BIOTECHNOLOGY

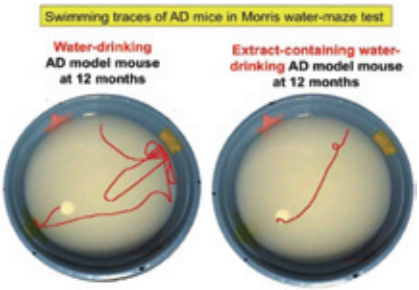
Identification of Plant Extracts Containing Inhibitory Activities on g-Sectetase

Identification of plant extracts that prevent Alzheimer disease

Professor Akira Kakizuka - Graduate School of Biostudies
Graduate Student (Doctor course) Norio Sasaoka - Graduate School of Biostudies

Prof. Kakizuka and his research team identified several plant extracts that contain inhibitory activities on γ-secretase, a key enzyme for Alzheimer disease (AD). They dissolved one showing the strongest inhibitory activity in water, and allowed AD mice to drink it freely. AD mice drinking the extract-containing water were able to quickly find the hidden platform in a Morris water maze test (Figure), showing apparently no impairment of learning and memory abilities.

In Chinese medicine, this plant extract has been used on humans for more than a thousand years. Thus, taking this plant extract itself or extract-containing drinks and/or foods would safely reduce the risk of suffering from AD.



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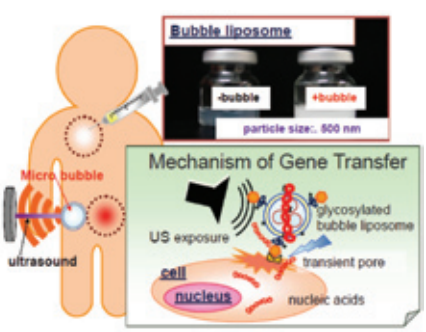
Glycosylated Liposomes for Cell-specific Delivery of siRNA and Plasmid DNA

Gene delivery for treating intractable disease

Professor Mitsuru Hashida - Graduate School of Pharmaceutical Science
Lecturer Shigeru Kawakami - Graduate School of Pharmaceutical Science

Targeted drug delivery via specific cellular receptors is a promising strategy for drug therapy. Prof. Hashida and Lecturer Kawakami have developed glycosylated (galactose, mannose, fucose, and mannose-6-phosphate modified) liposomes for cell-selective targeting of gene drugs and demonstrated their therapeutic activities. Recently, the researchers have developed a new gene delivery system in which glycosylated bubble lipoplexes are combined with ultrasound (US) exposure. Intravenous injection of mannosylated bubble lipoplexes followed by US exposure resulted in specific delivery of plasmid DNA (pDNA) and siRNA to splenic dendritic cells or hepatic endothelial cells (HECs) expressing a mannose receptor in mice. DNA vaccine with pDNA expressing melanoma-related antigen (gp100) exhibited high inhibition activities against tumors. The siRNA against intracellular adhesion molecule-1 (ICAM-1) administered with this system exhibited strong reduction of inflammatory responses by knocking out of ICAM-1 production in HECs and suppressed migration of neutrophil. Thus, glycosylated bubble lipoplexes combined with US exposure demonstrated efficient nucleic acids delivery and therapeutic efficacy.



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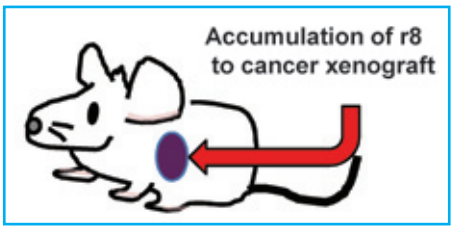
Delivery of Anti-cancer Drugs Using Oligoarginine Peptides

Oligoarginine peptides may provide novel methods of cancer targeting!

Professor Shiroh Futaki - Graduate School of Pharmaceutical Science

Prof. Futaki and his research team have developed a new approach of cancer targeting using oligoarginine peptides. Intravenous injection of D-form of octaarginine (r8) effectively led to the accumulation of r8 to tumor-xenograft in mouse. The sustained retention over 24 h in tumor was observed. The r8-doxorubcin conjugate (4 mg doxorubcin/kg) effectively suppressed the tumor proliferation without the decrease of mouse weight after intravenous injection of the conjugate. Unconjugated doxorubicin required higher dose (6 mg/kg) to obtain the same extent of tumor growth suppression, accompanied by a significant weight loss of the mice.



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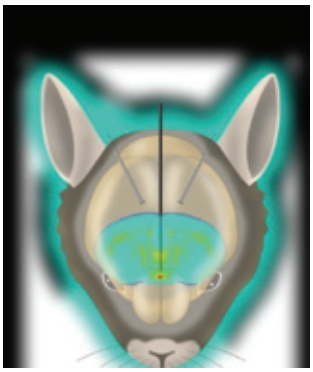
Molecular Dissection of Circadian Timing System for the Treatment of Life-Style Related Diseases and Sleep Disorders

Identification of clock-related genes involved in the development of metabolic syndrome, cancer and hypertension

Professor Hitoshi Okamura - Graduate School of Pharmaceutical Science

As the living environment changes rapidly, and the numbers of around-the-clock facilities and people staying awake all night increase in efficiency-oriented industries, the biological system that regulates our internal rhythms is being compromised. It is becoming clear that the disruption of the molecular system regulating biological rhythms is linked with the incidence of numerous lifestyle-related diseases and industrial accidents. Under these circumstances, it is now essential to investigate how time is generated by our body and how it can be tuned. Prof. Okamura and his team will approach these questions with a multi-layered perspective at the intracellular, intercellular and system levels. They have identified a number of genes that are strongly expressed in the mammalian circadian center, called the suprachiamatic nucleus (SCN). These genes therefore are likely to be involved in the generation, regulation and integration of time within the multi-neuronal network of the SCN. In parallel, Prof. Okamura and his team will also demonstrate the role of the circadian clock in the healthy function of tissues and organs by studying the pathologies that arise in genetically modified clock-less animals. These two complementary approaches will provide new potential targets for the treatment of diseases and disorders that have a circadian component in their etiology. Specific examples include hypertension, metabolic syndrome, diabetes and cancer, as well as jet-lag and sleep disorders.



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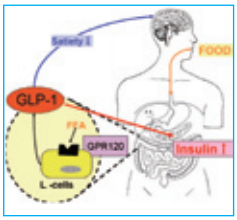
Lipid Sensor GPR120 Regulates Secretion of Gut Peptide Incretin Hormone GLP-1

Lipid sensor GPR120 is a drug target molecule for treating obesity and diabetes

Professor Gozoh Tsujimoto - Graduate School of Pharmaceutical Science
Associate Professor Akira Hirasawa - Graduate School of Pharmaceutical Science

Obesity and its associated disorders are a serious global health problem. Free fatty acids provide an important energy source and also act as signaling molecules in various cellular processes, including the secretion of gut incretin peptides. Prof. Tsujimoto and his research team found that a G-protein-coupled receptor, GPR120, which is abundantly expressed in intestine, functions as a receptor for unsaturated long-chain free fatty acids, especially omega-3 fatty acids. As GLP-1 is the most potent insulinotropic incretin, GPR120- is potentially important drug target for the treatment of obesity-related metabolic disorders.



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Activating Effects of Ethanolamines on Bovine Intestine Alkaline Phosphatase Activity

Enzyme for highly-sensitive enzyme immunoassay

Professor Kuniyo Inouye - Graduate School of Agriculture
Graduate student (PH. D. Candidate) Satoshi Sekiguchi - Graduate School of Agriculture

Bovine intestine alkaline phosphatase (BIALP) is widely used as a signaling enzyme in sensitive assays such as enzyme immunoassay (EIA). The sensitivity and rapidity of the assay increase with increasing the activity of the enzyme. Therefore, its activation and stabilization are of great interest. The assay of BIALP has been done conventionally in 0.05-0.5 M borate buffer at pH 9.8, 25 °C with the molecular activity (k_{cat}) value of 120-130 s^{-1} in the hydrolysis of *p*-nitrophenyl phosphate (*p*NPP). Prof. Inouye and his collegues evaluated the effects of various aminoalcohols and amines on BIALP activity. The k_{cat} values in the presence of ethanolamines were much higher than that observed in borate buffer, and the values increased with increasing their concentrations. In the presence of 1 M diethanolamine, triethanolamine, and *N*-methylethanolamine, the values were 1200, 1500, and 2300 s^{-1}, respectively.

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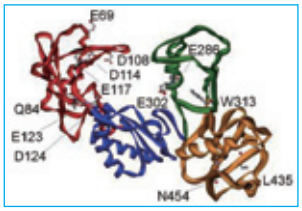
Increase in Thermal Stability of Moloney Murine Leukaemia Virus Reverse Transcriptase by Site-directed Mutagenesis

Thermostable reverse transcriptase suitable for use in research and clinical diagnosis

Associate Professor Kiyoshi Yasukawa - Graduate School of Agriculture
Professor Kuniyo Inouye - Graduate School of Agriculture



Reverse transcriptases act as DNA polymerase using both RNA and DNA as template. The reaction should be performed under increased temperature in order to prevent the formation of a secondary structure of RNA. It is, thus, desirable to develop thermostable and versatile reverse transcriptase. Associate Prof. Yasukawa and Prof. Inouye replaced certain amino acids of DNA interacting region of Moloney murine leukemia virus reverse transcriptase (MMLV RT) with positive or non-polar aminod acids. The multiple variant-type enzymes, MM3 and MM4, produced by this invention, are more thermostable than wild-type enzyme (WT) and a single variant-type enzyme D524A. The MMLV RT produced by this invention can be used as versatile reagents to analyze or detect virus, bacteria, and diseases, and there are no restrictions on types of RNA in samples.

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CHEMISTRY

Production of Novel β-Lactams from α-Amino Acids without Asymmetric Catalysts

Multi-substitued highly strained chiral β-lactams

Professor Takeo Kawabata - Institute for Chemical Research
Dr. Tomoyuki Yoshimura - Institute for Chemical Research

β-lactams constitute an important skeleton of antibacterial agents and are precursors of β-amino acids. Chiral β-lactams are also useful building blocks for the synthesis of biologically active natural and unnatural compounds. Prof. Kawabata and his research team have established a new method for the synthesis of multi-substituted highly strained β-lactams in high optical purity. The synthesis can be performed using abundant L-α-amino acids at room temperature without asymmetric catalysts. Therefore, a large quantity of the novel β-lactams can be synthesized at a low cost. Ring opening of the multi-substituted chiral β-lactams should give rise to novel amino acids that can be used for the construction of a unique peptide library and as novel glutamate analogues for the study of neuroscience.

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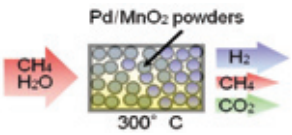
Pd/MnO_2-based Catalyst to Produce Hydrogen from Methane at Low Temperature

Improved hydrogen yield from natural gas in actual industrial plants/Optimization of output energy of fuel cell

Associate Professor Hideki Koyanaka - iCeMS
Mr. Masahiko Tsujimoto - iCeMS



A Pd/MnO_2-based catalyst to produce hydrogen (H_2) from methane (CH_4) has been synthesized successfully. The yield of H_2 from CH_4 (10% of the concentration in argon balance) reached over 200 mL per 1g of the catalyst in an hour under 300℃ without the co-production of toxic carbon monoxide (CO). Conventional catalysts such as Pd/Al_2O_3 and Pd/Carbon, produce CO that significantly decreases the yield of H_2 for the production plant and the efficiency of fuel cells. The Pd/MnO_2-based catalyst contributes to technologies of hydrogen production and utilization.

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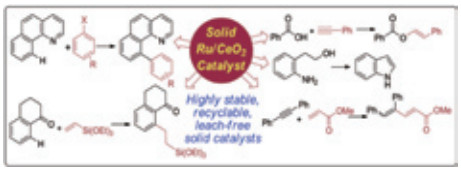
Ceria-supported Ruthenium Catalyst for Green Synthesis of Various Chemicals

Simple solid oxide catalysts for highly efficient, environmentally-benign synthesis of various chemicals,

Associate Professor Kenji Wada - Graduate School of Engineering



Associate Prof Kenji Wada and his research team have developed solid ceria-supported ruthenium (Ru/CeO_2) catalyst, which showed excellent activity towards a wide range of organic transformations, namely:(1) addition of aromatic C-H bonds to vinylsilanes, (2) direct arylation of aromatic C-H bonds to biaryls, (3) addition of carboxylic acids to terminal alkynes, (4) region- and stereoselective cross coupling of alkenes and alkynes, (5) selective synthesis of indole, and so on. The Ru/CeO_2 catalyst is easily prepared, stable towards air and moisture, and recyclable for several times without significant leaching of ruthenium species into the products, indicating its possibility as an attractive, environmentally benign alternative to homogeneous complex catalysts.

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MATERIALS

Utility of a Slightly Modified Collagen Scaffold

Development of a scaffold for use in the reconstruction of various internal organs

Associate Professor Tatsuo Nakamura - Institute for Frontier Medical Sciences
Research Fellow Akira Nakada - Institute for Frontier Medical Sciences

In regenerative medicine, a collagen is an excellent scaffold material. Therefore Associate Professor Tatsuo Nakamura and his research team focused on a characteristic of collagen, which has a molecular structure in the acidic region and forms a fibrous structure with increased strength in the neutral region. The researchers made neutral collagen into a scaffold.

They studied the biocompatibility and durability of this collagen scaffold by embedding it beneath the dorsal skin of rats. Biocompatibility was best when the freezing temperature of the collagen fiber suspension was -10℃, the thermal denaturation temperature was 140℃, and time was six hours. The slightly modified collagen fiber scaffold made in this way appears to be useful not only as a "scaffold" but also as a so-called "cell capsule" to carry cells to a designated location.

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A Single Molecule of Water Encapsulated in Fullerene C_{60}

Endohedral C_{60} encapsulating a water molecule

Professor Yasujiro Murata - Institute for Chemical Research
Dr. Kei Kurotobi - Institute for Chemical Research (present affiliation; iCeMS)

Prof. Yasujiro Murata and his research team synthesized fullerene C_{60} encapsulating a single molecule of water. A single molecule of H_2O without any hydrogen bonds is completely isolated within the confined sub-nano space inside fullerene C_{60}. With the concept of dynamic control of opening size, an open-cage C_{60} derivative was synthesized, whose opening can be enlarged in situ at 120℃ resulting in quantitative encapsulation of a molecule of H_2O under the high-pressure conditions. A simple method to restore the opening was developed to realize the organic synthesis of water-encapsulating C_{60}. The structure of $H_2O@C_{60}$ was determined by the single crystal X-ray analysis, and the properties of the single H_2O molecule as well as the spherical π-system encapsulating the water molecule were studied.

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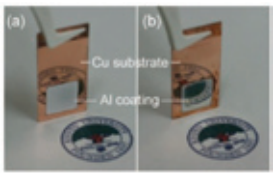
Electrodeposition of Aluminum Layers with Controlled Structures from Dimethylsulfone-based Baths

Fabrication of bright aluminum coatings and porous aluminum layers



Assistant Professor Masao Miyake - Graduate School of Energy Science
Professor Tetsuji Hirato - Graduate School of Energy Science

Assistant Prof. Masao Miyake and Prof. Tetsuji Hirato developed an electrodeposition method for the formation of bright aluminum (Al) coatings. Al coatings can be electrodeposited using dimethylsulfone-based baths; however, the coatings usually lack luster. The researchers have recently found that the addition of a certain additive to the bath resulted in the electrodeposition of bright Al coatings with mirror-like appearances. The coatings can potentially be used as decorative, corrosion-resistant coatings and light reflectors. They have also devised a new method for the fabrication of porous Al layers. In this method, the electrodeposition of Al is performed in a bath containing NaCl powder, yielding an Al layer containing NaCl particles. A porous Al layer can be obtained by washing the composite in water after the electrodeposition.

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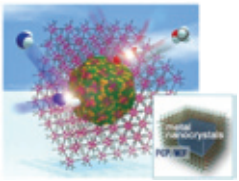
Development of Metal Nano-crystals Covered with Functional Porous Materials

Hybrid nano-catalysts for highly-selective energy-gas capture



Professor Hiroshi Kitagawa - Graduate School of Science
Dr. Hirokazu Kobayashi - Graduate School of Science

Prof. Hiroshi Kitagawa and Dr. Hirokazu Kobayashi are searching for novel methods for introducing functionalities into porous coordination polymers (PCPs) by hybridization with metal nanocrystals. PCPs are organic–inorganic hybrid solids with zeolite-like structures and porous properties. Due to their high surface area and designable pore size with hydrophilic or hydrophobic characteristics, PCPs have attracted much attention as practical adsorbents or membrane materials to separate gases on an industrial scale. Metal nano-crystals, on the other hand, play an important role as effective catalysts for various reactions. The hybridization of the two should deliver enhanced catalytic capabilities. The synergy effect between PCPs and metal nanocrystals is expected to be highly selective and active, and will hopefully provide a clean and green environment.

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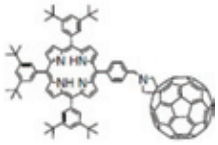
Photovoltaic Cell with Semiconducting Electrodes Modified with Composite

Thin film organic solar cell



Assistant Professor Tomokazu Umeyama - Graduate School of Engineering

Assistant Prof. Tomokazu Umeyama has developed a composite cluster of soluble single-walled carbon nanotube and porphyrin-linked C_{60}, which was prepared in a mixed solvent of o-dichlorobenzene and acetonitrile and then electrophoretically deposited onto a tin-oxide electrode. The photoelectrochemical measurements of the deposited film revealed enhanced photocurrent generation efficiency compared to the reference film without the soluble single-walled carbon nanotube. This technology may be applied to highly efficient photovoltaic devices.

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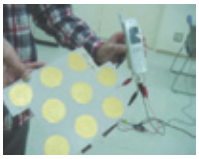
OTHERS

Wireless Power Transmission and Space Solar Power Satellite/Station as Its Application

Wireless Charging, Electric Charging, Wireless Sensor, Electric Vehicle, Mobele Phone, Energy Harvesting, Solar Power



Professor Naoki Shinohara - Research Institute of Sustainable Humanosphere
Assistant Professor Tomohiko Mitani - Research Institute of Sustainable Humanosphere

Wireless Power Transmission (WPT) is useful and convenient technology, which can be used to charge batteries in the equipments without the need for a wire connection. The WPT technologies can also be used to harvest broadcasted radio waves. At Kyoto University, Prof. Shinohara and Assistant Prof. Mitani have a long history of the research of the WPT, especially WPT via microwaves, and have carried out the WPT experiments for various applications. One exciting application of the WPT is wireless charging of an electric vehicle. Prof. Shinohara and Assistant Prof. Mitani can charge the mobile phones without any wires (Figure). They have various technologies and know-how of the WPT via microwaves. Their future dream is wireless power from space, by way of a Space Solar Power Satellite/Station (SPS).

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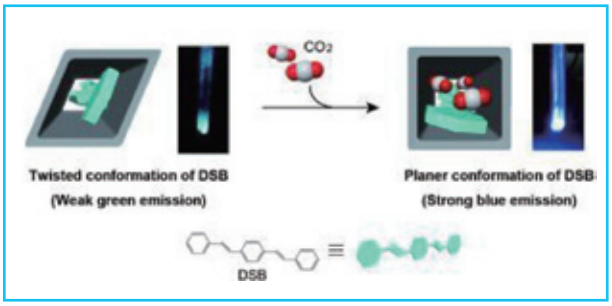
Gas Detection by Structural Variations of Fluorescent Guest Molecules in a Flexible Porous Coordination Polymer

Fast, cheap, and accurate: detecting CO_2 with a fluorescent twist

Associate Professor Takashi Uemura - Graduate School of Engineering
Professor Susumu Kitagawa - iCeMS and Graduate School of Engineering

Prof. Kitagawa and his research team reported a novel strategy in which gas molecules are detected by signals from a reporter guest molecule that can read out the structural transformation of a porous coordination polymer (PCP). A fluorescent reporter molecule, distyrylbenzene (DSB), was incorporated into a flexible PCP. The PCP-DSB composite selectively adsorbed CO_2 over other atmospheric gases, such as N_2, O_2, and Ar. This gas adsorption induced a transformation of the PCP framework, which was accompanied by conformational variations of the included DSB. This read-out process resulted in a critical change in DSB fluorescence at a specific threshold pressure. Their PCP-DSB system showed, for the first time, that fluorescent molecules can detect gas molecules without any chemical interaction or energy transfer.



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Automatic Generation of 3D Building Models Using Airborne LiDAR and Aerial Photograph

Automatic generation of 3D urban map

Associate Professor Junichi Susaki - Graduate School of Engineering and Graduate School of Global Environmental Studies

Associate Prof. Junichi Susaki has developed an algorithm that automatically generates 3D building models even in dense urban areas. The proposed algorithm uses the results of building segmentation from aerial photographs. Segmentation of buildings in urban areas, especially dense urban areas, by using remotely sensed images is also challenging because of unclear boundaries between buildings and shadows cast by neighboring buildings. He has developed another algorithm that segments buildings, including shadowed buildings, in dense urban areas from an aerial photograph. By considering the segmented regions and airborne light detection and ranging (LiDAR) data, models of actual building types—gable-roof, hip-roof, flat-roof and slant-roof buildings—are generated.

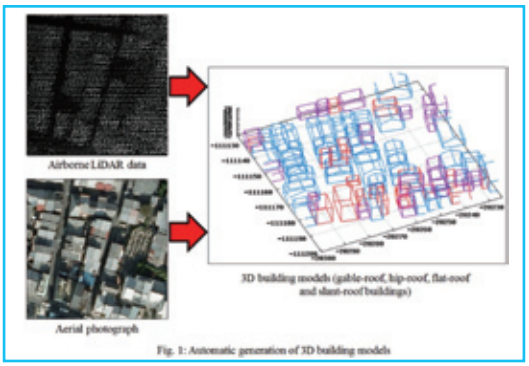

Fig. 1: Automatic generation of 3D building models

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