoya Iwanami, Yusuke Ito, Tomoyuki Miura, Shinji Nakaoka, Shingo Iwami, Revealing uninfected and infected target cell dynamics from peripheral blood data in highly and less pathogenic simian/human immunodeficiency virus infected Rhesus macaque, ***Journal of Theoretical Biology*, 479**, 29-36 (2019).

Shinji Nakaoka and Keita Matsuyama, Information and statistical analysis pipeline for high-throughput RNA sequencing data, ***Springer protocol Epidermis***, pp.1-10 (2019).

Shinji Nakaoka and Keisuke H. Ota, An information and statistical analysis pipeline for microbial metagenomic sequencing data, ***Handbook of Statistics* Vol.43** (2020).

Overview

Chemical Biology is interdisciplinary science to understand and manipulate the biological system by chemistry. Our research group focuses on chiral and lipid chemical biology. Our first topic, sphingolipids, are one of main membrane components and play important roles in signal transmission and cell recognition. We create enzyme inhibitors by utilizing synthesis, lipid chemical library and natural products toward lipid related diseases, such as obesity, atopic dermatitis, Alzheimer's disease, colon cancer. We also study for identification of binding mode by photo-affinity labelling as well as MS proteomics. Our second topic is to understand and regulate the higher-order structures of biomolecules by using spectroscopy and organic chemistry. We utilize Vibrational Circular Dichroism (VCD) method, which can determine stereochemistry with/without theoretical calculation. We apply this method to various molecules including small- to medium-sized, unique functional molecules and biomacromolecules.



RESEARCH THEME

Three-dimensional structural analysis of biological molecules by vibrational circular dichroism (VCD) spectrum / Creation of disease related molecules by lipid chemical biology

KEYWORDS

Chemical Biology, Chirality, Organic Synthesis, Inhibitors, Vibrational Circular Dichroism, Helix, Lipid Mediator, Glycoconjugate, Medicinal Chemistry

Laboratory of Molecular Chemical Biology

kmonde@sci.hokudai.ac.jp

Professor

MONDE Kenji

Selective Recent Publications

Taniguchi, T., Suzuki, T., Satoh, H., Shichibu, Y., Konishi, K., Monde, K., Preparation of Carbodiimides with One-Handed Axial Chirality, ***J. Am. Chem. Soc.,* 140**, 15577-15581 (2018)

Swamy, M. M. M., Murai, Y., Ohno, Y., Jojima, K., Kihara, A., Mitsutake, S., Igarashi, Y., Yu, J., Yao, M., Suga, Y., Anetai, M., Monde, K., Structure-inspired design of a sphingolipid mimic sphingosine-1-phosphate receptor agonist from a naturally occurring sphingomyelin synthase inhibitor, ***Chem. Commun.*, 54**, 12758 - 12761, (2018)

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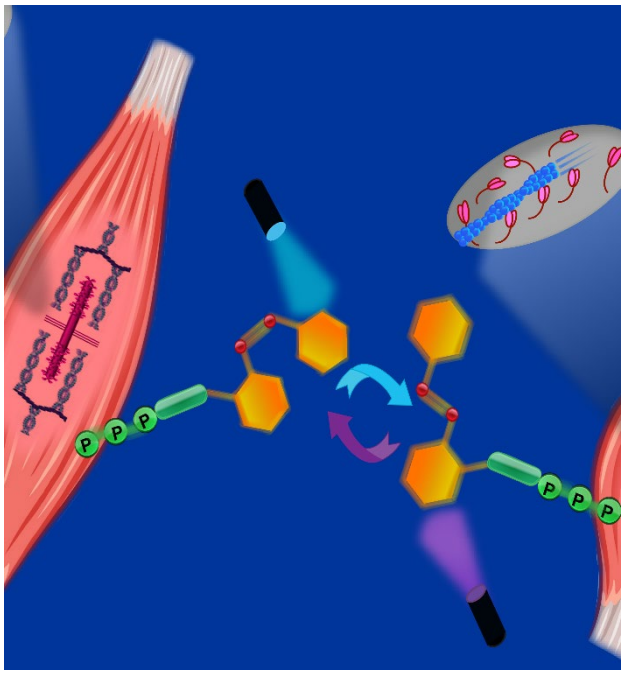
Taniguchi, T., Manai, D., Shibata, M., Itabashi, Y., Monde, K., Stereochemical Analysis of Glycerophospholipids by Vibrational Circular Dichroism., ***J. Am. Chem. Soc.,* 137**, 12191–12194 (2015)

Overview

Although living things consist of molecules as non-living things do, we smartly sense and judge surroundings and do the action by ourselves. It is still important topic in the present science to envisage what is special and what is not special in the molecular level for the outwardly special living things in comparison with non-living things. We think that constructing new artificial molecular systems with various information functions which are realized in the living systems will contribute to the deep understanding of the living things. This is the different way of the usual biology where we observe living things itself directly.



RESEARCH THEME

Creation of light-controlled molecular machines

KEYWORDS

molecular machine, motor protein, photochromic compound, azobenzene, liquid crystal, self-organization, inter-molecular interaction, organic synthesis, nano bio-machine, single molecular measurement, chirality

Laboratory of Smart Molecules

tamaoki@es.hokudai.ac.jp

Professor

TAMAOKI Nobuyuki

Selective Recent Publications

Noushaba Nusrat Mafy, Kazuya Matsuo, Shota Hiruma, Ryota Uehara and Nobuyuki Tamaoki, "Photoswitchable CENP-E inhibitor enabling the dynamic control of chromosome movement and mitotic progression", ***J. Am. Chem. Soc.*, 2020, 142(4),** 1763-1767

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Yuna Kim, Ken'ichi Aoki, Masaya Fujioka, Junji Nishii, and Nobuyuki Tamaoki, "Pressure-Induced Transition of Bisamide Substituted Diacetylene Crystals from Non-Photopolymerizable to Photopolymerizable State", ***ACS Appl. Mater. Interfaces*, 2018, 10(42)**, 36407-36414

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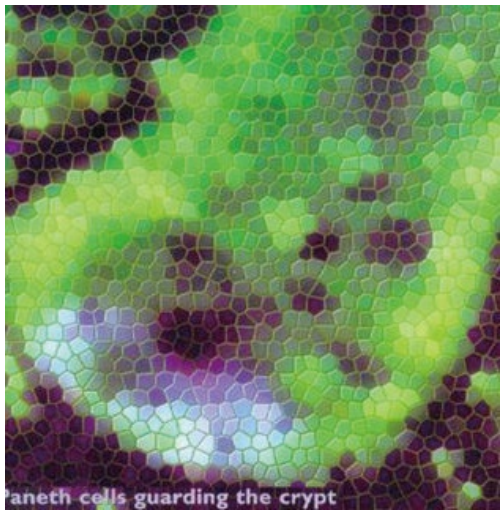
Overview

Mucosal immunity serves an important role in the host defense. One of our laboratory's goals is to understand molecular mechanisms that regulate function in the innate immune system in host defense. By focusing on antimicrobial peptides (AMPs) and cells that produce and secrete those molecules, we aim to create a new paradigm in the field of mucosal immunity. At the surface of gut epithelia, where huge microbes creates intestinal microbiota, the host must deal with both symbiotic microbes and potential pathogens that might cause infections and serious inflammation. Paneth cells in the small intestine of humans and other mammals secrete AMPs, termed α-defensins that is vital for innate enteric immunity and symbiosis. Our study contributes to maintaining health and developing new preventive medicine.



RESEARCH THEME

Regulation of innate immunity in mucosal immunity by Paneth cell alpha-defensin / Pathogenesis of inflammatory bowel disease and lifestyle diseases

KEYWORDS

innate immunity, antimicrobial peptide, mucosal immunity, intestinal epithelial cell, Paneth cell, alpha-defensin, stem cell, intestinal microbiota, intestinal environment, inflammatory bowel disease, lifestyle diseases, mental health, aging, cancer, allergy, food and medicine, preventive medicine, therapeutics

Laboratory of Innate Immunity

ayabe@sci.hokudai.ac.jp

Professor

AYABE Tokiyoshi

※Professor Ayabe will be retiring in the end of FY2022.

Selective Recent Publications

Kamioka M, Goto Y, Nakamura K, Yokoi Y, Sugimoto R, Ohira S, Kurashima Y, Umemoto S, Sato S, Kunisawa J, Takahashi Y, Domino SE, Renauld JC, Nakae S, Iwakura Y, Ernst PB, Ayabe T, Kiyono H. Intestinal commensal microbiota and cytokines regulate Fut2+ Paneth cells for gut defense. ***Proc Natl Acad Sci U.S.A.* 2022.**

Shimizu Y, Nakamura K, Kikuchi M, Ukawa S, Nakamura K, Okada E, Imae A, Nakagawa T, Yamamura R, Tamakoshi A, Ayabe T. Lower human defensin 5 in elderly people compared to middle-aged is associated with differences in the intestinal microbiota composition: the DOSANCO Health Study. ***GeroScience* 2021.**

Suzuki K, Nakamura K, Shimizu Y, Yokoi Y, Hagiwara M, Ohira S, Wang Y, Song Y, Aizawa T, Ayabe T. Decrease of alpha-defensin impairs intestinal metabolite homeostasis via dysbiosis in mouse chronic social defeat stress model. ***Sci Rep* 2021.**

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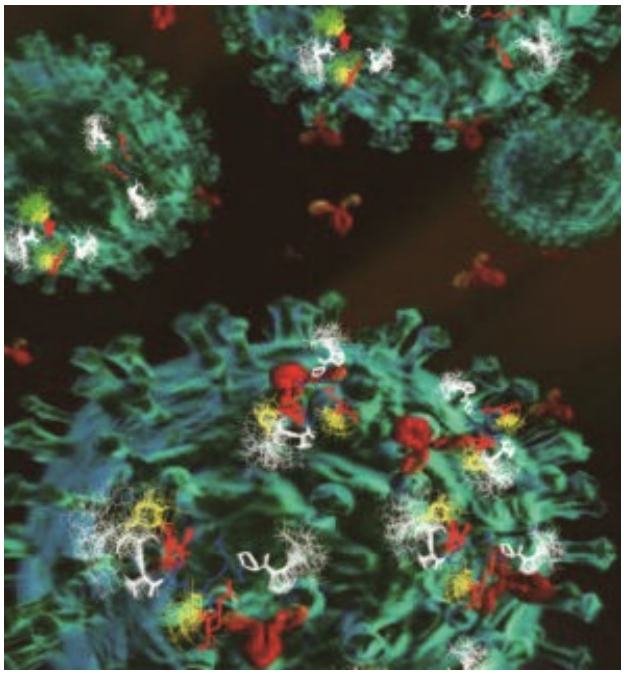
Shimizu Y, Nakamura K, Yoshii A, Yokoi Y, Kikuchi M, Shinozaki R, Nakamura S, Ohira S, Sugimoto R, Ayabe T. Paneth cell alpha-defensin misfolding correlates with dysbiosis and ileitis in Crohn's disease model mice. ***Life Science Alliance* 2020**. 3(6):e201900592.

Yokoi Y, Nakamura K, Yoneda T, Kikuchi M, Sugimoto R, Shimizu Y, Ayabe T. Paneth cell granule dynamics on secretory responses to bacterial stimuli in enteroids. ***Sci Rep* 2019**.

Overview

Toward personalized medicine, our goal is to establish a promising strategy for the rational drug discovery system from disease-relevant “dynamic epitopes” based on the specific posttranslational modification of the key glycoproteins. Our new glycotechnology platform, notably glycoblotting-based high throughput glycomics and microarray displaying robust synthetic glycopeptides library, allowed for the development of epitope-defined antibodies showing potent anti-cancer activities.
At the core of our focused library construction technology, we are continuing to innovate molecular-based life technology such as microarrays and absolute quantification technology of specific key structures in life.



RESEARCH THEME

Rational drug discovery based on a theory of dynamic epitope and innovative glycotechnology platform

KEYWORDS

Chemical biology, Medicinal chemistry, Glycomedicine, Automated glycosynthesis, Glycomics, Glycobiology, Biomarker discovery, Dynamic epitope, Glycopeptide, Antibody drug, Glycoconjugates probe, Microarray

Laboratory of Advanced Chemical Biology

shin@sci.hokudai.ac.jp

Professor

NISHIMURA Shin-Ichiro

Selective Recent Publications

Koide R., Hirane N., Kambe D., Yokoi Y., Otaki M., Nishimura S-I., “Antiadhesive nanosome elicits role of glycocalyx of tumor cell-derived exosomes in the organotropic cancer metastasis” ***Biomaterials*** **280**, 121314

Yokoi Y., Nishimura S-I. “Effect of Site-specific O-Glycosylation on the Structural Behavior of NOTCH1 Receptor Extracellular EGF-like Domains 11 and 10” ***Chem. Eur. J.*** **26**, 12363-12372 (2020)

Wakui H., Tanaka Y., Ose T., Matsumoto I., Kato K., Yao M., Tachibana T., Sato M., Naruchi K., García-Martín F., Hinou H., Nishimura S-I. “A straightforward approach to antibodies recognising cancer specific glycopeptidic neoepitopes” ***Chem. Sci.*** 11, 4999-5006 (2020)

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Koide R., Nishimura S-I., “Antiadhesive nanosomes facilitate targeting of lysosomal GlcNAc salvage pathway through derailed cancer endocytosis” ***Angew. Chem. Int. Ed*****. 58**, 14513-14518 (2019)

Somovilla V.J., Bermeijo I.A., Albuquerque I.S., Martínez-S. N., Castro-Lopez J., Garcia-Martin F., Companon I.., Hinou H., Nishimura S-I., Jimenez-Barbero J., Asensio J.L, Avenoza G., Busto J.H., Hurtado-Guerrero. R., Peregrina J.M., Bernardes G.J.L., Corzana F., “The use of fluoroproline in MUC1 antigen enables efficient detection of antibodies in patients with prostate cancer”, ***J. Am. Chem. Soc.*** **129**, 18255-18261 (2017)

Overview

Gene functions and mechanisms of disease process, at the level of live organisms, can be analyzed by using model animals. We create genetically modified experimental model mice to investigate genetic diseases.

RESEARCH THEME

Development of the treatment for genetic disorders based on the use of model animals

KEYWORDS

neurodegenerative disease, poly-glutamine disease, autophagy, model mice, embryonic engineering

Laboratory of Embryonic and Genetic Engineering

t-koda@sci.hokudai.ac.jp

Professor

KODA Toshiaki

Selective Recent Publications

Nobutaka Hanagata, Taro Takemura, Keiko Kamimura, Toshiaki Koda, Effect of immunosuppressants on a mouse model of osteogenesis imperfecta type V harboring a heterozygous Ifitm5 c.-14C > T mutation., ***Sci. Rep.*** **10(1)**: 21197 (2020)

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Kan Yaguchi, Takahiro Yamamoto, Ryo Matsui, Yuki Tsukada, Atsuko Shibanuma, Keiko Kamimura, Toshiaki Koda, Ryota Uehara, Uncoordinated centrosome cycle underlies the instability of non-diploid somatic cells in mammals., ***J. Cell Biol.*** **217(7)**: 2463-2483 (2018)

Shigeko Kijimoto-Ochiai, Tokuko Matsumoto-Mizuno, Daisuke Kamimura, Masaaki Murakami, Miwako Kobayashi, Ichiro Matsuoka, Hiroshi Ochiai, Hideharu Ishida, Makoto Kiso, Keiko Kamimura, Toshiaki Koda, Existence of NEU1 sialidase on mouse thymocytes whose natural substrate is CD5., ***Glycobiology*** **28**, 306-317 (2018)

Overview

A main focus of my research is to elucidate the structural principle for the biological activities of functional proteins, especially which can be utilized for bioproduction and bioprocessing of the novel biomaterials. By using X-ray crystallography, we have analyzed the 3D structures of functional proteins including various antifreeze proteins and industrial enzymes. Based on detailed insights of the 3D structure of functional proteins, combined with other biochemical and molecular biological study, we have clarified the molecular mechanism of their function to product modified proteins with advanced properties.

RESEARCH THEME

Characterization and improvement of industrial proteins

KEYWORDS

structural biology, antifreeze protein, industrial protein, industrial enzyme

Laboratory of Biomolecular Adaptation Science

h.kondo@aist.go.jp

Visiting Professor

KONDO Hidemasa

Selective Recent Publications

Okumura, S.; Hirano, Y.; Komatsu, Y. Stable Duplex-Linked Antisense Targeting MiR-148a Inhibits Breast Cancer Cell Proliferation. ***Sci. Rep.*** **11**, 11467 (2021).

Khan, N.M.M.U., Arai, T., Tsuda, S., and Kondo, H., Characterization of microbialantifreeze protein with intermediate activity suggests that a bound-water network is essential for hyperactivity. ***Scientific Reports*** **11,** 5971 (2021).

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Arai, T., Fukami, D., Hoshino, T., Kondo, H., and Tsuda, S.: Ice-binding proteins from the fungus Antarctomyces psychrotropicus possibly originate from two different bacteria through horizontal gene transfer. ***FEBS J.*** **(2019) 286**, 5, 946-962.

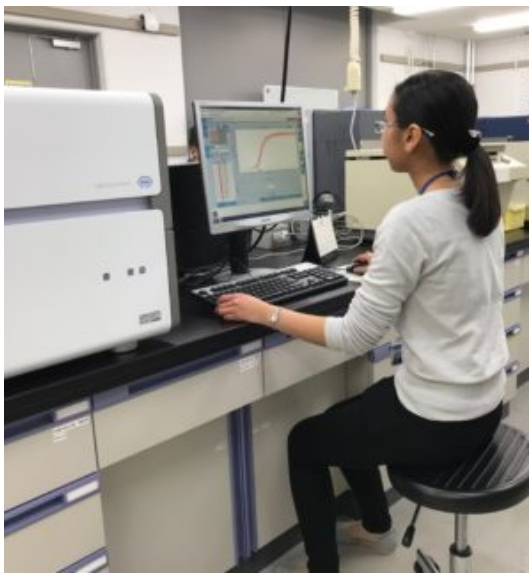
Mahatabuddin, S., Fukami, D., Arai,T., Nishimiya, Y., Shimizu, R., Shibazaki, C., Kondo, H., Adachi, M., and Tsuda, S.: Polypentagonal ice-like water networks emerge solely in an activity-improved variant of ice-binding protein. Proc. ***Natl. Acad. Sci. USA*****,115** (21), 5456-5461 (2018).

Mahatabuddin, S., Hanada, Y., Nishimiya, Y., Miura, A., Kondo, H., Davies, PL., and Tsuda, S. Concentration-dependent oligomerization of an alpha-helical antifreeze polypeptide makes it hyperactive. ***Sci. Rep.*** **(2017), 7**, 42501.

Overview

The National Institute for Materials Science (NIMS) and the Graduate School of Life Science of the Hokkaido University have established a joint Doctoral Program in the Field of Frontier Biomaterials Science. The laboratory is located in NIMS in Tsukuba city, Ibaraki.

When pathogens infect us, our cells recognize DNA or RNA molecules of bacteria and viruses and the immune system is activated. With attention to this biological immune system, we are developing nucleic acid-based nanomedical molecules, and also nanoparticle-conjugated nanomedicines, and applying these to the treatment of infectious diseases and allergies.



RESEARCH THEME

Development of nucleic acid nanomedicines for immunomodulation / Study on mechanism of osteogenesis imperfecta type V (OI-V) and the treatment of OI-V by nucleic acid nanomedicines / Molecular mechanism on cytotoxicity of nanoparticles / Control of cellular function on material surface

KEYWORDS

Nanomedicine, nanobiotechnology, nucleic acid drug, immune system, comprehensive gene analysis, nano particles, DNA delivery, nanotoxicity

Laboratory of Frontier Biomaterials Science

HANAGATA.Nobutaka@nims.go.jp

Visiting Professor

HANAGATA Nobutaka

Selective Recent Publications

Anh Thi Tram Tu, Kazuaki Hoshi, Miwako Shobo, Tomohiko Yamazaki. G-Quadruplex-Based CpG Oligodeoxynucleotide/DOTAP Complex Strongly Stimulates Immunity in CpG Motif-Specific and Loop-Length-Dependent Manners. Nanomedicine: ***Nanotechnology, Biology and Medicine*** **40** (2022) 102508

Fika Ayu Safitri, Anh Thi Tram Tu, Kazuaki Hoshi, Miwako Shobo, Arief Budi Witarto, Sony Heru Sumarsono, Ernawati Arifin Giri-Rachman, Kaori Tsukakoshi, Kazunori Ikebukuro, Tomohiko Yamazaki. Enhancement of the Immunostimulatory Effect of Phosphodiester CpG Oligodeoxynucleotides by an Antiparallel Guanine-Quadruplex Structural Scaffold. ***Biomolecules*** **11** [11] (2021) 1617

Hongxin Wang, Han Zhang, Bo Da, Dabao Lu, Ryo Tamura, Kenta Goto, Ikumu Watanabe, Daisuke Fujita, Nobutaka Hanagata, Junko Kano, Tomoki Nakagawa, and Masayuki Noguchi. Mechanics biomarker for cancer cells unidentifiable through morphology and elastic modulus. ***Nano Letter*** **21** (2021) 1538-1545

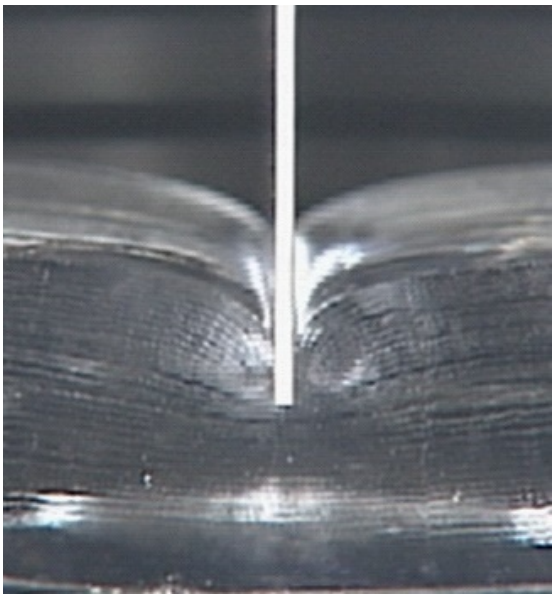
Anh Thi Tram Tu, Kazuaki Hoshi, Kazunori Ikebukuro, Nobutaka Hanagata, Tomohiko Yamazaki. Monomeric G-Quadruplex-Based CpG Oligodeoxynucleotides as Potent Toll-Like Receptor 9 Agonists. ***Biomacromolecules.*** **21** [9] (2020) 3644-3657

Shanmugavel Chinnathambi, Nobutaka Hanagata, Tomohiko Yamazaki, Naoto Shirahata. Nano-Bio Interaction between Blood Plasma Proteins and Water-Soluble Silicon Quantum Dots with Enabled Cellular Uptake and Minimal Cytotoxicity. ***Nanomaterials*****. 10** [11] (2020) 2250

Overview

Gels are biotissue-like soft, wet and deformable materials. The aim of our study is to create novel tough and functional gels, to investigate their toughening or functionalizing mechanism, and to apply our novel gels as artificial bio-substituting materials. Our research also aims to generalize the principles of novel tough gel development for other types of soft materials towards application in industrial fields.

Selected topics are listed below: 1) design and fabrication of tough gels and elastomers 2) Investigation of fracture mechanics and dynamics of soft materials 3) Synthesis of gels with low surface friction and investigation of their lubrication mechanism 4) Fabrication of tough and soft composites and investigation of the toughening mechanism 5) Mechanochemistry of gels 6) Fabrication of soft ceramics through biomineralization 7) Biomaterials and artificial cartilage.



RESEARCH THEME

Creation and application of polymer gels with excellent functions inspired by biological structures

KEYWORDS

Soft & wet matter, polymer gel, double network gel, gel more durable than metal, self-healing gel, self-growing gel, bonding gel, thermal toughening gel, low friction gel, super lubricating gel, color changing gel , Sea glue gel, artificial cartilage, cell scaffold gel

Laboratory of Soft & Wet Matter

gong@sci.hokudai.ac.jp

Professor

GONG Jian Ping

Selective Recent Publications

H. Fan, J. P. Gong, "Fabrication of Bioinspired Hydrogels: Challenges and Opportunities," ***Macromolecules,* 53(8)**, 2769-2782 (2020).

C. Yu, H. Guo, K. Cui, X. Li, Y. N. Ye, T. Kurokawa, J. P. Gong, "Hydrogels as Dynamic Memory with Forgetting Ability," ***Proceedings of the National Academy of Sciences*, 117**(32), 18962-18968 (2020).

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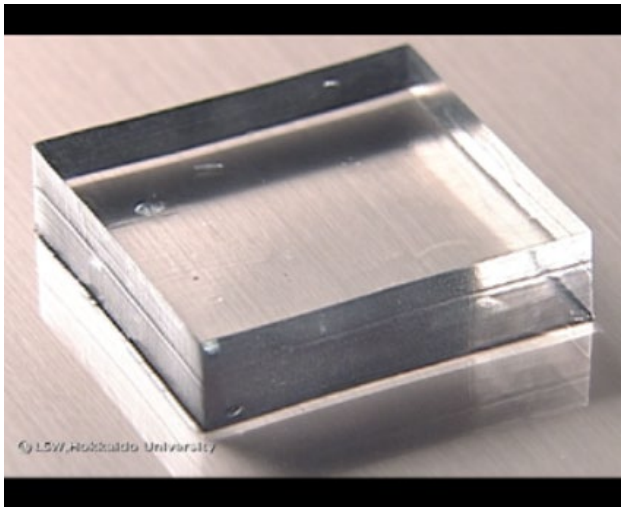
P. Rao, T. L. Sun, L. Chen, R. Takahashi, G. Shinohara, H. Guo, D. R. King, T. Kurokawa, J. P. Gong, "Tough Hydrogels with Fast, Strong, and Reversible Underwater Adhesion Based on a Multi-Scale Design", ***Advanced Materials*, 30(32)**, 1801884 (2018).

Overview

We create functional polymer hydrogels, understand the mechanism of their functions, and use the knowledge obtained as a guideline for designing new functional gels. By repeating the cycle of creating even more highly functional materials, we can enhance the usefulness of polymer gel materials as if climbing a spiral staircase. In the middle of the spiral staircase, some technologies lead to biomaterials and new physical property measurement methods, which lead to the exit for "real world" applications.



RESEARCH THEME

Understanding Friction Using Gels as a Model / Analysis of the Internal Structure of Gels by Donnan Potential Measurements / Creation of Soft Composites with Unique Mechanical Properties / Biomaterials Investigation and Development

KEYWORDS

Polymer gel, Double network gel, Friction of gel, Artificial cartilage, Cell culture substrate, Soft composite material, Adsorption and adhesion, Donnan potential

Laboratory of Transformational Soft Matter

kurokawa@sci.hokudai.ac.jp

Professor

KUROKAWA Takayuki

Selective Recent Publications

S. Hirayama, T. Kurokawa*, J. P. Gong, "Non-Linear Rheological Study of Hydrogel Sliding Friction in Water and Concentrated Hyaluronan Solution," ***Tribology International*, 147**, 106270 (7 pages) (2020).

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D. R. King*‡, T. Okumura‡, R. Takahashi, T. Kurokawa, Gong, J. P.* "Macroscale Double Networks: Design Criteria for Optimizing Strength and Toughness." ***ACS Applied Materials & Interfaces*. 2019, 11** (38): 35343-35353.

Overview

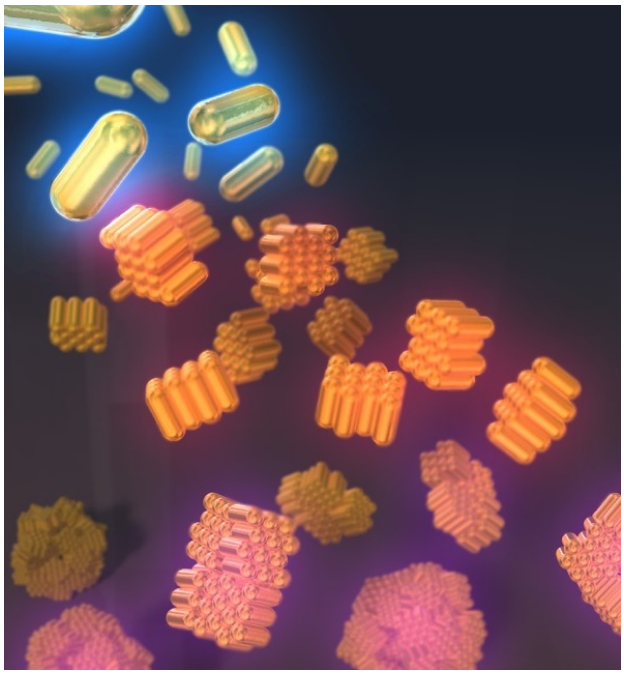
Bio organisms are capable of efficient energy transformation, selective synthesis of biomolecules and interactive information processing. All these processes are based on effective molecular recognition at highly organized supramolecular assemblies. This research group is concerned with the construction of hierarchical molecular devices by the combination of nanosize molecular assemblies with micro size structures derived from dissipative processes. The following themes are in progress.
1) Development of novel drug delivery system using nanostructures, 2) Control of self-assembly of nanoparticles and creation of functions, 3) Development of supersensitive gel based plasmonic biosensors, 4) Development of high efficient nanoparticle vaccine

RESEARCH THEME

Development of self-assembled nanoparticles for bioengineering applications

KEYWORDS

Self-organization, self-assembly, functional device, biosensor, DNA, protein, biomolecule, cell, molecular recognition, drug delivery system, vaccine, gold nanoparticle, surface plasmon, stimuli- responsivity, capsule



Laboratory of Molecular Device

ijiro@poly.es.hokudai.ac.jp

Professor

IJIRO Kuniharu

Selective Recent Publications

Kun Xiong, Hideyuki Mitomo, Xueming Su, Yier Shi, Yusuke Yonamine, Shin-ichiro Sato and Kuniharu Ijiro, "Molecular configuration-mediated thermo-responsiveness in oligo(ethylene glycol) derivatives attached on gold nanoparticles", ***Nanoscale Advances*****, 3**, 3762-3769 (2021). (Front Cover)

Satoshi Nakamura, Hideyuki Mitomo, Yu Sekizawa, Takeshi Higuchi, Yasutaka Matsuo, Hiroshi Jinnai, Kuniharu Ijiro, "Strategy for Finely Aligned Gold Nanorod Arrays using Polymer Brushes as a Template", ***Langmuir,*** **36**, 3590-3599 (2020). (Front Cover)

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Taiyu Tazaki, Koshiro Tabata, Akira Ainai, Yuki Ohara, Shintaro Kobayashi, Takafumi Ninomiya, Yasuko Orba, Hideyuki Mitomo, Tetsuo Nakano, Hideki Hasegawa, Kuniharu Ijiro, Hirofumi Sawa, Tadaki Suzuki and Kenichi Niikura, "Shape-dependent adjuvanticity of nanoparticle-conjugated RNA adjuvants for intranasal inactivated influenza vaccines", ***RSC Adv.,*** **8**, 16527-16536 (2018).

Ryo Iida, Hideyuki Mitomo, Kenichi Niikura, Yasutaka Matsuo, and Kuniharu Ijiro, "Two-step assembly of thermoresponsive gold nanorods coated with a single kind of ligand", ***Small*****, 14,** 1704230 (2018). (Inside Front Cover)

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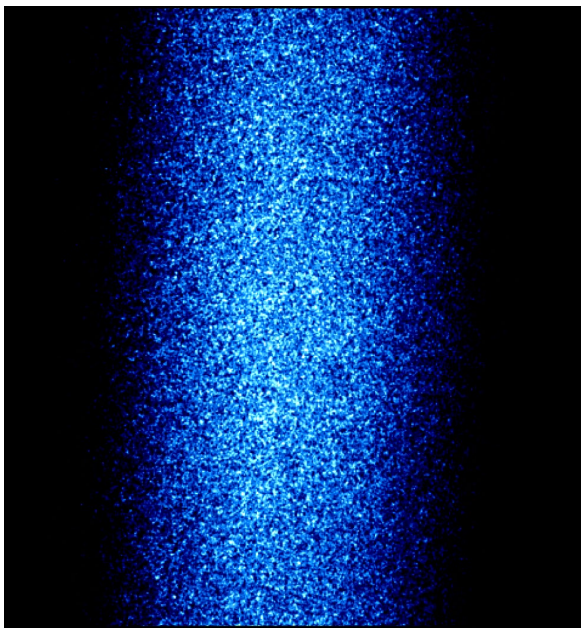
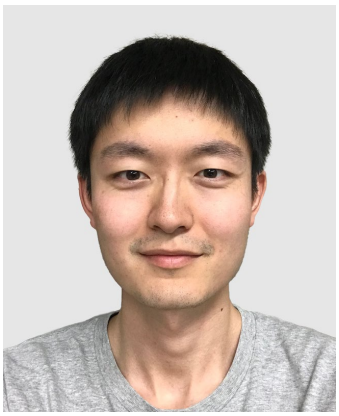
Overview

We are engaged in understanding the polymer structure and dynamics of soft materials, including polymer solutions, gels, elastomers, micelles, colloids, and cells. We employ a combination of scattering techniques (neutron, X-ray, and light), rheological measurements, and spectroscopy to reveal the underlying mechanism between nanostructures and physical properties. We also develop new high-performance soft materials using the revealed mechanism from the structure analysis.





RESEARCH THEME

Elucidation of correlation between the structure and the physical properties of soft matter / Development of high-performance soft materials / Structure and dynamics analysis using light, X-ray, and neutron scattering

KEYWORDS

Polymer solution, polymer gel, rubber, nanostructure, molecular dynamics, light scattering, X-ray scattering, neutron scattering, Raman spectroscopy, rheology, polymer synthesis, polymer physics

Laboratory of Soft Matter Structure & Physics

x.li@sci.hokudai.ac.jp

Associate Professor

LI Xiang

Selective Recent Publications

Y. Tsuji, S. Nakagawa, C. I. Gupit, M. Ohira, M. Shibayama, and X. Li, Selective Doping of Positive and Negative Spatial Defects into Polymer Gels by Tuning the Pregel Packing Conditions of Star Polymers, ***Macromolecules* 53**, 7537 (2020).

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Overview

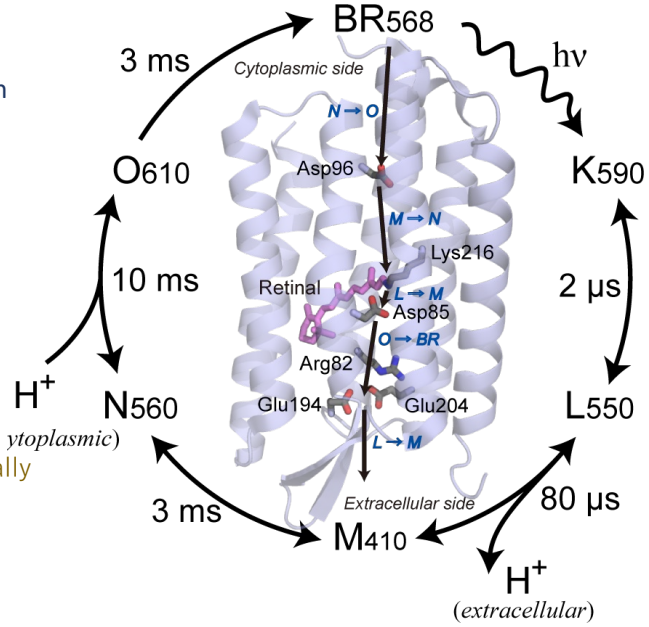
Organisms express photoactive proteins to utilize sunlight for cellular metabolic processes. Rhodopsins are the most ubiquitous photoactive proteins and have diverse functions, such as photosensors, ion pumps, and ion channels. We are analyzing their essential mechanisms for light-energy utilization and functional differentiation. Our goal is to develop the novel photoactive proteins applicable to environmental and medical problems.

RESEARCH THEME

Elucidation of the light-energy conversion mechanisms of photoactive proteins / Development of photoactive systems by featuring functionally modified photoactive proteins

KEYWORDS

Photoactive proteins, photobiology, rhodopsin, optogenetics, laboratory evolution, membrane protein, ion pump, membrane transport, transporter, flash photolysis



Laboratory of Biological Information Analysis Science

demura@sci.hokudai.ac.jp

Professor

DEMURA Makoto

Selective Recent Publications

Sasaki, S., Tamogami, J., Nishiya, K., Demura, M., Kikukawa, T., Replaceability of Schiff base proton donors in light-driven proton pump rhodopsins, ***J. Biol. Chem.* 297**, 101013 (2021)

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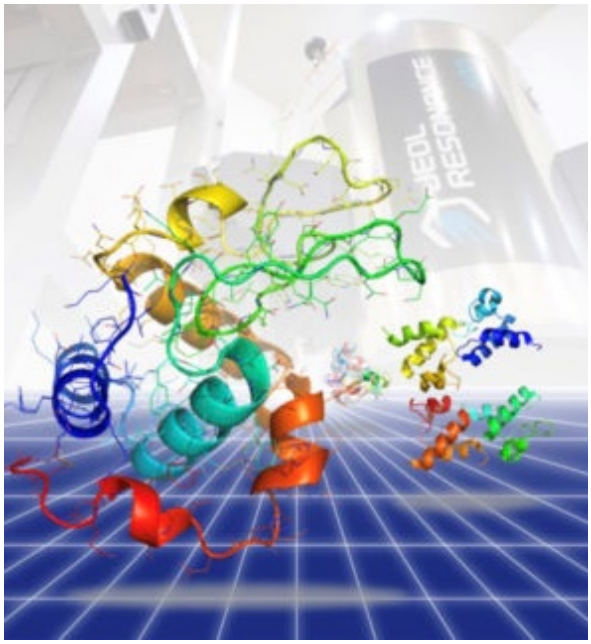
Overview

Our main research targets are NMR analysis of proteins and peptides, development of novel production methods of heterologous proteins and peptides. Our final goals of the research are to create the artificial proteins with complete control. We also utilize NMR for metabolomics researches. Our group are conducting research on NMR metabolomics which comprehensively analyzes metabolites of living organisms in various body fluids related to health and diseases.



RESEARCH THEME

Studies on production methods for recombinant proteins and peptides / Research on proteins and peptides using NMR spectroscopy and genetic engineering / NMR metabolomics

KEYWORDS

protein science, structural biology, protein engineering, NMR, metabolome, biomarker research, biological defense, innate immunity, antimicrobial peptides, allergen, cytokines, microbiological control

Laboratory of Protein Science

aizawa@sci.hokudai.ac.jp

Professor

AIZAWA Tomoyasu

Selective Recent Publications

Komatsu Y, Shimizu Y, Yamano M, Kikuchi M, Nakamura K, Ayabe T, Aizawa T., Disease Progression-Associated Alterations in Fecal Metabolites in SAMP1/YitFc Mice, a Crohn's Disease Model., ***Metabolomics*, 16**, 48 (2020)

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Overview

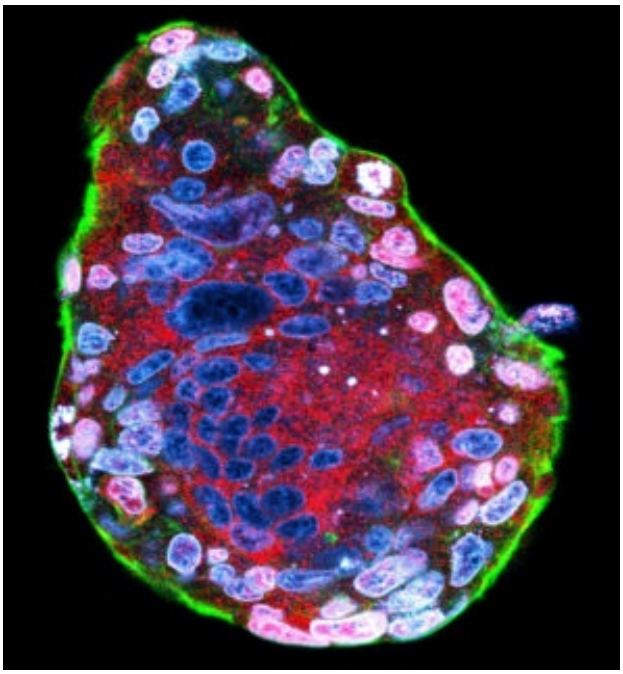
We are interested in the behaviors of cells and tissues, especially collective cell migration, 3D morphogenesis, and tissue construction. To understand these phenomena, we utilize soft biomaterials (e.g. collagen gels, Matrigels) for cell culture to mimic biological environments and analyze the behaviors with approaches of both molecular biology and mechanobiology. Furthermore, we are using extracellular matrices of different stiffness and investigating the mechanism of cancer progression induced by substrate stiffening. We are able to contribute to improve regenerative medicine and cancer therapy with our research approaches.

RESEARCH THEME

Collective cell migration in 3D morphogenesis Cancer metastasis Structures and physical properties of polymeric materials and connective tissues

KEYWORDS

Cell Mechanics, Collective Cell Behavior, 3D Morphogenesis, Cancer Invasion, Atomic Force Microscopy



Laboratory of Cell Dynamics

haga@sci.hokudai.ac.jp

Professor

HAGA Hisashi

Selective Recent Publications

H. Oyama, A. Nukuda, S. Ishihara, and H. Haga: Soft Surfaces Promote Astrocytic Differentiation of Mouse Embryonic Neural Stem Cells via Dephosphorylation of MRLC in the Absence of Serum, ***Scientific Reports*****, 11**, 19574, 1-11 (2021).

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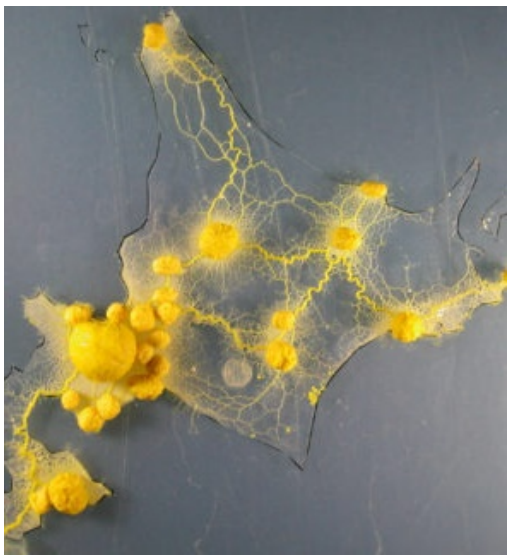
Akiyama, T. Sushida, S. Ishida, and H. Haga: Conformational Mathematical Model of Collective Cell Migrations Based on Cell Polarity, ***Dev. Growth Differ.*****, 59**, 471-490 (2017).

Overview

Soft matter physics that deals with soft and largely deformable materials is a necessary tool for mechanical understanding of motion, deformation and growth of biological systems such as cells, tissues and organisms. Based on these ideas, we are investigating characteristic and functional behaviors of various biological systems, by inventing unique experimental setup. Explicit themes in our lab are as follows. (1) Ethology of protozoa (slime molds, ciliates, amoebae, etc.). (2) Biophysical study on intracellular regulation of amoeboid and ciliary movement. (3) Rheology of solutions of biopolymers such as actin filaments and microtubules. (4) Animal behavior and biomechanics of nematodes. (5) Mechanics of peristaltic crawling of snails and earthworms. (6) Mechanical properties and functions of trees and bones. (7) Mechanical modeling for development of multicellular organisms. (8) Shape, function and development of transport networks in slime mold and the other living systems. (9) Ethological dynamics in diorama environments



RESEARCH THEME

Searching for an elementary algorithm of behavioral intelligence that may be common from amoeba to human/ Biophysical study on amoeboid and ciliary movement/Study on active soft matter in relation to bio-mechanics

KEYWORDS

ciliate, amoeba, slime mold, protozoa, nematode, live cell imaging, field work, evolutionary ecology, biomechanics, locomotion, memory and learning, mathematical modeling, computer simulation, nonlinear dynamics, active soft matter, Belousov-Zhabotinski reaction, pattern formation, scaling theory, network of biochemical reactions

Laboratory of Physical Ethology

nakagaki@es.hokudai.ac.jp

Professor

NAKAGAKI Toshiyuki

Selective Recent Publications

S. Kuroda, N. Uchida, T. Nakagaki: “Gait switching with phase reversal of locomotory waves in the centipede Scolopocryptos rubiginous”, ***Bioinspiration & Biomimetics*, 17(2)**, 026005 (2022),

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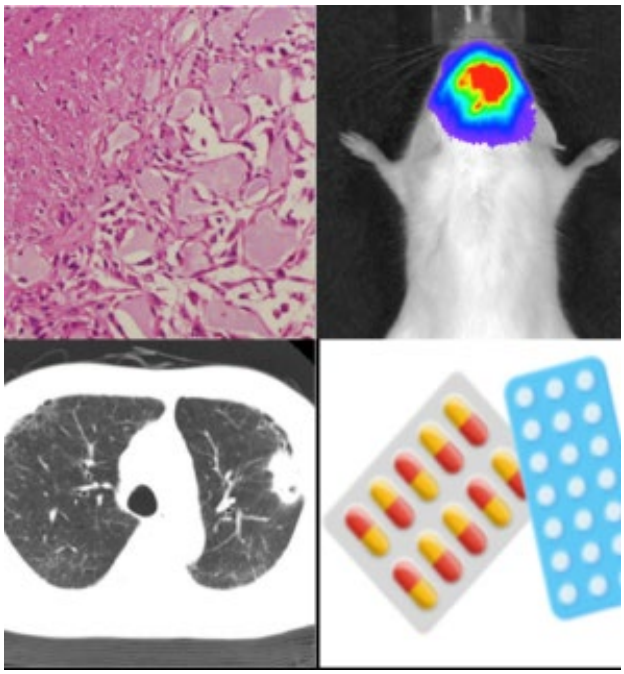
D. Akita, I. Kunita, M. D. Fricker, S. Kuroda, K. Sato and T. Nakagaki : “Experimental models for Murray's law”, ***J. Phys. D: Appl. Phys.,* Vol. 50**, 024001(11pp) (2017).

Overview

Students acquire basic knowledge of basic medicine, clinical medicine, and regenarative medicine necessary for medical application of soft matter (synthetic polymer hydrogel). Particularly, by analyzing cell phenomena and *in vivo* reactivity on soft matter that mimics *in vivo* environment, students deepen their understanding of diseases in the field of cancer treatment, articular cartilage, and regenerative medicine. Ultimately, we aim to contribute to medical development toward an advanced precision medicine and aging society, by fusing medicine and soft matter.



RESEARCH THEME

Analysis of cellular responses to functional polymer gels and their medical application

KEYWORDS

biomaterial, cancer stem cell, molecular targeted therapy, regenerative medicine, cartilage regeneration, neuroregeneration

Laboratory of Pathology

tsudam@med.hokudai.ac.jp

Associate Professor

TSUDA Masumi

Selective Recent Publications

Suzuki R, Yamasoba D, Kimura I, Wang L, Kishimoto M, Ito J, Morioka Y, Nao N, Nasser H, Uriu K, Kosugi Y, Tsuda M, Orba Y, Sasaki M, Shimizu R, Kawabata R, Yoshimatsu K, Asakura H, Nagashima M, Sadamasu K, Yoshimura K, The Genotype to Phenotype Japan (G2P-Japan) Consortium, Sawa H, Ikeda T, Irie T, Matsuno K, Tanaka S, Fukuhara T, Sato K. Attenuated fusogenicity and pathogenicity of SARS-CoV-2 Omicron variant. ***Nature*** **110**:747-760, 2022

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Suzuka J, Tsuda M, Wang L, Kohsaka S, Kishida K, Semba S, Sugino H, Aburatani S, Frauenlob M, Kurokawa T, Kojima S, Ueno T, Ohmiya Y, Mano H, Yasuda K, Gong JP, Tanaka S. Rapid reprogramming of tumour cells into cancer stem cells on double-network hydrogels. ***Nat Biomed Eng.*** **5**:914-925, 2021

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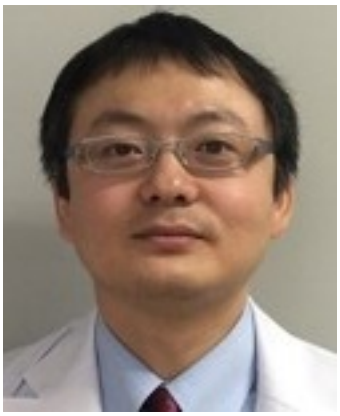
Overview

Our laboratory aims to develop bioactive soft-matter materials as a scaffold for undifferentiated progenitor cells for the purpose of fast implementation in clinical application. By carrying out animal experiments and clinical research, which is a position as a translational research, clinical practical application of the materials will be realized.



RESEARCH THEME

To elucidate the mechanism of cartilage metabolism and tissue regeneration. / Development of innovative treatments for musculoskeletal diseases leading to clinical application.

KEYWORDS

Orthopaedic Surgery, Joint Surgery, Regenerative Medicine, Musculoskeletal System, Animal Model, Scaffold, Cartilage, Bone, Meniscus, Biomaterials, Soft Matter, Clinical Application, Translational Research

Laboratory of Reconstructive Surgery and Rehabilitation Medicine

tomozou@med.hokudai.ac.jp

Lecturer

ONODERA Tomohiro

Selective Recent Publications

Onodera T, Baba R, Kasahara Y, Tsuda T, Iwasaki N., Therapeutic effects and adaptive limits of an acellular technique by ultrapurified alginate (UPAL) gel implantation in canine osteochondral defect models. ***Regen Ther.*** 2020/02

Kim W, Onodera T, Kondo E, Terkawi MA, Homan K, Hishimura R, Iwasaki N., Which Contributes to Meniscal Repair, the Synovium or the Meniscus? An In Vivo Rabbit Model Study With the Freeze-Thaw Method. ***Am J Sports Med***. 2020/1

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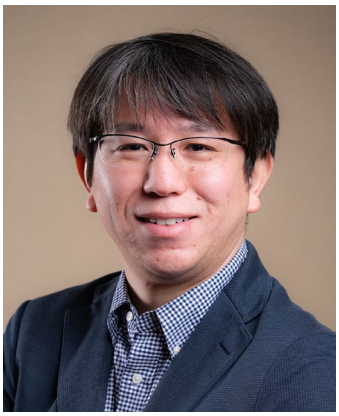
Kim W, Onodera T, Kondo E, Kawaguchi Y, Terkawi MA, Baba R, Hontani K, Joutoku Z, Matsubara S, Homan K, Hishimura R, Iwasaki N, Effects of Ultra-Purified Alginate Gel Implantation on Meniscal Defects in Rabbits., ***The American journal of sports medicine*** 363546518816690 2018/12

Overview

Target of our research is to develop novel optoelectronically functional liquid as well as self-regulatable smart soft gel materials based on the design for low molecular weight pi-conjugated unit, ionic liquid, and block copolymer building blocks. Accompanying with gaining insight into physicochemical property/structure/function for these soft matter, we develop highly functional energy conversion/stimuli-responsive materials (i.e. sensor, actuator, synthetic cellular matrix) which can be potentially utilized for advanced stretchable electronics, robotics, and biomedical applications.



RESEARCH THEME

Development of novel energy conversion soft material systems / Stimuli-responsive, molecular and polymer materials based on molecular softness

KEYWORDS

molecular liquid, ionic liquid, polymer gel, block copolymer, stimuli-responsive materials, optoelectronic function, self-assembly, dynamic biomimetics, sensor, actuator

Laboratory of Functional Soft Matter

NAKANISHI.Takashi@nims.go.jp

Visiting Professor

NAKANISHI Takashi

Selective Recent Publications

T. Machida, T. Nakanishi, "Alkyl-π functional molecular liquids towards soft electronics", ***J. Mater. Chem. C,*** **9**, 10661-10667 (2021).

Z. Guo, A. Shinohara, C. Pan, F. J. Stadler, Z. Liu, Z.-C. Yan, J. Zhao, L. Wang, T. Nakanishi, "Consistent red luminescence in p-conjugated polymers with tuneable elastic moduli over five orders of magnitude", ***Mater. Horiz.*****, 7,** 1421-1426 (2020).

A. Ghosh, M. Yoshida, K. Suemori, H. Isago, N. Kobayashi, Y. Mizutani, Y. Kurashige, I. Kawamura, M. Nirei, O. Yamamuro, T. Takaya, K. Iwata, A. Saeki, K. Nagura, S. Ishihara, T. Nakanishi, "Soft chromophore featured liquid porphyrins and their utilization toward liquid electret applications", ***Nature Commun.,*** **10**, 4210 (2019).

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F. Lu, K. Jang, I. Osica, K. Hagiwara, M. Yoshizawa, M. Ishii, Y. Chino, K. Ohta, K. Ludwichowska, K. J. Kurzydlowski, S. Ishihara, T. Nakanishi, "Supercooling of functional alkyl-π molecular liquids", ***Chem. Sci.*****, 9**, 6774-6778 (2018).

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