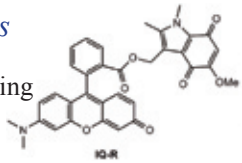
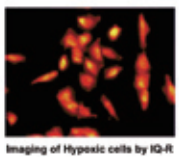
BIOTECHNOLOGY

Indolequinone-Rhodol (IQ-R) Conjugate as a Fluorescent Probe for Hypoxic Tumor Cells

Fluorescent probe for visualization of hypoxic tumor cells

Associate Professor Kazuhito Tanabe - Graduate School of Engineering
Professor Sei-ichi Nishimoto - Graduate School of Engineering




Imaging of Hypoxic cells by IQ-R

Hypoxia is an important feature of many diseases such as malignant solid tumors, inflammatory diseases and cardiac ischemia. Associate Prof. Tanabe and his research group herein focused on the development of a novel hypoxia-sensitive fluorescent probe, IQ-R, consisting of an indolequinone unit and a rhodol fluorophore. IQ-R has good solubility in water and longer wavelength for absorption and emission, which are favorable for cellular bio-imaging. While the fluorescence of rhodol in the IQ-R conjugate was quenched by the function of intramolecular indolequinone unit, it was restored under hypoxic conditions through the enzymatic one-electron reduction of IQ-R by NADPH:cytochrome P450 reductase to release the nonconjugated free rhodol. When administered to A549 cells, IQ-R was activated and reduced by endogenous reductase preferentially under hypoxic conditions, thereby visualizing hypoxic cancer cells by robust fluorescence.

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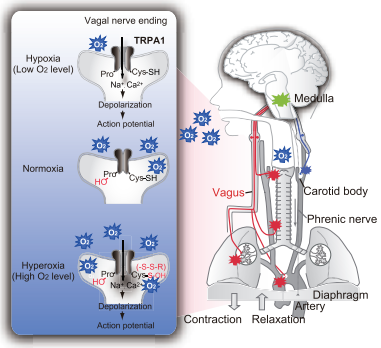
TRPA1 Underlies a Sensing Mechanism for Oxygen

Applications to clinical treatment of respiratory disorders

Professor Yasuo Mori - School of Global Environmental Studies
Specific Assistant Professor Nobuaki Takahashi - Center for the Promotion of Interdisciplinary Education and Research



Oxygen (O_2) is a prerequisite for cellular respiration in aerobic organisms but also elicits toxicity. To understand how animals cope with the ambivalent physiological nature of O_2, it is critical to elucidate the neuronal and molecular mechanisms responsible for O_2 sensing. Prof. Mori and Specific Assistant Prof. Takahashi have conducted a systematic evaluation of TRP cation channels using reactive disulfides with different redox potentials to reveal the capability of a TRP channel to sense O_2. O_2-sensing is based upon disparate processes: while prolyl hydroxylases (PHDs) exert O_2-dependent inhibition on the TRP channel activity in normoxia, direct O_2 action overrides the inhibition via the prominent sensitivity of the TRP channel to cysteine-mediated oxidation in hyperoxia. Surprisingly, the TRP channel is activated through relief from the same PHD-mediated inhibition in hypoxia. In mice, gene disruption of the O_2-sensitive TRP channel impedes in vivo activity induced by hyperoxia and hypoxia in the vagus nerve – known to innervate the trachea and lung – and in sensory neurons. The results suggest a novel O_2-sensing mechanism in vagus nerves, and contribute also to understanding respiratory and sensory disorders mediated by defects of TRPA1.

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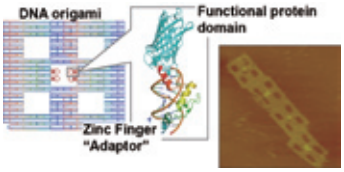
Site-specific Arrangements of Proteins on DNA-origami Structures

Molecular switchboards facilitate arranging of enzymes and receptors in nanometer-scale precision

Professor Takashi Morii - Institute of Advanced Energy
Lecturer Eiji Nakata - Institute of Advanced Energy



DNA nanostructures can be equipped with specific docking sites for proteins. Cellular processes and chemical transformations take place in several reaction steps, with multiple enzymes cooperating in specific fashion to catalyze sequential steps of chemical transformations. Such natural systems are effectively reconstructed in vitro when the individual enzymes are placed in their correct relative orientations. DNA-origami structures can be used as "molecular switchboards" to arrange enzymes and other proteins with nanometer-scale precision.

A new method was developed based only on proteins, to locate specific proteins by means of special "adapters" known as zinc-finger proteins. Zinc fingers are suitable site-selective adapters that attach to specific locations within DNA-origami structures. Several different adapters carrying different proteins can bind independently to defined locations on this type of nanostructure.

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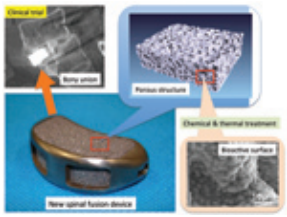
Development and Clinical Trial of Porous Bioactive Titanium Metal for Lumbar Spinal Fusion

Surgical treatment using a new synthetic material for low back pain

Senior Lecturer Shunsuke Fujibayashi - Kyoto University Hospital
Assistant Professor Mitsuru Takemoto - Kyoto University Hospital



The objective of this study was to establish the efficacy and safety of porous bioactive titanium metal for use in a spinal fusion device, based on a prospective human clinical trial. A high-strength spinal interbody fusion device was manufactured from porous titanium metal. A bioactive surface was produced by simple chemical and thermal treatment. Five patients with unstable lumbar spine disease were treated surgically using this device in a clinical trial approved by the university Ethics Review Committee and the University Hospital Medical Information Network.

Clinical and radiological results were reported at the minimum follow up period of 1 year. Successful bony union was achieved in all cases within 6 months without the need for autologous iliac crest bone grafting. All clinical parameters improved significantly after the operation and no adverse effects were encountered during the follow-up period. Although a larger and longer-term follow-up clinical study is mandatory to reach any firm conclusions, the study results show that this porous bioactive titanium metal is a promising material for spinal fusion devices.

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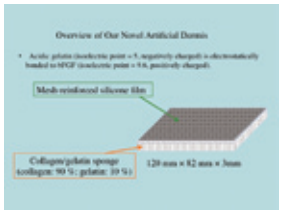
Development of a Novel Artificial Dermis for Sustained Release of Growth Factors

Development and clinical applications of functional artificial dermis

Professor Shigehiko Suzuki - Graduate School of Medicine
Lecturer Naoki Morimoto - Graduate School of Medicine



Professor Suzuki and Lecturer Morimoto developed a novel artificial dermis that adds cell growth factor retention and controlled-release functions to conventional artificial dermis. The researchers confirmed that this novel artificial dermis impregnated with bFGF (basic fibroblast growth factor) had 50% residual bFGF content one week after application (in contrast to 10% for conventional artificial dermis) and 20% residual bFGF content 10 days after application.

The novel artificial dermis incorporating 7 to 14 μg/cm^2 bFGF offered superior wound healing effects over conventional artificial dermis in cases of full-thickness skin defects on mice, chronic skin ulcers (pressure ulcer) on diabetic mice, and mucoperiosteum defects of beagle dogs. This novel artificial dermis is excellent in encouraging wounds to heal and can also be applied to chronic skin ulcers that were conventionally difficult to treat with artificial dermis. Clinical trials have already begun as the first step toward commercialization.

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CHEMISTRY

Silicon-based Cross-coupling Reagents for Synthesis of Organic Compounds

Stable but highly reactive novel tetra-organosilicon compounds

Senior Lecturer Yoshiaki Nakao - Graduate School of Engineering
Professor Emeritus Tamejiro Hiyama - Graduate School of Engineering

Senior Lecturer Yoshiaki Nakao and Prof. Emeritus Tamejiro Hiyama have developed 2-(hydroxymethyl) phenyl-substituted tetra-organosilanes (HOMSi®), which undergo cross-coupling reactions. The proximal hydroxy group allows transmetalation of alkyl, alkenyl, and aryl groups on silicon to palladium, nickel, or copper to participate in the cross-coupling reaction under mild conditions employing weak base activators with excellent chemoselectivity. Highly efficient synthesis of functional molecules, such as oligoarenes, can be achieved through iterative cross-coupling/O-deprotection sequences by simply switching their reactivity with orthogonal O-protection/deprotection. Silicon residues of the HOMSi reagents can readily be recovered and reused for the synthesis of the reagents.

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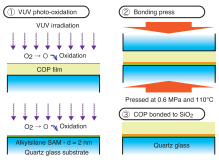
MATERIALS

Photochemical Surface Modification of Organic Materials through Vacuum Ultraviolet Irradiation for Adhesive-less Bonding

Photo-activation bonding of synthetic resin to inorganic substrate

Professor Hiroyuki Sugimura - Graduate School of Engineering
Dr. Hideya Nagata - Graduate School of Engineering



Prof. Hiroyuki Sugimura and Dr. Hideya Nagata have developed an adhesive-less organic-inorganic bonding technology applicable to the production of mechanical, optical, electrical, chemical and bio-logical devices. As schematically illustrated in Fig. 1, bonding is conducted by a simple two-step process. A cyclo-olefine polymer (COP) film and a quartz glass substrate had been activated with vacuum ultra-violet (VUV) irradiation in air (Step 1). Both of the surfaces were oxidized with atomic oxygen species generated by VUV-irradiation so as to be chemically activated. The COP film was adhered to the quartz substrate using only a low-temperature press facing the bonding surfaces (Step 2). A key to attaining the reproducible bonding is an alkyl self-assembled monolayer (SAM), which was VUV-oxidized as well, on the inorganic surface.

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Optically Transparent Bio-based Nanocomposites

Optically transparent low thermal expansion bendable nanocomposites

Professor Hiroyuki Yano - Research Institute for Sustainable Humanoshere
Researcher Fumiaki Nakatsubo - Research Institute for Sustainable Humanoshere
Assistant Professor Kentaro Abe - Research Institute for Sustainable Humanoshere

Figure 1
[left] Chemically modified pulp fiber sheet
[right] After resin impregnation

Recently, Prof. Yano and his research team were successful in producing a completely transparent crab-shell, keeping its original shape and substantial morphological detail. An important application for the finding is demonstrated in the micro- to mm-scale nanostructured crab shell chitin particles that can be used to process transparent nanocomposites. The incorporation of these chitin particles not only retains the transparency of the matrix resins but also drastically reduces the CTE (coefficients of thermal expansion) of the polymer. Moreover, the optical transmittance of the composite is stable over a large range of temperatures despite significant inhomogeneity at the mm-scale and large changes in the refractive index of the resin in its isolated state. Encouraged by the production of this transparent crab powder sheet, the research team undertook to create optically transparent pulp-fiber composites. The pulp-fiber sheet was acetylated, with care taken to maintain a never-dried condition, and was then dried and impregnated with acrylic resin. Despite the heterogeneous paper structure, the sheet became transparent (see Figure 1, right). Since a nanofibrillation process was unnecessary and the dewatering speed of the acetylated pulp fibers is very high, the production efficiency of optically transparent composites improved drastically.

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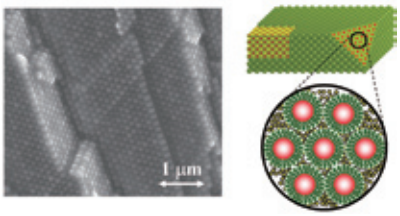
Novel Solid-State Polymer Electrolyte of Colloidal Crystal Decorated with Ionic-Liquid Polymer Brush

On the basis of a completely new concept, a novel solid electrolyte was developed, realizing a bipolar lithium-ion battery

Professor Yoshinobu Tsujii - Institute for Chemical Research
Professor Takaya Sato - Tsuruoka National College of Technology

Prof. Tsujii, Prof. Sato and their research team have successfully fabricated a leak/vapor-free, non-flammable and solid-electrolyte membrane by three-dimensional self-assembly. In this membrane, the hybrid silica particles (PSiPs) with "concentrated" polymer brushes (CPBs) of ionic-liquid polymers assembled themselves into a crystal state in the presence of a small amount of ionic liquid (IL) as a plasticizer. Solidification as well as ionic conduction is owing to the regular array of PSiPs thereby producing, between cores, a high ion-conductive, networked path containing IL. From this point of view, this is completely different from the previously reported electrolyte reinforced with nanoparticles, which are in an amorphous state in IL but not in a crystal. The CPB plays an important role not only in forming such higher-order structures but also in enhancing ionic conduction; a highly ordered structure, that is the face-centered cubic (fcc) crystal, was verified, and its conductivity was in the highest level among solid polymer electrolytes. This solid electrolyte was demonstrated to be successfully applied to a bipolar lithium-ion rechargeable battery operated at room temperature, with a double operation voltage and a capacity at the mAh level.



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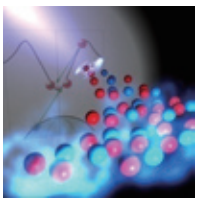
OTHERS

Terahertz Pulse Generates 1,000-Fold Increase in Electron Density

Findings point to advances in transistor and solar cell development



Assistant Professor Hideki Hirori - Institute for Integrated Cell-Material Sciences
Professor Koichiro Tanaka - Institute for Integrated Cell-Material Sciences

The study of carrier multiplication has become an essential part of many-body physics and materials science, since this multiplication directly affects nonlinear transport phenomena in ultra-high-speed transistors and plays a key role in designing efficient solar cells and electroluminescent emitters and highly sensitive photon detectors. Assistant Prof. Hideki Hirori and co-workers observed that when exposed to a single-cycle electric field pulse at the 1000 GHz (terahertz) frequency range, a sample of standard semiconductor material (gallium arsenide, GaAs) burst an avalanche of electron-hole pairs (excitons) 1,000-times more abundant than initial states only on the picosecond (10^{-12} s) time scale. The observed bright luminescence associated with carrier multiplication suggests that carriers coherently driven by a strong electric field can efficiently gain enough kinetic energy to induce a series of impact ionizations. These just-released results with the world strongest terahertz pulses demonstrate the rich potential that lies in the study of terahertz radiation.

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