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8548-1, Session 1a

Impact of polymeric nanomedicine on miRNA, cancer stem cells and chemoresistance *(Keynote Presentation)*

Ram I. Mahato, The Univ. of Tennessee Health Science Ctr. (United States)

Most cancers relapse due to the generation of chemoresistance rendering first-line chemotherapy ineffective. Combination therapy using biodegradable copolymeric systems may treat advanced cancers. I will discuss the roles of miRNA and cancer stem cells on chemoresistance and how the combination therapy of cyclopamine (CYA) and paclitaxel (PTX) or CYA and gefitinib can be used to treat resistant cancer. I will also discuss why our novel biodegradable copolymers can be used for deliver these hydrophobic drugs. Drug sensitivity and apoptosis assays showed significantly higher cytotoxicity with the combination therapy of PTX and CYA. To distinguish the presence of cancer stem cell like side populations (SP), Hoechst 33342 flow cytometry method was used. Drug resistant cancer cell lines and human cancer tissues possess a distinct SP fraction and have higher expression of stem cell markers. SP cell fraction was increased following PTX monotherapy and treatment with CYA either alone or in combination with PTX effectively reduced their numbers, suggesting the effectiveness of combination therapy. SP fraction cells were allowed to differentiate and reanalyzed by Hoechst staining and gene expression analysis. Post differentiation, the % of viable SP cells decreased significantly on treatment with CYA. The expression levels of P-gp efflux protein were also significantly decreased on treatment with PTX and CYA combination. There was significant decrease in the expression of tumor suppressor miRNAs. Treatment with this combination therapy restored the expression of miR200c and 34a, confirming their role in modulating chemoresistance.

8548-3, Session 1a

Construction of high fluorescent gold nanoclusters conjugated with DOX and PEG as a multi-functional and potential drug carrier

Shu-Yi Hsieh, Research Ctr. for Applied Sciences (Taiwan) and National Tsing Hua Univ. (Taiwan)

As a carrier in drug delivery, gold nanoparticles have been researched widely in the past few years. Gold nanoclusters could not induce immune response by the very small size and can be tracked after deliver drug in cells in confocal by high fluorescent.

In this study, we demonstrated that highly fluorscent gold nanoclusters can be a potential drug carrier by coupling with drug doxorubicin (DOX) and poly(ethylene glycol) (PEG). Functional groups are modified on the surface of ~2 nm nanoclusters by exchanging tetrakis(hydroxymethyl) phosphonium chloride (THPC) with 11-mercaptoundecanoic acid (MUA). Drugs can be easily coated on gold nanoclusters by amine bond formation with 1-Ethyl-3-[3-dimethylaminopropyl]carbodiimide hydrochloride (EDC) and N-Hydroxysuccinimide (NHS). From the confocal images, gold nanoclusters must have entered into cells by green fluorescent and DOX must be delivered into cells by the red fluorescent. Interestingly, nucleus has much red fluorescent than green. Moreover, the green fluorescent was outside nucleus and inside cells like a circle. We suggest that there must be some protease could cleave DOX from nanoclusters, then DOX can enter into nucleus to inhibit topoisomerase II then kill cancer cells.

Moreover, the cytotoxicty of nanoclusters were assayed by MTT in normal (MRC-5) and cancers cells (CL1-0, CL1-5 and A549). Fortunately, PEG nanoclusters with NH2 group on surface do not cause remarkable cytotoxicity in low concentration in normal or cancer cells. However, PEG nanoparticles have higher cytotoxicity in high concentration in days. From these results, we purpose 2 nm MUA-Au nanoclusters must be a powerful, potential and efficient drug carrier by the outside carboxylic group to couple with kinds of drugs.

8548-4, Session 1a

Smart nanoconjugate platforms for systemic administration of Ad *(Keynote Presentation)*

Chae-Ok Yun, Hanyang Univ. (Korea, Republic of)

A challenge to develop adenovirus (Ad)-mediated therapeutics has been issued to treat metastatic cancer via systemic administration. For effective gene therapeutics against primary and metastatic lesions, a systemically injectable tumor-targeting Ad vector system must be developed. In this study, versatile strategies involving the modification of viral surfaces with polymers and nanomaterials such as PEG, chitosan, and arginine-grafted bioreducible polymer (ABP) have been attempted to maximize Ad antitumor activity and specificity by systemic administration. Her2/neu-targeted and PEGylated oncolytic Ad (DWP418-PEG-HER) showed Her2/neu-dependent oncolytic activity, indicating that the Herceptin-targeting moiety directed selective entry of this Ad nanocomplex into Her2/neu-positive cells. Systemic administration of DWP418-PEG-HER elicited greater antitumor activity towards Her2/neu-positive SK-OV3 and MDA-MB435 xenograft tumors than naked DWP418 or DWP418-PEG. Moreover, DWP418-PEG-HER showed a 1010-fold increase in the liver-to-tumor biodistribution compared with naked Ad. The formation of Ad complex with chitosan polymers has been achieved by electrospinning, making steady production on a large scale possible. Ionic crosslinking of chitosan formed a stable positive layer as an outer shell of the Ad. When tumor-targeting folic acid (FA) was further conjugated, the entry of Ad/chitosan-PEG-FA was dependent on the expression of the FA receptor on the cell surface. Another advanced design of Ad complexes with ABP has been also attempted. ABP-conjugated hepatoma-specific oncolytic Ad retained specificity as well as the potency of oncolytic Ad. Biodistribution, blood circulation time, immune response, and therapeutic effect of these Ad nanocomplexes will be discussed, proposing the future direction of viral/nonviral combinatory delivery for cancer therapy.

8548-5, Session 1a

Interaction of nanoparticles with light or ultrasound for tumor therapy or drug delivery

Rinat O. Esenaliev, The Univ. of Texas Medical Branch (United States)

Our noninvasive therapy approach is based on interaction of

nanoparticles with optical or ultrasound radiation that produces direct thermal or mechanical damage to tumors or enhances delivery of anti-cancer macromolecular drugs and genes in tumors. Poor penetration of drugs and genes in malignant tumors limits efficacy of cancer chemo- and biotherapy. Interaction of light or ultrasound with strongly-absorbing or porous nanoparticles may enhance drug and gene delivery. The nanoparticles can selectively be delivered in tumor blood vessels using enhanced permeability and retention (EPR) effect or using targeting molecules. In this work we obtained enhanced delivery of drugs and genes in vitro in a variety of cancer cell lines and in vivo in tumors when ultrasound was used in combination with microbubbles or biodegradable polymer poly (lactic-co-glycolic acid) (PLGA) air-filled nanoparticles. The nanoparticles were manufactured in our laboratory. We also studied kinetics of the nanoparticles injected in the tail vein of mice bearing human tumors using an high-resolution ultrasound imaging system Vevo developed by VisualSonics. The ultrasound imaging system operating at 80 MHz was used to visualize tumors with high resolution and to study kinetics of the nanoparticles in the tumors. Experiments were performed also with ultrasound contrast agents (microbubbles) for comparison with the nanoparticles. Our results demonstrated that interaction of light or ultrasound with these nanoparticles can be used for substantial enhancement of drug and gene delivery or for cancer therapy without drugs using thermal or mechanical damage to tumors.

8548-51, Session 1a

Engineering and application of collagen binding fibroblast growth factor 2 for collagen based bone graft

Jun-Hyeog Jang, Eunyi Jeon, Inha Univ. (Korea, Republic of)

Collagen is a widely used bone graft in tissue repair and regeneration for bone tissue engineering. Here, we genetically engineered collagen binding FGF2 and applied in the collagen based bone grafts. We investigated cellular functions such as cell adhesion, proliferation, and differentiation of MC3T3-E1 cells on collagen based bone grafts.

8548-54, Session 1b

Microfabricated miniature biofuel cells with nanoengineered enzyme electrodes *(Keynote Presentation)*

Matsuhiko Nishizawa, Syuhei Yoshino, Takeo Miyake, Tohoku Univ. (Japan)

Nanostructured carbons have been widely used for fabricating enzyme-modified electrodes due to their large specific surface area. We present here a method to achieve ideal enzyme electrodes having suitable intra-nanospace automatically regulated to the size of enzymes. We utilize a carbon nanotube forest (CNTF) consisting of extremely long (~1 mm) single-walled CNTs, which can be handled with tweezers, as a 100% binder-free carbon film. When liquids are introduced into the as-grown CNTF (CNTs with a pitch of 16 nm) and dried, the CNTF shrinks to a near-hexagonal close-packed structure (CNTs with a pitch of 3.7 nm) because of the surface tension of the liquids. By using an enzyme solution as the liquid, the CNTF is expected to dynamically entrap the enzymes during the shrinkage. The fructose dehydrogenase (FDH), glucose oxidase (GOD), laccase (LAC) and bilirubin oxidase (BOD) were successfully entrapped in the CNTF films. This “in-situ regulation” approach has led to reproducible activity of enzyme electrodes, to the first free-standing flexible character, and to high-power density biological fuel cells. The free-standing, flexible composite film can be used by winding on a needle device, for example, a self-powered sugar monitor.

8548-55, Session 1b

Nanocomposite sensor electrodes for smartphone enabled healthcare garments: e-bra and smart vest

Prashanth S. Kumar, Pratyush Rai, Sechang Oh, Hyeokjun Kwon, Vijay K. Varadan, Univ. of Arkansas (United States)

The financial burden of hospital readmissions and treatment of chronic diseases are global concerns. Point of Care (POC) has been presented as an elegant solution for healthcare cost reduction. However, large scale adoption of POC systems requires an intuitive, unobtrusive and easy to use health monitoring system from patient’s perspective. Healthcare textiles are sensor systems mounted on textile platform that function as wearable unobtrusive health monitoring systems. Nanomaterials based devices and technology can be employed in healthcare textiles for improved electrical characteristics of the sensors- Free standing nanostructure gold electrodes and nanotube composite ink based printable conductive electrodes are textile adaptable nanomaterial technologies. However, this technology needs to be complemented with cyber-infrastructure for data handling to facilitate POC diagnostics and health management. The systems presented here are a vest and a bra, which incorporate the nanomaterials based sensor electrodes for human cardiac biopotential (Electrocardiography, EKG) sensing and cyber infrastructure for POC. A smartphone is used to provide cyber-infrastructure connectivity for the healthcare data from the healthcare garment. They can be used to monitor young or elderly recuperating /convalescent patients either in hospital or at home. They can also be used by young athletes to monitor important physiological parameters to better design their training or fitness programs.

8548-56, Session 1b

Medical application of Fresnel micro spectrometer chip

Yeonjoon Park, National Institute of Aerospace (United States); Hargsoon Yoon, Norfolk State Univ. (United States); Uhn Lee M.D., Gachon Univ. of Medicine and Science (United States); Glen C. King, Sang H. Choi, NASA Langley Research Ctr. (United States)

Newly developed miniaturized solid-state optical spectrometer chip will be demonstrated for medical research. While conventional spectrometers cannot be miniaturized smaller than a few centimeter sizes because of the limit of Fraunhofer diffraction, the new micro spectrometer can be miniaturized into millimeter sizes in device volume because it is based on Fresnel diffraction. Although the optical fiber can easily enter the patient body, a bulky and large conventional spectrometer which is attached to the optical fiber has hindered in-vivo medical applications so far. We review the design and performance of Fresnel micro-spectrometer and find the potential medical applications for embedded in-vivo patient monitoring.

8548-57, Session 1b

Nanoporous electrochemistry for electrochemical biosensors and abiotic sugar cell *(Keynote Presentation)*

Taek Dong Chung, Seoul National Univ. (Korea, Republic of)

The nanoporous electrodes, especially mesoporous platinum, offer an authentic system to investigate the potential profile in the electric double layer, and also have profound implication of potential substrates for sensory devices. We significantly extended the research scope that had been limited within lyotropic liquid crystalline template or potential

controlled self-assembly producing 1D nanopores, and propose a new way to mass production of nanoporous metal thin films. 3D nanoporous thin film was prepared from L2 phase and possessed 1~3 nm wide 3D pores with several hundreds of high roughness factors. This new film turned out to be greatly practical for electrocatalytic applications that require fast mass transport and remarkably alleviated pore clogging. A representative example of the novel applications is the electrochemical determination of glucose concentration without using enzyme, which will lead to possible breakthroughs in achieving the enzymeless glucose sensor. Another class of its valuable applications include solid-state reference electrode and thin film-based pH sensor which can be miniaturized into a microfluidic system. Substantial suppression of impedance at the nanoporous s interfaces allows neural stimulator, extracellular recording probes, and many others. In this talk, a series of its uses as well as fundamental electrochemical behavior at nanoporous interfaces will be briefed.

8548-58, Session 1b

A nanofluidic bioarray chip for fast and high-throughput detection of antibodies in biological fluids

Jonathan Lee, Naveed Gulzar, Jamie Scott, Paul C. Li, Simon Fraser Univ. (Canada)

We are developing a novel nanofluidic bioarray (NBA) chip intended for fast detection of antibodies present in biological fluids such as mouse ascites fluid. This capability has applications in diagnosing disease, and in monitoring efficacy of therapy or vaccination. To begin designing and testing this system, the synthetic peptide (HA; a 12 amino-acid residue fragment from hemagglutinin A glycoprotein of influenza virus) was used as a model antigen to be detected by the monoclonal antibody (MAb), 17/9, produced from the murine 17/9 hybridoma cell line. By introducing the intersection approach on a NBA chip, we developed various arrays whereby multiple samples each reacted with multiple probes, resulting in a system that conducted a variety of different tests on multiple samples within an hour. This chip design allows for simultaneous delivery of the 96 samples using centrifugal pumping, and our lab has previously used it to deliver multiple DNA-containing samples to multiple oligonucleotide probes in 3 min. Our approach introduces the sample and probes using microfluidic channels with dimensions of 200μm width and 50μm depth, which reduces the required liquid volumes from >50μL/sample to 0.5μL/sample, and distributes samples uniformly, thereby enhancing reproducibility. In our protein detection system, several MAb samples were tested by reacting each with multiple antigen probes. Multiple tests were conducted in a single run either on a single sample, or on multiple samples, with sensitivity comparable or better than ELISA, but with faster detection and higher throughput offered by the NBA chip.

8548-29, Session 1c

Biomimetic approaches for engineered organ chips and skin electronics for in-vitro diagnostics *(Invited Paper)*

Kahp-Yang Suh, Seoul National Univ. (Korea, Republic of); Changhyun Pang, Seoul National University (Korea, Republic of); Kyung-Jin Jang, Wyss Institute for Biologically Inspired Engineering, Harvard University (United States); Hong Nam Kim, Seoul National University (Korea, Republic of); Alex Jiao, University of Washington (United States); Nathaniel S. Hwang, Min Sung Kim, Do-Hyun Kang, Seoul National University (Korea, Republic of); Deok-Ho Kim, Seoul National University (Korea, Republic of) and University of Washington (United States)

Two kinds of biomimetic systems including engineered organ chip and flexible electronic sensor are presented. First, in vivo, renal tubular epithelial cells are exposed to luminal fluid shear stress (FSS) and a transepithelial osmotic gradient. In this study, we used a simple collecting-duct-on-a-chip to investigate the role of an altered luminal microenvironment in the translocation of aquaporin-2 (AQP2) and the reorganization of actin cytoskeleton (F-actin) in primary cultured inner medullary collecting duct (IMCD) cells of rat kidney. We demonstrate that several factors (i.e., luminal FSS, hormonal stimulation, transepithelial osmotic gradient) collectively exert a profound effect on the AQP2 trafficking in the collecting ducts, which is associated with actin cytoskeletal reorganization. Furthermore, with this kidney-mimicking chip, renal toxicity of cisplatin was tested under static and fluidic conditions, suggesting the physiological relevancy of fluidic environment compared to static culture. Second, we present a simple architecture for a flexible and highly sensitive strain sensor that enables the detection of pressure, shear and torsion. The device is based on two interlocked arrays of high-aspect-ratio Pt-coated polymeric nanofibres that are supported on thin polydimethylsiloxane layers. When different sensing stimuli are applied, the degree of interconnection and the electrical resistance of the sensor changes in a reversible, directional manner with specific, discernible strain-gauge factors. We show that the sensor can be used to monitor signals ranging from human heartbeats to the impact of a bouncing water droplet on a superhydrophobic surface.

8548-103, Session 1c

Interactions of stem cells with nanostructured surfaces *(Keynote Presentation)*

Kyu-Back Lee, Korea Univ. (Korea, Republic of)

No Abstract Available

8548-104, Session 1c

Microneedles for delivery of drugs to vascular tissues *(Invited Paper)*

WonHyoung Ryu, Yonsei University (Korea, Republic of)

Vascular diseases such as atherosclerosis or intimal hyperplasia are caused by damage to endothelium or abnormal growth of smooth muscle cells. For the treatment of diseased blood vessels, drug eluting stents (DES) or perivascular devices (wraps or rings) have been explored. Despite many advances, DES still has an issue of relatively low efficiency of drug delivery to vascular tissues. Perivascular devices demonstrated reduction of intimal hyperplasia that occurs after vascular bypass grafting surgery. However, the delivery efficiency and spatial distribution of drug by the perivascular devices are uncertain. In this research, we have developed biodegradable microneedle cuffs (BMC) that wrap around target blood vessels and deliver drugs from the ends of microneedles that are inserted into internal layers of the blood vessels. Insertion of microneedles into either tunica adventitia or media layers increases the efficiency and precision of drug delivery. Thermal drawing and post annealing processes were employed to construct three-dimensional cuff structure containing an array of microneedles. In this talk, the fabrication of BMC using biodegradable polymers will be introduced. Particular emphasis will be given on the formation of ultra-sharp tip using a spatially-discrete thermal drawing method. Mechanical properties and drug delivery function of the BMC will also be discussed depending on the shape and materials of microneedles. Finally, in vitro and in vivo drug delivery performance of the BMCs will be presented and discussed.

8548-105, Session 1c

Functional nanomaterials for chemical sensing and bioengineering applications *(Invited Paper)*

Inkyu Park, KAIST (Korea, Republic of)

In this talk, we present the fabrication, characterization, and applications of functional nanomaterials for chemical sensing and bioengineering purposes. One dimensional (1D) nanostructures such as nanowires and nanotubes have been actively researched due to their unique physical and chemical properties. Their applications range from electronic devices to power conversion devices and to smart windows. One of the main challenges of the applications of 1D nanostructures is their controlled and reliable integration to the device platforms. We have recently developed a facile route to the controlled synthesis and integration of 1D nanomaterials and their structural and chemical conversion for specialized applications. Various composite nanostructures such as nanoparticle-decorated nanowires and porous multi-component metal nanotubes are fabricated by simple wet-chemical synthesis processes on flexible substrates and microfluidic chips for sensing and bioengineering applications.

8548-107, Session 1c

Spectral-domain optical coherence phase microscopy for quantitative biological studies *(Invited Paper)*

Chulmin Joo, Yonsei Univ (Korea, Republic of)

Quantifying depth-resolved optical path-length alteration in transparent biological specimens (e.g., cells) provides a new dimension of study, which may serve as a means of phenotypically differentiating cellular responses to external stimuli. Spectral-domain optical coherence phase microscopy (SD-OCPM) represents a novel optical microscopy technique, capable of measuring optical path-length changes inside the cells. It is based on common-path spectral-domain optical coherence reflectometry to produce depth-resolved reflectance and quantitative phase images with high phase stability. The phase sensitivity of SD-OCPM was measured as nanometer-level for cellular specimens and sub-nanometer level for reflective surfaces (e.g, glass), demonstrating the capability for detecting small structural variation of the specimens.

Here, we will describe a multi-modal microscope that combines unique features of SD-OCPM and multi-photon fluorescence microscopy, and will summarize its biological applications, including quantifying fast and slow intracellular dynamics of human epithelial ovarian cancer cells, as well as multiplexed molecular interaction measurement on activated sensor surfaces.

8548-109, Session 1c

Stretchable photovoltaics *(Invited Paper)*

Jongho Lee, GIST (Korea, Republic of)

This talk presents, using a combination of theory and experiment, the essential mechanics, and the ideas in stretchable solar modules that use ultrathin, single junction GaAs and dual junction GaInP/GaAs solar microcells.

8548-501, Session PLEN1

Nanomaterials in biomedical applications

Meyya Meyyappan, NASA Ames Research Ctr. (United States)

Nanomaterials such as carbon nanotubes (CNTs), graphene and inorganic nanowires have been gaining much attention due to their interesting electronic, mechanical and other properties in a variety of applications. Of these, biomedical applications such as diagnostics, drug delivery and many others have benefitted from the novel properties of these materials. This talk will provide an overview of our long term efforts on biosensors for lab-on-a-chip needs, nanoelectrodes for deep brain stimulation, chemical sensors for detecting biomarkers in human breath and others. Also, a description of the new collaborative program at POSTECH on Ubiquitous health (U-Health) combining advances in information, bio and nanotechnologies. The author acknowledges contribution from J. Koehne, J. Li, Y. Lu, Dr. Kendall Lee, Professor Jeong-Soo Lee, and colleagues at Mayo Clinic and POSTECH.

8548-502, Session PLEN2

MR molecular imaging: Is it promising for cancer theragnostics?

Jin-Suck Suh, Yonsei Univ. College of Medicine (Korea, Republic of)

Molecular imaging is aiming at visualizing molecular events in biologic systems from single cells to whole organisms. Hence it is a right imaging tool to provide information on cell, tissue, organ function and ultimately it will enable us to guide diagnosis and treatment for individualized therapy. There are several imaging means of molecular imaging: Optical imaging, radioisotope imaging, ultrasound imaging, and MR imaging and so on. Regarding MR molecular imaging (in-vivo) we have been focusing on, it is crucial to develop high-specificity / high-sensitivity probes. A novel MR molecular imaging probe will be presented that we have developed. The probe was found to show the utmost sensitivity for the cancer detection in preclinical animal experiments and it implies that there are great potential for clinical implementation. MR molecular imaging will broaden its field by developing tools and probes toward multi-modal imaging as well as multifunctional diagnostic and therapeutic perspectives. In the future it will find new application fields over cancer research.

8548-6, Session 2a

Polymer-based gene carrier for gene delivery and silencing *(Keynote Presentation)*

Won Jong Kim, Pohang Univ. of Science and Technology (Korea, Republic of)

Tremendous impetus has been directed toward the development of various nonviral synthetic delivery systems which could be safer and more efficient. However, the induced cytotoxicity and non-biodegradability of these non-viral polymeric vectors impede the prevalent practical realization of gene therapy. Therefore, in our quest to develop a highly coveted vector which could provide all these attributes, we have devised several highly efficient vector systems. Irrespective of the vector types, efficient gene transfection demands appreciable concentration of efficient cell-binding delivery vectors at the target site at the onset of gene delivery. To address the issue we developed hybrid magnetic nanomaterial composed of superparamagnetic nanoparticles having polyethylene glycol (PEG) pendent and low molecular weight branched polyethylenimine. This covalently conjugated superparamagnetic nanomaterial (BPEI-SPION), displayed transfection efficiency even higher than high molecular weight BPEI (HMW BPEI) and the high transgene expression has been achieved at very low vector dose within very short incubation time.

Our endeavor also encompasses the target specific gene delivery endowed with bioreducibility. We developed multifunctional gene carrier which has incorporated reducible moiety, tumor targeting ligands as well as PEG to achieve efficient release of pDNA, enhanced tumor- specificity and long circulation, respectively.

In conclusion, we have developed polymer-inorganic nanomaterials as a multifunctional gene carrier and smart reducible gene carriers, and confirmed their efficacy as a efficient gene carrier as well as imaging

agent. The success of their gene carriers should drive further research into multipurpose therapeutic biomaterials

8548-9, Session 2a

Applications of magnetic nanomaterials in biomedicine

Leisha M. Armijo, Yekaterina I. Brandt, Antonio C. Rivera, Nathaniel C. Cook, John B. Plumley, Nathan J. Withers, Gennady A. Smolyakov, Natalie L. Adolphi, The Univ. of New Mexico (United States); Todd C. Monson, Dale L. Huber, Sandia National Labs. (United States); Hugh D. Smyth, The Univ. of Texas at Austin (United States); Marek Osinski, The Univ. of New Mexico (United States)

Bacterial biofilms pose a significant public health problem occurring in stents, indwelling catheters, dental implants, and other biological interfaces. Bacterial biofilm infections in lungs are the leading cause of death of patients suffering from cystic fibrosis (CF). CF disease complications, such as chronic inflammation and the presence of highly viscous respiratory tract mucus, severely limit the ability to treat such patients with standard antibiotics. The inflammatory response causes increased respiratory tract tissue damage, and the highly viscous mucus limits mechanical clearance of inhaled microbes, while producing anoxic environmental conditions, thus promoting bacterial biofilm production. The average lifespan of CF patients today is only 35 years with intensive treatment. Methods for for enhanced drug delivery to the lungs of patients with CF using nanoparticles have provided insight to the complexity of the problem, and it appears that an active transport method is necessary. We are exploring the use of magnetic-field-gradient-guided nanoparticles as drug carriers for CF. The use of superparamagnetic nanoparticles as active transporters for this application also allows the exploitation of magnetic hyperthermia, which may further increase transport rates by reducing the viscosity of the CF mucus and reducing bacterial biofilm production. We have selected iron oxide as the superparamagnetic material of choice, due to its high biocompatibility. We have synthesized and characterized iron oxide nanoparticles of various sizes and morphologies for this application. Hyperthermia contributions are characterized using field frequencies from 100 kHz to 1 MHz. In order to take advantage of inherent multifunctionality of colloidal nanoparticles, core/shell type nanoparticles with photoluminescent properties have been synthesized as a model system to allow single-particle tracking studies through an alginate model. Comparison of transport rates for nanoparticles of different sizes and morphologies will be presented.

8548-52, Session 2a

Advanced biohybrid materials based on nanoclays for biomedical applications *(Keynote Presentation)*

Eduardo Ruiz-Hitzky, Materials Science Institute of Madrid, CSIC (Spain)

Bio-nanohybrids prepared by assembling natural polymers (polysaccharides, proteins, nucleic acids, etc) to nanosized silicates (nanoclays) and related solids (layered double hydroxides, LDHs) give rise to the so-called bionanocomposites constituting a group of biomaterials with potential application in medical purposes. In this way, biopolymers, including chitosan, pectin, alginate, xanthan gum, ι-carrageenan, gelatin zein, DNA, etc. have been incorporated in layered host matrices by means of ion-exchange mechanisms producing intercalation composites. Also bio-nanohybrids have been prepared by the assembly of diverse bio-polymers with sepiolite, a natural microfibrous magnesium silicate. The properties and applications of these biomaterials for drug delivery and gene transfection systems, scaffolds for tissue engineering, active phases of ion-sensors and biosensors will be introduced. It should be also discussed the use of synthetic bionanocomposites as new substrates to immobilize microorganisms, as for instance to bind Influenza viral nanoparticles, allowing their application as effective low-cost vaccine adjuvant.

8548-59, Session 2b

Polymer nanoparticle-based nitric oxide (NO) photodonor for novel therapeutics *(Keynote Presentation)*

Yukio Nagasaki, Univ. of Tsukuba (Japan)

Nitrogen oxide is known to play versatile roles in vivo. Excessive NO generation reported to cause antitumor effect in vivo. We started to design new polymer micelle based NO-photodonor for novel anticancer chemotherapy. PEGylated polymer micelles containing 4-nitro-3-trifluoromethylphenyl units within the core moiety were prepared, and their photo-triggered nitric oxide (NO)-generating ability was confirmed by electron spin resonance (ESR) spin-trapping and the Griess method. These micelles were found to be able to deliver exogenous NO into tumor cells in a photo-controlled manner and showed an NO-mediated antitumor effect, indicating the usability of this molecular system in NO-based tumor therapy.

8548-60, Session 2b

Design optimisation of multi-analyte evanescent field biosensor

Kang Nan Khor, Mukhzeer Mohamad Shahimin, Univ. Malaysia Perlis (Malaysia)

Evanescent field has been widely used in optical biosensor to sense the refractive index change of cover layer where target analyte is bound. This method is simple and label-free, thus it can be developed for multianalyte detection. However, sensitivity of sensor has not been fully optimised because important parameters such as thickness and width of waveguide, polarization of optical field are not investigated in detail. In this paper, 1 to 8 Y-branch splitter is designed to detect multianalyte simultaneously at each different output branching waveguides. Design of output waveguides is optimised to maximise the evanescent field while design of Y-branch splitter is optimised to minimise the power loss. Beam propagation method (BPM) is used to simulate the Y-branch splitter and output waveguide. In the simulation, parameters such as thickness and width of channel waveguide, polarization of optical field, effective angle of 1 to 8 Y-branch splitter, type of S-bend waveguide, taper structure of branching point are investigated. The simulation results conclude that strongest evanescent field at cover layer is observed at specific thickness and width of output waveguide. The optimum thickness and width of silicon nitride waveguide with refractive index of 1.98783 at 1um wavelength and TE polarization are 40nm and 800nm respectively. Optimum thickness and width is served as reference in the fabrication of channel waveguide to realize evanescent field biosensor with optimised sensitivity.

8548-61, Session 2b

Development of a reliable biosensor based on Photoluminescence emission in single-walled carbon nanotubes for mutation detection in diseased DNA

Pramod K. Bhatnagar, Jyoti Bansal, Univ. of Delhi (India); Parmatma C. Mathur, Univ of Delhi (India)

SWNTs have been used as target for sequence detection of ssDNA

for medical diagnostics. In order to disperse the bundle of SWNTs, we have used an aqueous solution of alternating G and T sequence of ssDNA attached with diseased DNA in pure water. The free ssDNA, which has not been wrapped on the SWNT surface, has been removed using high molecular-weight dialysis. The PL spectrum of the DNA-SWNT complex has been studied in the nIR region. Afterthat we add ssDNA having complementary sequence (cDNA) into the above solution and incubate it at about 45oC for 20minutes to achieve steady state hybridization with ssDNA already wrapped on the SWNT target. The fluorescence spectrum of the cDNA-DNA-SWNT complex has been studied and the resulting blue shift with respect to DNA-SWNT fluorescence peak has been measured as a function of concentration of cDNA. We will also examine the effect of mutated DNA on photoluminescence spectrum.

8548-62, Session 2b

Disposable biosensors made with cellulose and nanomaterials hybrid composites

Jaehwan Kim, Inha Univ. (Korea, Republic of); Hyun-U Ko, Abu Hasan Khondoker, Mohammad Maniruzzaman, Inha University (Korea, Republic of)

Biosensors work on the physiochemical changes caused by the interaction between bioreceptor and the analyte such as change of light absorption or electrical charge or frequency of oscillation. Several types of biosensors have been reported so far, including clays, nanoporous alumina membranes, SnO_2/ITO and metallic nanotubes arrays, etc. Recently there has been increasing trend to utilize the polymer-metal oxide hybrid composite as a biosensor.

Herein we report inexpensive, flexible and disposable biosensors based on cellulose and inorganic nanomaterials such as tin oxide (SnO_2), titanium dioxide (TiO_2) and multi-walled carbon nanotubes. We use a regenerated cellulose membrane as a base material because of its advantages in terms of biodegradable, biocompatible, flexible characteristics as well as low price. A thin layer of inorganic nanomaterials was introduced onto the cellulose surface via liquid-phase deposition technique. We present a systematic study on the detection of glucose and urea by employing cellulose-inorganic hybrid nanocomposites on which proper enzyme is immobilized via physical adsorption process. Effect of inorganic material deposition and glucose concentration on their electrical properties of biosensors will be evaluated by measuring the current in the presence of electrical potential.

8548-108, Session 2c

In vivo nano-molecular imaging of cancer *(Keynote Presentation)*

Keon Wook Kang, Seoul National Univ. College of Medine (Korea, Republic of)

In vivo molecular imaging is used for early detection, characterization of disease and an early assessment of treatment efficacy through imaging molecular/cellular events in living organisms. Molecular imaging is useful not only for clinical studies but also for developing new drugs and new treatment modalities such as gene or stem cell therapy. Multifunction nanoparticles can be used for diagnostic in vitro/in vivo and therapeutic purpose as well. PET/MRI/fluorescent triple modality imaging using multifunctional nanoparticles can guide surgical interventions especially minimal invasive procedures such as endoscopic, laparoscopic or robotic ones. If multimodal molecular probes are used targeting cancer in patients, the locations of tumors and metastatic lymph nodes can be assessed using whole body PET/MRI. The surgeon can locate the tumor, its margin and lymph nodes by fluorescent signal using videoscope during surgery, the pathologist can assess tumor margin and lymph nodes using fluorescent microscope. Nanoparticles are able to carry fluorescent dye, radioisotope, drugs, genes, and targeting biomarkers on their surface and inside. We can add targeting function to the triple-modality nanoparticles by conjugating 3D scaffold such as antibodies, peptides, and aptamers. The particles can trace targets and reveal the lesions after systemic administration. We validated a molecular targeted nano-drug delivery system using in vivo SPECT/CT imaging of an I-125 labeled gold nanoparticle conjugated with cyclic RGD peptide in a U87MG tumor bearing mouse model. Combining nanotechnology and in vivo imaging, personalized targeting therapy might be possible in the future after validating the targeting efficiency using multimodal imaging.

8548-111, Session 2c

Noninvasive delivery of nanomedicine through vascular barriers using ultrashort pulsed laser *(Invited Paper)*

Chulhee Choi, KAIST (Korea, Republic of)

Biopharmaceuticals such as peptides, protein and nucleic acids are considered as next-generation medicine due to their high selectivity to disease-specific targets and superior bioavailability; however, difficulty in targeting specific organs due to relatively large size compared to conventional chemical drugs should be solved. Especially, the cerebral vasculatures are practically impermeable to nanoscale drugs due to highly organized blood-brain-barrier (BBB), imposing a challenge to develop effective CNS drugs. Our group has recently demonstrated that brief irradiation of femtosecond lasers (FL) can evoke a repertoire of cellular events and induce a transient permeabilization of BBB, suggesting that FL can be used for drug delivery into the CNS or other organs. Current issues for FL-induced drug delivery involve understanding the molecular mechanisms related to photon-endothelial cell interactions, safety and potential applications. As molecular mechanisms responsible for noninvasive photon-tissue interactions, photochemical reaction, mainly reactive oxygen species (ROS), are speculated to be the major one because selective blockade of ROS using chemical scavengers abrogated FL-induced permeability through endothelial junctions. To minimize the unwanted toxicity, it is important to understand not only the mechanisms responsible for FL-induced physiological events but also FL-evoked cell death or tissue injuries. Potential mechanisms for FL-associated toxicity and clinical applications will be discussed.

8548-177, Session 2c

Targeted cancer imaging using terahertz technique

Seung Jae Oh, Yong-Min Huh, Yonsei Univ College of Medicine (Korea, Republic of); SeungJoo Haam, Department of Chemical & Biomolecular Engineering, Yonsei University (Korea, Republic of); Joo-Hiuk Son, University of Seoul (Korea, Republic of); Jin-Suck Suh, Yonsei Univ College of Medicine (Korea, Republic of)

Terahertz imaging has been used to diagnose the cancer as a novel medical imaging technique due to its high sensitivity of water molecular dynamics. This imaging system, however, has not classified the differences at the molecular and cellular levels. The recently developed terahertz molecular imaging (TMI) technique enhanced the sensitivity of the THz imaging by employing nanoparticle probes (nanoprobes). The nanoprobe in solution increases the ambient temperature of water under the irradiation of the optical beam. The change of temperature enables the THz wave to sense the existence of gold nanorods (GNRs). Herein, we showed that the target specific in vivo imaging of cancers was obtained by TMI with the phase conjugated GNRs. The Cetuximab-PEGylated gold nanorods (CET-PGNRs) were used as targeted nanoprobes. The CET-GNRs were injected into the mouse bearing the A431 epidermoid carcinoma tumor through the tail vein. The TMI image of cancer was obtained in vivo and TMI images of tumor, liver, spleen, kidney, and brain also were showed and compared

with the conventional THz image. The amplitudes of the TMI images of the tumor, liver, and spleen were higher than those of the brain and kidney. It implied that the nanoprobes were delivered into the targeted tumor via circulation system. The results displayed that TMI could be used as the early cancer diagnostic method.

8548-10, Session 3a

Arginine-engrafted biodegradable polymer for siRNA-mediated treatment of melanoma *(Keynote Presentation)*

Sang-Kyung Lee, Hanyang Univ. (Korea, Republic of)

The RNAi technology has great potential for use in cancer therapy and a plethora of genes have been identified and evaluated as effective RNAi targets. However, tumor regression is highly dependent on the type and the stage of cancer, the gene target chosen for silencing and the method of RNAi-drug delivery. We have investigated whether the efficacy of siRNAs in cancer therapy could be improved by the simultaneous blockade of several gene products and pathways implicated in cancer biogenesis. We chose to target the gene products of bcl-2, c-Myc and VEGF that are frequently overexpressed in multiple tumors, including melanomas. Further we use a novel polymer – a arginine-grafted bioreducible polydisulfide amine (ABP) with increased siRNA encapsulating properties and reduced toxicity for siRNA delivery. Combinatorial treatment with all three siRNAs not only allowed extended control of B16.F10 melanoma cell proliferation in culture but also in vivo in a mouse model of solid tumor engraftment. Intratumoral injection with a siRNA cocktail targeting the three genes almost completely regressed a larger tumor volume in contrast to single or dual siRNA treatments. Further, systemic intravenous administration of the ABP/siRNA cocktail enabled enhanced permeability and retention (EPR) with a significant anticancer activity. Our results suggest that multiplexing siRNAs can results in a synergistic inhibitory effect on cancer progression and combination therapy incorporating multiple RNAi targets with current modalities would vastly improve the prognosis of cancer.

8548-11, Session 3a

Near-infrared light-responsive intracellular drug and siRNA release using Au nanoensembles with oligonucleotide-capped silica shell

Fong-Yu Cheng, Chen-Sheng Yeh, National Cheng Kung Univ. (Taiwan)

Au nanorods (NRs) with strong surface plasmon resonance are highly absorbent of light in the NIR region and can act as nanoheater by absorbing the NIR laser.11 Herein, we started with Au NRs as a template to buildup mesoporous silica ($mSiO_2$) shell. The double-stranded oligonucleotides (dsDNA) were tethered to mesopore pore openings to encapsulate anticancer Doxorubicin (Dox) drug. Contrary to use of femtosecond laser, a continuous-wave diode laser (808 nm), with advantages of less expense and easy to handle, was employed to irradiate Au NR@mSiO2 (AuMS) hybrid nanocontainers. The remotely NIR-triggered intracellular drug release was achieved by means of the photothermal conversion of the Au NRs, which induced dehybridization of the DNA duplexes. Different from other gating agents, such as inorganic nanoparticles, organic and polymeric molecules, the oligonucleotide bio-gate can be replaced with functional nucleic acids to provide additional gene delivery. In this regard, we have demonstrated using siRNAs attaching to the openings of pores. Upon NIR irradiation, the released GFP-interfered siRNAs silenced GFP expression in GFP expressing HeLa cells (human epithelial carcinoma cell line, HeLa-GFP). Both Dox drug and GFP-interfered siRNA can be released in response to a sequential laser ON-OFF manner. Scheme 1 illustrates the design of the Au NRs with oligonucleotides-capped silica shell and the experimental performance.

8548-12, Session 3a

Synthesis of iron oxide nanotubes and their drug loading and release capabilities

Linfeng Chen, Jining Xie, Kiran R. Aatre, Vijay K. Varadan, Univ. of Arkansas (United States)

Due to their structural and magnetic properties, iron oxide nanotubes are extremely attractive for biomedical applications, and are among the most widely used nanomaterials in nanomedicine. This paper reports the synthesis of iron oxide nanotubes, and their potential applications in drug delivery. Three types of iron oxide nanotubes, i.e., hematite, maghemite, and magnetite, were synthesized using different methods, and the effects of synthesis methods on the morphological and crystalline properties of the synthesized nanotubes were analyzed. The hematite nanotubes synthesized by template assisted thermal decomposing method have uniform walls and good crystallinity. The maghemite nanotubes synthesized by hydrothermal method may have cup-like or tube-like shapes, and they also have good crystallinity. The magnetite nanotubes synthesized by template filtering method have nonuniform walls and acceptable crystallinity. The maghemite and magnetite nanotubes respond obviously to external magnetic fields, indicating their stronger magnetic properties than those of hematite nanotubes. To explore their applications in drug delivery, a preliminary experimental study on the drug loading and release capabilities of the synthesized iron oxide nanotubes was conducted, with ibuprofen sodium salt (ISS) as the drug model. It was found that drugs could be efficiently loaded in iron oxide nanotubes, and the loaded drugs could be released in hours. Two approaches for controlled drug release are proposed in the final part of this paper, which could be helpful in decreasing or eliminating the undesired drug release in the drug delivery procedure.

8548-13, Session 3a

Coloring Brain Tumor with Multi-potent Micellar Nanoscale Drug Delivery System

Kyuha Chong M.D., Kyungsun Choi, EunSoo Kim, Eun Chun Han M.D., Jungsul Lee, Junghwa Cha, Taeyun Ku M.D., Jonghee Yoon, Ji Ho Park, Chulhee Choi M.D., KAIST (Korea, Republic of)

Brain tumor, especially glioblastoma multiforme (GBM), is one of the most malignant tumors, which not only demands perplexing approaches to treat but also requires potent and effective modality to deal with recurrence of the tumor. Standard treatment of GBM is following concurrent chemoradiation after surgical resection, which prolong mean survival of patients only to 12 to 15 months. Even though many alternatives were introduced with many laboratory and clinical trials to overcome malignant progress of GBM, advancement of prognosis is still stagnant. Photodynamic therapy (PDT) is a treatment that uses photosensitizing agent to destroy tumor cells under photoactivated condition, and has been recommended as a third-level treatment. We are trying to investigate possibility of the PDT as an efficient adjuvant therapeutic modality for the brain tumor. With adequate photon-delivery system and photosensitizer, suppressed viability of tumor cells was verified, in vitro. Hydrophobic photosensitizer was modified as micellar nanoparticle to maximize tumor specificity of photosensitizer. Applying micellar nanoscale drug delivery system, localization of the tumor was identified, in vivo, which is able to be referred as photodynamic diagnosis. Herein, we are suggesting photodynamic diagnosis and therapy are able to be performed simultaneously in our nanoscale drug delivery system.

8548-14, Session 3a

Polypeptide thermogel as an injectable biomaterial *(Keynote Presentation)*

Byeongmoon Jeong, Ewha Womans Univ. (Korea, Republic of)

Polypeptides develop unique secondary structures such as random coils, beta-sheets, and alpha-helix. Based on the control of these structures, we have developed a series of polypeptide-based block copolymers of which aqueous solutions undergo sol-to-gel transition as the temperature increases. Depending on the composition and molecular weight of the polypeptide, the self-assembled nano structures and enzymatic degradability of the in situ formed gel could be controlled. Mechanism of sol-to-gel transition involves the secondary structural changes of polypeptide as well as the dehydration of the hydrophilic block. As an injectable depot system, protein delivery and three dimensional cell culture were investigated. The in-situ formed gel provided a biocompatible microenvironment for protein drug delivery and 3D culture of the encapsulated cells, where the secondary structure of the polypeptide and modulus of the in-situ formed gel play a significant role in controlling the proliferation of the cell and biomarker expression.

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8548-15, Session 3a

Ultrasound thermally triggered rapid drug release system composed of liposomes with gaseous precursor inside

Hsiang-Fa Liang, Industrial Technology Research Institute (Taiwan); Min-Fan Chung, National Tsing Hua Univ. (Taiwan); Ming-cheng Wei, Industrial Technology Research Institute (Taiwan); Hsin-Wen Sung, National Tsing Hua Univ. (Taiwan)

The ABC has a decomposition temperature of 36°. After heating ABC filled liposomes (ABC liposomes) to 42°, the ABC converts to gas form and then explodes liposomes to release drugs inside. From our preliminary data, calcein was released from the ABC filled liposome immediately after heating at 42°. More than 60% of calcein was released at t = 60 min, in contrast, only 20% calcein was released at 37. In addition, the calcein released from PBS filled liposome showed similar release profiles at 37 and 42°. These observations indicated that the calcein release was due to the presence of temperature sensitive ABC. The ultrasonic contrast enhanced images were also observed after heating the ABC liposomes to 42°. The results suggested that after heating ABC liposomes to 42°, ABC was vaporized to explode the liposomes, thus made calcein release and ultrasonic contrast available. The properties of prepared ABC liposome are suitable for the combination with ultrasound instrument for diagnosis and drug trigger release.

8548-16, Session 3a

Fluorescent Au8@PAMAM nano-clusters as carriers for efficient gene delivery

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Gene therapy is now a promising treatment for some diseases, such as hemophilia.However, how to carry genes to the target is a main issue. Recent works have devel- oped many drug carrier systems for this purpose.

For the successful delivery of genes or drugs into target cells, the carriers must possess 3 main functions. 1) Specificity, help to been recognized and uptaken into cells. 2) Protection, genes can't be decomposed during the transport. 3) Payload, genes need to be released when they achieve their destinations, the nucleus.

There are two main categories of delivery systems, one group is the capsules-like vehicles, including micelles and liposomes. The other group is by combing the genes or drugs on to the carriers. Such carriers include linear polymers, dendrimers and diverse nanoparticles.

PAMAM, a polycationic dendrimer, is well known that have high efficiency for gene delivery. The successful delivery of genes is main due to the proton sponge effect.

We fabricate Au nanoclusters by using PAMAM as the templates. The as-prepared gold nanoclusters possess 8 Au atoms which were confirmed through the high resolution mass spectrometer. The Au nanoclusters have a fluorescence peak at 450 nm that we can simultaneous track the distributions of genes by measuring fluorescence from the nanoclusters.

We used them to carry a plasmid DNA that will transfect the green fluorescent proteins(GFP) on actins. Surprisingly, the GFPs expressed in each cells are much more uniform by using Au8@PAMAM as the carriers. In the contrary, by using PAMAM as carriers, GFPs only over-expressed in few cells while others show low transfection efficiency. While the Au8@PAMAM shows less cytotoxicity on normal cell (MRC-5) than cancel cells (Cl1-0 & A549). This selective property makes it more potential to be a suitable drug carrier system.

8548-63, Session 3b

Sensoring, monitoring and control of protease activities in theragnosis *(Keynote Presentation)*

Ick Chan Kwon, Korea Institute of Science and Technology (Korea, Republic of)

In recent years, advances in medical imaging technology have been emphasized along with new advances in the field of cellular and molecular biology. Emerging field of medical imaging, i.e. Molecular Imaging, allows not a traditional image of anatomical changes, but a biological characterization of disease state at molecular or cellular lever. Interdisciplinary research at the interface of nanotechnology and molecular imaging had led to elucidate key factors that determine specificity in diagnosis and therapeutics. For example, with combining molecular imaging technology and drug delivery system, a novel design of drug screening or new approaches in drug development can be performed in animal models. Polymer nanoparticles bearing near-infrared fluorescent dyes can be utilized in determining optimized therapeutic dosages or frequencies of drug administration. These nanoparticles also can be utilized as molecular probes for visualization of therapeutic efficacy in small animals. Design of novel polymeric nanoparticles with high specificity in cellular or molecular responses, application of molecular imaging probes toward the era of Personalized Medicine will be presented in current study.

8548-65, Session 3b

Surface functionalisation on optical channel waveguide for biological cell manipulation

Mukhzeer Mohamad Shahimin, Sohiful Anuar Zainol Murad, Univ. Malaysia Perlis (Malaysia)

Surface functionalisation has emerged as a powerful tool for mapping limitless surface-cell membrane interaction in diverse biomolecular applications. Inhibition of nonspecific biomolecular and cellular adhesion to solid surfaces is critical to device performance, particularly for in vitro bioassays. In this paper, polyethylene glycol

(PEG) based surface passivation techniques have been demonstrated on optical channel waveguide to reduce friction, to prevent biological cell adhesion and to facilitate in the optical sorting of particles and biological cells. The PEG layers with different fabrication parameters have been characterised in terms of its thickness and friction coefficient via ellipsometry and friction force microscopy to provide the optimised parameters within the specified range. Results from the Brownian and propulsion of particles and biological cells on the optical channel waveguides shows 25% increment in their mobility on the PEG functionalised surface.

8548-66, Session 3b

Comparison of functionalized and non-functionalized multi-walled carbon nanotubes for sensing applications

Parmatma C. Mathur, Amandeep Kaur, Inderpreet Singh, Univ. of Delhi (India)

The sensors fabricated with Carbon nanotubes (CNTs) have various advantages over conventional sensors. The gas sensing property of the CNTs at room temperature is applicable to many kinds of applications due to the fact that CNTs have nano-sized morphology and high surface-to-volume ratio, resulting in high sensitivity and rapid gas adsorption. In the present work both functionalized (f-MWNT) and non- functionalized multi walled carbon nano-tube(n-MWNT) in polymethyl methacrylate (PMMA) matrix have been fabricated keeping nitro methane as solvent. MWNT/PMMA solution is prepared by dispersing MWNT powder in PMMA and nitro methane Then, the solution is ultrasonicated and later centrifuged for 10minutes.The upper 80% portion of the suspension is decanted off. Thin film is prepared by drop casting the prepared solution on patterned indium tin oxide (ITO) coated glass. The percolation limit of the both MWNT composite films is calculated using the percolation model following the procedure reported in our earlier work with Single walled carbon nanotubes. Conductivity measurements have been carried out using keithly source meter 2400 for two gases(ethanol and LPG-liquid petroleum gas)with different concentration of gases in ppm. The resistance of the film is found to increase sharply in few seconds on exposure to gases (when gas is adsorbed), which is attributed to the charge transfer induced by adsorption of polar organic molecules on f-MWNT. The degree of change in resistance of f-MWNT is much higher than that for n-MWNT. The response and recovery time for different polymer matrix for e.g.PMMA,PVA(Polyvinyl alcohol),HDPE(high density polyethylene) has also been studied which is of the order of a few seconds.Results for typical f-MWNT/ PMMA for ethanol sensing will be presented. The observed change in resistance is due to swelling of film by adsorption of gas there by increasing distance between the MWNT. This swelling has been verified by Atomic force microscopy(AFM) measurements.It is concluded that f-MWNT is better for sensing applications.

8548-67, Session 3b

Biomarkers for diagnosing changes in blood: from nanotoxicity to neurodegeneration *(Keynote Presentation)*

Seong Soo An, Gachon Univ. (Korea, Republic of)

Biomarkers are tools to measure and to evaluate normal biological processes, pathogenic processes or pharmacological response, as indicators with specially characteristics or signatures. Various biomarkers were thought after for all pathological situations. Blood Pathogen Laboratory has been focusing in developing qualitative and quantitive biomarkers for least invasive monitoring methods from the neurotoxic ramifications by genetic and environmental factors. For the assessing neurotoxic effects by nanoparticles, protein coronas (bound proteins) on the surface of nanoparticles from blood were analyzed for the potential recommendations or branched correlations for pathological conditions. Hence, underlying hypothesis is that nanoparticles will interact with various proteins in blood for causing their influenced pathways. Same concept was applied to various neurodegenerative diseases for developing biomarkers, especially with prion protein, causing Transmissible spongiform encephalopathies (TSEs). Determinant biomarkers will be presented, amyloid-beta for Alzheimer's disease, alpha-synuclein for Parkinsons's disease, Tau for Taupathy, and huntingtin for Huntington's disease.

8548-68, Session 3b

Nanostructure based SPR sensor for cell secretion study

Shuhan Wu, National Yang-Ming Univ. (Taiwan)

No Abstract Available

8548-69, Session 3b

Implantable and bio-integrated flexible GaN LED *(Invited Paper)*

Keon Jae Lee, KAIST (Korea, Republic of)

III-V LEDs have superior characteristics, such as long-term stability, high efficiency, and strong brightness compared to OLED. However, due to the brittle property of inorganic materials, III-V LED limits its applications for the flexible electronics. This seminar introduces the flexible GaN LED on plastic substrates that is transferred from bulk GaN wafers. The superb properties of the flexible GaN LED in terms of its wide band gap and high efficiency enable the dramatic extension of not only consumer electronics but also the implantable biomedical applications. A bio-integrated LED is demonstrated as a prototype for detecting a cancer or even treating a disease in invivo condition. These results show that the III-V based flexible LED can be used as the future flexible light source and a type of implantable LED biomedical applications.

This seminar also introduces a highly efficient and printable BaTiO3 thin film nanogenerator on plastic substrates. Energy harvesting technologies converting external biomechanical energy sources (such as heart beat, blood flow, muscle stretching and animal movements) into electrical energy is recently a highly demanding issue in the materials science community. Herein, we describe procedure suitable for generating and printing a lead-free microstructured BaTiO3 thin film nanogenerator on plastic substrates to overcome limitations appeared in conventional flexible ferroelectric devices.

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8548-112, Session 3c

Nanostructure of human internal mammary arteries measured by coherent anti-Stokes Raman scattering microscopy *(Keynote Presentation)*

Eun-Soo Lee, University of Science and Technology (Korea, Republic of) and Korea Research Institute of Standards and Science (Korea, Republic of); Dae Won Moon, Korea Research Institute of Standards and Science (Korea, Republic of) and University of Science and Technology (Korea, Republic of); Se-Hwa Kim, Korea Research Institute of Standards and Science (Korea, Republic of)

Human internal mammary artery (IMA) is known for the rare incidence of atherosclerosis due to resist the cholesterol buildup remarkably. However, the structure-based studies for IMA's resistance to atherosclerosis are not known due to the limit of tools. Here, we examined the en-face nano-structures of IMA using coherent anti-Stokes Raman scattering (CARS) microscopy, specially focusing on the distribution of lipid droplets and the structure of extracellular matrix. Human IMAs were harvested from 5 individuals and subjected to 3-dimensional CARS imaging (300 nm of lateral resolution, 900 nm of axial resolution). The structure of IMA was characterized by 3 major layers by en-face CARS imaging. Interestingly, intmal regions showed more compact matrix structures than media regions. Also, we found that lipid droplets were uniform (diameter: 2.5±0.6 μm) and dominantly observed at superficial intima (Z=0 - 15 μm). The restricted localization of lipid droplets might be caused by not only compact intmal structures but also elevated expression of fatty acid binding protein 4 in IMAs measured by confocal microscopy. These results represent that en-face fine structures of IMA by CARS can provide a new perspective to understand the relatively low incidence of atherosclerosis.

8548-113, Session 3c

Surface plasmon enhanced biomolecular imaging of intra/extracellular processes *(Invited Paper)*

Donghyun Kim, Yonsei Univ (Korea, Republic of); Youngjin Oh, Wonju Lee, Yonsei University (Korea, Republic of)

There has been an exponential growth of interests in nanoplasmonics for enhanced optical characteristics useful in various biomedical engineering applications. While traditional thin film-based plasmon detection allows molecular imaging and sensing by localizing evanescent fields axially, nanoplasmonics further enables localization of near-fields in the lateral plane and empowers researchers with novel approaches that were previously deemed unrealizable.

Surface-enhanced nanoplasmonic substrates can create locally amplified electromagnetic near-field or hot spots as a result of evanescent field localization. The production and maintenance of hot spots have been explored in many studies because of the potential for enhanced detection sensitivity and improved resolving power in imaging applications.

In this direction, three key aspects need to be considered, i.e., surface plasmon enhanced localization and amplification of near-fields, management of target distribution, and novel detection strategies. In particular, this presentation will describe recent approaches for efficient excitation of localized surface plasmon using nanostructures aimed at diverse target interactions including DNA hybridization, antigen-antibody binding, and intra/extracellular protein dynamics. Also discussed are the efforts to manage and control target molecular distribution. The colocalization of target molecules with localized near-fields may be critical to the enhancement of optical signatures by making an optimal use of field localization. In addition, novel detection schemes such as phase imaging, which may be combined with nanoplasmonics for enhanced sensing and imaging, will be presented.

8548-114, Session 3c

Combined two-photon microscopy and optical coherence tomography for in vivo tissue imaging *(Invited Paper)*

Ki Hean Kim, Pohang Univ of Science and Technology (Korea, Republic of); Beomjoo Kim, Taejun Wang, Yeorum Yoon, Minsung Jang, Bo-Gie Yang, Myung Ho Jang, Junsang Doh, Pohang University of Science and Technology (Korea, Republic of)

The combination of two-photon microscopy (TPM) and optical coherence tomography (OCT) is useful in conducting in-vivo tissue studies, because they provide complementary information regarding tissues. In the present study, we developed a new combined system using separate light sources and scanners for individually optimal imaging conditions. TPM used a Ti-Sapphire laser and provided molecular and cellular information in microscopic tissue regions. Meanwhile, OCT used a wavelength-swept source centered at 1300 nm and provided structural information in larger tissue regions than TPM. The system was designed to do simultaneous imaging by combining light from both sources. TPM and OCT had the field of view values of 300 μm and 800 μm on one side respectively with a 20x objective. TPM had resolutions of 0.47 μm and 2.5 μm in the lateral and axial directions respectively, and an imaging speed of 40 frames/s. OCT had resolutions of 5 μm and 8 μm in lateral and axial directions respectively, a sensitivity of 97dB, and an imaging speed of 0.8 volumes per second. This combined system was tested with simple microsphere specimens, and was then applied to image small intestine and ear tissues of mouse models ex-vivo. Molecular, cellular, and structural information of the tissues were visualized using the proposed combined system.

8548-115, Session 3c

Photoacoustic tomography to mapping sentinel lymph nodes with carbon nanotubes *(Invited Paper)*

Junghwan Oh, Pukyong National Univ (Korea, Republic of)

The current study has presented the feasibility of noninvasive in vivo PA mapping of sentinel lymph nodes with injection of SWNTs-ICG into a rat. Injection of SWNTs-ICG helped SLNs to be apparently visualized and distinguished from the peripheral blood vessels. A noninvasive method for accurately mapping axillary SLNs could be used to map sentinel lymph nodes in breast cancer patients and monitor vascular disease. In addition, a clinical PAT system with higher sensitivity may allow us to use relatively low concentration of SWNTs-ICG with sub-nM sensitivity and sub-mm spatial resolution, and thus its consequent clinical translation ability becomes high.

8548-116, Session 3c

Reengineering the delivery of contrast medium in clinical medical imaging *(Keynote Presentation)*

Kyongtae Ty Bae, Univ. of Pittsburgh Medical Ctr. (United States)

In many clinical CT and MR examinations, contrast enhancement is extremely valuable for the visualization of normal tissue as well as the diagnosis of soft tissue diseases. Although there is an intrinsic contrast between a lesion and surrounding tissue, it is critical to selectively enhance the pathology or the structure of interest by administering a contrast agent. In recent years, there have been dramatic improvements in speed of CT and MR data acquisition because of rapid advances in hardware and software technology. However, the technical developments in contrast administration and scan timing have been slow and lagging behind the technical developments in

image acquisition. We can certainly improve and optimize our practice of contrast medium enhancement. The purpose of this presentation is to introduce and discuss various components such as contrast pharmacokinetics, physiology, computer modeling, and injector that are involved in 'reengineering' the delivery of contrast medium in clinical medical imaging.

8548-117, Session 3c

Digital holographic microscopy by using fresnelets basis

Nazeer Muhammad, Hanyang Univ. (Korea, Republic of)

A new method of digital off-axis hologram reconstruction based on the Fresnelets basis has been proposed. For this a combination of composite filtering, Abbe's limitation and digital lens formulae with an appropriate handling of Fresnelets coefficients are used. Unlike other similar approaches, the proposed method provides the information at larger distance with reconstruction of large size image noticeably. The method can facilitate the spontaneous and transverse resolution of microscopic image, identical to that in classical optical microscopy, which has better applicability. Moreover the proposed method is promising to analyse the texture of phase contrast by using the brushlet application.

Key-words: Fresnelets basis: Lens Formula; Composite Filtering; Brushlet; Holography Microscopy.

8548-118, Session 3c

Autoconfocal transmission microscopy based on nonlinear detection

Chulmin Joo, Yonsei University (Korea, Republic of)

Laser-scanning confocal microscopy (LCSM) is capable of producing high-contrast, high-resolution images of biological specimens with depth-sectioning capability. The improved image contrast and depth resolvability in LCSM is enabled by a physical pinhole in the image plane, which allows in-focus portion of light to be measured while rejecting stray light from out-of-focus background. Among the various modes of operation in LCSM, the transmission mode, which measures the transmitted light through the specimen, has an advantage over the reflection (or epi-detection) mode, in that the transmitted light has higher intensity, alleviating a need for highly sensitive detectors (e.g. PMT). Yet, to acquire images, a dedicated mechanism is required to descan the beam or to move the pinhole synchronously with the illumination beam.

We developed a simple, self-aligned (pinhole-less) confocal transmission microscopy based on nonlinear optical detection with a silicon photodiode. Silicon detectors produce photocurrents in quadratic dependence on incident optical intensity under the pulsed illumination of light with wavelengths longer than 1.2 um. We exploit this nonlinear absorption process to reject out-of-focus diffuse background and to perform depth-sectioning microscopic imaging. We will demonstrate a comparable background rejection capability of our method to linear confocal detection, and present three-dimensional images of biological tissues.

8548-43, Session PSMon

Nano-structured microparticles for prolonged residence time on preocular surface

Chun Gwon Park, Min Park, Sung Yoon Choi, Ji Eun Lee, Seung Ho Lee, Gyeong-Seon Shin, Young Bin Choy, Seoul National Univ. College of Medicine (Korea, Republic of)

Topical drug administration is widely used to treat diverse eye diseases owing to ease of administration and high patient compliance. However, this still poses problems, such as short residence time and low bioavailability of drug, needing multiple daily doses. To resolve this, we fabricated nano-structured microparticles (NM) of large surface area as a potential drug carrier to increase the retention time of microparties on the eye in this study. For this purpose, nanofibrous sheets of poly (lactic-co-glycolic acid) and polyethylene glycol (PEG) as a wall material and mucoadhesion promoter, respectively, were freeze-milled to produce NM, hence enhanced retention time. To further increase retention time of NM on the preocular surface, NM was embedded in polyvinyl alcohol (PVA) matrix to form a dry table, which was rapidly dissolved, when administrated into eye, to release only NM on the eye. In vivo animal study, using a rabbit model, revealed that 73 % of NM with PEG still resided on the preocular surface 10 min after administration as a table form while more than 70% of the other types of microparticles disappeared during the same period. Also, more than 13 % of NM with PEG was ept on the preocular surface for up to 90 min due to the synergetic effects of particle geometry, mucoadhesive promoter and tablet formulation. Therefore, we conclude that mucoadhesive nano-structed microparticle in a dry tablet form, proposed in this study, is a promising carrier for ophthalmic drug delivery.

8548-45, Session PSMon

Properties of herbal extracts against Propionibacterium acnes for biomedical application

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Topical erythromycin and clindamycin are also used frequently to treat acne. Propionibacterium acnes (P. acnes), one of the anaerobic bacterium, causes inflammatory acne. Topical antibiotics reduce the number of P. acnes and have an anti-inflammatory activity, but these treatments have a major disadvantage of a rapid increase in bacterial resistance. The widespread use of antibiotics for treatment of acne has resulted in an increase in the resistance of skin bacteria. The problem of bacterial resistance is now increasingly affecting the treatment of acne vulgaris. Recently, several herbs with inhibitory activity against P. acnes growth and the inflammatory response have provided encouraging benefits for people suffering from acne vulgaris. Medicinal herbs have been used worldwide in many kinds of therapeutic agents since the earlier days.

8548-102, Session PSMon

A portable microfluidic chip system for cancer diagnosis with simultaneous detection methods

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In clinical and biological fields, circulating tumor cells (CTCs) attracts much attention for the valuable information about cancer progression, cancer status, and prognosis after the treatment with metastatic cancer. Recently, many researchers have studied to count CTCs efficiently. Representative methods of CTC detection are the immune-

reaction based method and the morphology-based method. However, the immune-reaction based method is weak due to the imperfect markers, and morphology-based method has a defect because of the unclear criterion. In this paper, we described the CTC detection system based on flow cytometry technique with morphology and immue-reaction based methods. The size and the immune-reaction information can be simultaneously obtained from DC impedance based detection and fluorescence detection, respectively. The performance of our system was evaluated with fluorescence beads (Bangs Lab.). To apply the proposed system to biological samples, the human ovarian cancer cell lines (OVCAR-3) suspended in phosphate buffered saline (PBS) were tested. OVCAR-3 cells were stained by fluorescence tagged anti-epithelial cancer adhesion molecule (EpCAM). The portable flow cytometer system could detect the cancer cells with these methods. The proposed system has sufficient potential for point-of-care testing type cancer cell counter and many valuable clinical applications in the near future.

8548-150, Session PSMon

Absorption, distribution, metabolism, and excretion of zinc oxide nanoparticles

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Zinc oxide (ZnO) nanoparticle is one of the most widely applied materials in diverse fields due to its UV light absorption, antimicrobial, catalytic, semi-conducting, and magnetic properties. However, toxicological effects of ZnO nanoparticles in animal models were not evaluated, particularly, with respect to particle size. Moreover, any research on kinetics of ZnO nanoparticles in vivo has not been yet performed. The aim of this study was, therefore, to evaluate the pharmacokinetics of ZnO nanoparticles of two different sizes (20 nm and 70 nm) in male and female rats. The blood, tissues, urine, and feces were collected and Zn concentration was measured with inductively coupled plasma-atomic emission spectroscopy (ICP-AES). The result showed that the plasma zinc concentration of both ZnO nanoparticles increased during 24 h post-administration in a dose-dependent manner and they were distributed to the main target organs such as liver, lung and kidney within 72 h without any significant difference between particle sizes or gender. Elimination kinetics showed that small amount of ZnO nanoparticles were excreted via urine, while most of nanoparticles were excreted via feces. It seems that small particles could be more rapidly cleared from the body than larger ones. ZnO nanoparticles below 300 mg/kg were distributed into the tissues and excreted within 24 h, thereby implying their low toxicity. These findings will provide crucial information on possible target organs for toxicity as well as chronic toxicity potential of ZnO nanoparticles.

8548-151, Session PSMon

Controlled bio-nanoparticle structures by programmable DNA self-assembly

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Nanomaterials with different structures have been extensively investigated owing to their interesting properties and potential applications in nanotechnology. In nanoscale system, however, organization of nanoparticle is very difficult because nanoparticles have strong interactions each other. The molecular-level control of nanoparticles is a bottleneck in the field of nanomaterial technology. Here, we have developed a very simple, yet accurate approach to generate molecular controlled nanostructures of ferritin by designed DNA self-assembly. This process allows us to assemble largely open designs with zigzag-, linear-, and Y-shape arrays. Electochemical property of controlled ferritin nanostructure was increased as compared to the f-SWNT and length effect (2 times) to electrochemical property was more than junction effect (1.75 times) of that. Therefore, these ferritin nanostructures may have significant applications as electron mediators and electronic nanocircuits in diverse areas including nanobionics and biomedical engineering.

8548-152, Session PSMon

The effect of P-glycoprotein on the brain uptake of [18F]MEFWAY in rats

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Introduction: The activity of the multidrug efflux transporter P-glycoprotein (P-gp) in the blood-brain barrier (BBB) restricts the brain uptake of many tracers for positron emission tomography (PET). Recently, [18F]MEFWAY was developed as a useful radioligand for the imaging post-synaptic serotonin 1A (5-HT1A) receptors. However, whether [18F]MEFWAY is the substrate of the P-gp has not been reported previously.

Objectives: The aim of this research is to determine if the brain uptake of [18F]MEFWAY is influenced by the action of P-gp.

Method: Male Sprague-Dawley (SD) rats were used for in vivo imaging of microPET. Each rat was anesthetized with 2.0 % isoflurane in oxygen and placed in the gantry with its head centered in the field of view. A catheter was inserted into the tail vein and fluconazole was injected at an infusion rate for 1 h. In the experimental group, a tariquidar (TQD) which is a vivid inhibitor of Pgp was intravenous bolus administrated and then radioactivity (13.1-19.6 MBq) was promptly injected over 1 min to the catheter and dynamic PET scans (Siemens, Inveon PET/CT) were performed for 120 min. In the control group after fluconazole pretreatment, radioactivity was injected over 1 min and we performed the PET experiment. PET data were reconstructed in user-defined time frames in length by 2-dimentional order-subset expectation maximization (OSEM) algorithm. Regions of interests are hippocampus, frontal cortex, and cerebellum. Non-displaceable binding potential (BPND), commonly used as an indication of receptor density, is the ratio of the peak values of specific binding curve to the non-specific binding curve at the time of the peak. The cerebellum was used as the reference region because it contains very few 5-HT1A receptors in the rats.

Result: After TQD administration, the hippocampal uptake of radioactivity was 4-fold higher than baseline. Moreover, the ratio of specific binding (SUVtarget-SUVcerebellum) to non-specific binding (SUVcerebellum) was also 2-fold higher than the control group. The increase in the ratio of specific binding to non-specific binding implied that available 5-HT1A receptors in the plasma membrane was augmented since the permeability to the BBB of [18F]MEFWAY was enhanced through the inhibition of Pgp.

Conclusion: Our research firstly demonstrated that inhibition of Pgp causes significant incensement of [18F]MEFWAY brain uptake. From these experiment, we conclude that [18F]MEFWAY is the substrate for Pgp.

8548-154, Session PSMon

Nanogap-based PNA chips for the detection of genetic polymorphism related to cytochrome P450 2C19

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The INEs were prepared by the combination of the photo lithography and the surface-catalyzed chemical deposition, without using the

e-beam lithography. And average gap distance and effective gap length were about ~70 nm and ~140 μm, respectively. In the case of coupled PNA-DNA pair, nanogap-based IDE exposes like a short circuit by an event of target DNA molecules functionalized with Au nanoparticles which play a key role as a conductive probe. Four different types of target DNAs were successfully detected and discriminated by the INE-based PNA chips.

8548-155, Session PSMon

Glioma brain tumor imaging using terahertz technique

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Terahertz (THz) wave has the high sensitivity of water molecular and safeness to humans and these advantage permits the THz imaging as new medical imaging technique. In the medical application of THz imaging method, the cancer imaging is interesting subject and has been studied extensively, in of the skin, breast, tongue and liver cancer. But the study of brain is insufficient and has not been reported yet. A glioma cancer is most common brain tumor and has the ambiguous margin between normal and abnormal regions. The THz imaging method can be used as a novel imaging technique which found the margin. In this paper, we displayed the THz images of whole brain of rat with and without tumor. A rat glioma model, the brain tumor model, was established by surgically implanting 9L/lacZ glioma cells. The rat brain tumors were extracted about 3-4 weeks after implantation. We got the photography, THz images and magnetic resonance imaging (MRI) images for fresh brain with and without tumor. The margin of tumor was distinguished clearly with normal region. The peak intensity of THz pulse in the region of tumor was about 10% larger than that of a normal region. It means that the tumor has larger water content than normal tissue. This result demonstrates that the THz imaging technique was useful for diagnosing brain cancers.

8548-156, Session PSMon

Synthesis of hybrid organic-inorganic near-IR responsive magnetic nanoparticles for cancer theragnosis combined with localized therapy

Doyeon Bang, Taeksu Lee, Jihye Choi, Joseph Park, Byunghoon Kang, Yong-Min Huh, Seungjoo Haam, Yonsei university (Korea, Republic of)

Hybrid organic-inorganic near-infrared responsive magnetic nanoparticles were synthesized for theragnosis combined with localized therapy. In detail, inorganic super-paramagnetic nanoparticles were embedded inside organic polyaniline matrix, which enables localized photothermal therapy upon NIR illumination under intracellular acidic/oxidative condition. In this structure, super-paramagnetic nanoparticle works as MRI contrast agent, that enables the visualization of a tumor and polyaniline works for near-infrared responsive tumor ablation.

8548-157, Session PSMon

Investigation of redox state for conducting polymer nanoparticles using scattering imaging

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Scattering imaging is a technique used to observe unstained samples causing them to appear brightly lit against a dark, almost purely black, background. When light hits an object, rays are scattered in all directions. The design of the dark field microscopes is such that it removes the dispersed light, so that only the scattered beams hit the samples.

On the other hand, polyaniline (PANI) is a conducting polymer that changes its color from blue to green according to its redox state. We formulate the nanoparticles based on PANI. In low pH (below pH 2), PANI is in the oxidized state (emeraldine base: EB), and in high pH (upper pH2), PANI is in the reduced state (emeraldine salt: ES). In the EB state of PANI, the color of PANI is blue, and in this case, SCATTERING image shows its complementary color, yellow, because only the scattered light can reach to a CCD camera. On the contrary to this, in the ES sate of PANI, the color is green, and pink color is observed in scattering image.

8548-158, Session PSMon

CD44-targetable NIR-sensitive supramolecular hydrogel for targeted imaging of stem-like gastric cancer cells

Minhee Ku, Yonsei University (Korea, Republic of)

Molecular imaging technologies have emerged as a key method to analyze cancer cells with molecular level for effective therapeutics via in vivo monitoring. Hence, We fabricated NIR-sensitive supramolecular hydrogel (NIRSH) using the HA for the sensitive optical imaging of CD44-expressing stem-like gastric cancer cells.To create this probe, the polycationic branched polyethyleneimine (PEI) was conjugated with Cy5.5 (a near-infrared exciting imaging-moiety). The Cy5.5 conjugated PEI was polyplexed with polyanionic HA and used for non-invasive in vivo imaging of CD44. This CD44-targetable, NIRSH was stably fabricated and exhibited specificity to and imaging potential for CD44-expressing cancer cells and heterotopic/orthotopic xenograft mouse models. NIRSH also neutralized cytotoxicity induced by PEI alone, was stable under harsh conditions, biocompatible, and displayed a long in vivo circulation time suitable for diagnosing.

8548-159, Session PSMon

Membrane type 1 matrix metalloproteinase targetable molecular imaging [robes using nanoparticle surface energy transfer phenomenon

Minhee Ku, Yonsei University (Korea, Republic of)

Membrane type 1 matrix metalloproteinase (MT1-MMP) is one of the major causes of tumor invasion and a promising drug target during early steps of the invasive cascade in primary tumors. For effective diagnosis of cancer invasion, thus, we fabricated MT1-MMP targetable probes by Nanoparticle surface energy transfer phenomenon. Gold Nanoparticles that can be used to target tumors and provide detection are produced by reduction of chloroauric acid. To specifically target MT1-MMP, gold nanoparticles are conjugated with activatable fluorogenic peptide (ActFP). The morphology and colloidal size of the prepared GNP-ActFP was confirmed by a transmission electron microscopy, dynamic light scattering and dark field microscopy.

Significant properties such as targeting ability of MT1-MMP of GNP-ActFP was investigated by Fluorophotometer, UV spectrometer. In conclusion, cleavage of specific peptide by MT1-MMP result in large changes in FRET efficiency. Thus such an approach using nanoparticle surface energy transfer phenomenon may take advantage of monitoring in tumor cell invasion.

8548-160, Session PSMon

Magnetic resonance imaging of Glioblastoma using aptamer conjugated magnetic nanoparticles

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Here we introduce a new class of smart imaging probes hybridizing polysorbate 80 coated-magnetic nanoparticles (MNPs) with vascular endothelial growth factor receptor 2 (VEGFR2)-targetable aptamer for specific magnetic resonance (MR) imaging of angiogenesis from glioblastoma. MNPs showed single crystallinity and high magnetism with superparamagnetic property. The conjugation of VEGFR2-targetable aptamer with polysorbate 80-coated MNPs was confirmed by FT-IR and NMR analysis. VEGF-MNPs were selectively delivered to VEGFR2 positive (PAE/KDR) cell with no cytotoxicity. T2-weighted MR imaging showed significant enhancement of brian tumor site in animal model because of selective delivery and accumulation of VEGF-MNPs at the VEGFR2 over expressed glioblastoma. VEGF-MNPs exhibit excellent glioblastoma-targeting ability with no cytotoxicity. Prolonged stability in the blood circulation and aptamer-mediated delivery also contributed to highly efficient accumulation in VEGFR2 over expressed glioblastoma. Consequently, these advantageous features of VEGF-MNPs allowed us to obtain outstanding selective tumor MR imaging results, demonstrating the utility of this nanoprobe design in future clinical applications.

8548-162, Session PSMon

Magneto-optical and plasmonic properties of thin film ternary alloy sensors

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Improvements to magneto-optical (MO) and plasmonic sensors have been sought through new materials and molecular architectures. For example, incorporation of a ferromagnetic material into a noble metal plasmonic sensor increases the sensitivity of the device by coupling the MO and plasmonic properties. These devices have typically been fabricated using segregated noble metal / ferromagnetic multilayers where interfacial effects hinder the sensitivity. A suitable single-layered material would eliminate these interfacial effects. Certain ternary alloys exhibit a ferromagnetic phase with plasmonic properties under specific deposition conditions and these MO and plasmonic properties will be discussed within the context of MO and plasmonic sensors.

8548-163, Session PSMon

Thermogeling behavior of PEG-PAF and its application for sustained release of hGH

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In the present study poly(ethylene glycol)–poly(L-alanine-co-L-phenylalanine) (PEG–PAF) aqueous solution as a polypeptide-based thermogelling system and its application as an injectable sustained release system is reported for human growth hormone (hGH).

The PEG–PAF aqueous solution underwent sol-to-gel transition at 16–34 0C in a polymer concentration range of 6.0–14.0 wt% as the temperature increased.

Dynamic light scattering, circular dichroism, FTIR, and 13C-NMR spectra indicated that the secondary structure of PAF was preserved however, PEG was dehydrated in the sol-to-gel transition temperature range. A micelle aggregation model was suggested for the sol-to-gel transition of the current PEG–PAF. The polymer was quite stable in water, and therefore, the molecular weight of the polymer did not significantly change and pH of the aqueous polymer solution was maintained at 7.2–7.8 during the 1 month storage of the polymer as an aqueous solution at room temperature. This point is clearly distinguished from previous thermogelling polymers based on polyesters, polyorthoesters, polyphosphazenes, poly (b-aminoester urethane) s, and polyanhydrides, which generate acid degradation products or can be degraded during storage as an aqueous polymer solution. Therefore, the current system can be used as a ready-to-use injectable implant for biomedical applications. When the polymer aqueous solution (0.5 mL) was injected into the subcutaneous layer of rats, the gel was formed by temperature-sensitive sol-to-gel transition, and the gel was completely eliminated from the implanted site in 15 days. A haematoxylin and eosin (H&E) staining study suggested the good histocompatibility of the gel in the subcutaneous layer of rats. As a sustained release formulation for hGH, the PEG–PAF showed a 4 day release profile with a pharmacological effective concentration range in vivo, suggesting that the system is promising as a once-per week delivery system for the hGH.

8548-164, Session PSMon

Effects of dispersants on physicochemical property and biological responses of ZnO nanoparticles

Hae Eun Chung, Choi Soo-Jin, Seoul Women's University (Korea, Republic of)

Among various inorganic materials widely applied to industrial fields and human-related products, zinc oxide nanoparticles have attracted much attention as sunscreen agents and nutrient supplements due to high UV absorption and essential trace element properties, respectively. For biological application of ZnO nanoparticles, they should be well dispersed in solution where some dispersants are indispensably added for better stabilization.

However, dispersants themselves can also affect the cellular response, uptake behaviors, and toxicity of ZnO nanoparticles, which are probably associated with their different physicochemical property in the presence of dispersants. In this study, therefore, we evaluated the effects of ZnO nanoparticles dispersed in different agents such as citrate, carboxymethyl cellulose (CMC), and water or cell culture medium without any dispersant on cytotoxicity, cellular uptake behaviors, and pharmacokinetics. Physicochemical characteristics of ZnO nanoparticles such as surface charge, particle size, morphology, and ionization property in each dispersant were also analyzed to understand their biological responses. The results demonstrated that the cytotoxicity, cellular uptake and pharmacokinetic behaviors of ZnO nanoparticles strongly depend on dispersant types, which resulted from their physicochemical stability. These findings suggest the choice of appropriate dispersants is of importance to evaluate biological response of nanoparticles.

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8548-165, Session PSMon

Effect of particle size on tissue distribution and excretion of silica nanoparticles

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Silica nanoparticles have been widely applied in diverse fields including such as manufacturing, sensing, coating, medicine, drug delivery, and food additives. Despite their wide range applications, toxicity of silica nanoparticles has not been clearly determined. In particular, any research on kinetic behaviors of silica nanoparticles in vivo has not been yet performed. The aim of this study was, therefore, to evaluate the kinetics of silica nanoparticles with respect to particle size (20 nm and 100 nm) in terms of plasma concentration-time profile, tissue distribution, and excretion after oral administration in rats. The results demonstrated that silica nanoparticles were mainly distributed to organs such as liver and kidney. Elimination kinetics showed that most of silica nanoparticles were excreted via the feces. However, any significant effect of particle size on the kinetics was found. All the results will be important to interpret toxicological effects caused by silica nanoparticles and to predict their chronic toxicity potential in long-term.

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8548-167, Session PSMon

Flexible, transparent, and free-standing nanomembrane for biomedical applications

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Biocompatibility of Poly (3,4-ethylenedioxythiophene), (PEDOT) has been studied for neural stimulation of biomedical applications. We report mechanically robust, electrically conductive, free-standing, transparent and bio-compatible hybrid nanomembranes made of densified carbon nanotube sheets that were coated with PEDOT using vapor phase polymerization and their performance. Flexible, free-standing, and electrically conducting ultrathin (< 100nm) nanomembranes can be used as electrodes for sensors, actuators, optical devices, fuel cells and separation of biological macromolecules. Carbon nanotube aerogel sheets drawn from multi walled carbon nanotube forests provide an excellent platform for the formation of conductive and transparent membranes. Carbon nanotube aerogel sheets densified by ethanol vapor turn into carbon nanotube sheets (CNSs) with well aligned nanotube structures and thickness of ?50 nm. The hybrid nanomembranes with thickness of ~66 nm and showed high mechanical strength and modulus. The hybrid nanomembrane of electrochemical property had good volumetric capacitance, volumetric energy and power density. The nanomembrane composite of PEDOT and CNS has a potential applications.

8548-169, Session PSMon

Directional wetting property on a fabricated asymmetric micro structure in microfluidic device

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Most of semi-aquatic insects like water strider, fisher spider have micro/nano hair on their legs and body that can help them repel liquid to specific direction. Inspired by micro/nano structure, researchers take an effort to apply the structures to microfluidic devices. Nowadays, Controlling fluidic characteristics like spreading velocity and direction in microchannel is of significant interest for broad range of microfluidics, including DNA microarrays, lab-on-a-chip, inkjet printing. With advancements in micro/nano fabrication, patterned surface have enabled control microfluidic characteristics. However, most of the surfaces have symmetric spreading property.

Herein, we demonstrate that we can control asymmetric liquid spreading property by regulate asymmetry of structure. For the formation of asymmetric micro pillar structure, fill the UV-cured polymer in microfluidic channel bonded with microhole patterned Cr glass substrate. Then, backside UV exposure after contacting backside of Cr glass with Lucius prism enables to from an asymmetric micro structure. As previously reported, the Lucius prism can allocate light to specific direction by oblique metal deposition technique. Hence, micro structure is formed following in the UV light pathway. The fabricated asymmetric micro structure has uni-directional wetting property. It is because of the critical angle effect on edge side. It is expected to apply to the flowing control in a microfluidic device.

8548-170, Session PSMon

Rational design of bio-inspired dry adhesive for drug delivery biomedical skin patch

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With rapid transition to an aging society, a skin-attachable U-health device would play a key role in future diagnostics and healthcare systems.[1] Therefore, there are increasing demands on less-irritating, biocompatible medical bandage or tapes as the aging skin is more sensitive and vulnerable to chemical-based adhesives.

Recognizing such needs for a new biocompatible medical patch, we have shown in our recent study[2] that the dry adhesive skin patch possesses several potential advantages as compared to acrylic-based chemical adhesives. First, it can show repeatable and restorable adhesion with the help of self-cleaning capability. Second, it is less affected by surface contamination, oxidation, and other environmental stimuli since the adhesion largely originates from structural characteristics of high-density microstructures. Third, it provides better biocompatibility in a prolonged exposure up to two days presumably due to increased ventilation of air and skin residues with minimal contact with potentially irritating chemical species. Despite these advantages, relatively low normal adhesion (maximum adhesion: ~1.3 Ncm-2), which is typically 30 ~ 40% of the acrylic wet medical patch (~3 Ncm-2), has been a hurdle to practical uses of the material.

To address this limitation, we present here an enhanced dry adhesive skin patch with composite micropillars; the stem region of micropillars is formed by a relatively rigid material like hard polydimethyl siloxane (h-PDMS) (Young's modulus: ~8.2 MPa) or PDMS with a higher amount of curing agent, typically at 15% (Young's modulus: ~2.8 MPa). The top layer is additionally integrated by inking a soft PDMS layer with a lower amount of curing agent, the amount of which ranges from 2.5 to 15 wt%. In this way, monolithically integrated composite PDMS micropillars are prepared with better adhesion strength and durability.

8548-171, Session PSMon

Effective suppression method of [18F] MEFWAY defluorination in rat brain in vivo for imaging 5-HT1A receptors

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PURPOSE: [18F]MEFWAY was developed as a F-18 radioligand for imaging the serotonin 1A receptor in the brain to overcome severe defluorination in vivo. This defluorination give rise to problem in exact quantification of receptor density due to spill over of radioactivity. However, there is no report about its biological evaluation in small animal in vivo. The aims of this study were i) to measure the degree of defluorination in small animal in vivo, ii) to find out the inhibition method of defluorination, iii) assess the efficacy of [18F]MEFWAY in rat brains in vivo.

METHODS: MicroPET of rat head after administration of [18F]MEFAY was used to confirm that distribution of radioactivity in the brain and to evaluate the degree of defluorination. Binding potential to 5-HT1A receptors in ventral hippocampus (HP), medial prefrontal cortex (MPFC) and cerebellum (CB) were analyzed. Miconazole and fluconazole were tested for the ability to suppress defluorination of [18F]MEFWAY in vitro and in vivo. For further evaluation, we conducted blockade and competition experiment by pre or post injection of WAY-100635 which is a high selective antagonist to 5-HT1A receptor before administration of [18F]MEFWAY.

RESULTS: In PET experiment, [18F]MEFWAY in rat brain revealed significant defluorination before administration of inhibitors. In inhibition study against parent decreasing activity in liver microsome in vitro, miconazole and fluconazole was effectively suppress the defluorination of [18F]MEFWAY. In detail, miconazole (IC50 = 0.54) was a more potent drug than fluconazole (IC50 = 3.81). However, in brain PET study, fluconazole showed favorable suppression ability than miconazole. In the blockade and competition study, we confirmed that [18F]MEFWAY is a specific radioligand to 5-HT1A receptors.

CONCLUSION: We concluded that authentic [18F]MEFWAY undergoes significant defluorination in rat brain in vivo. And this problematic defluoriation was effectively suppressed by pretreatment of fluconazole. From this data, inhibitor treated [18F]MEFWAY may serve as an effective radioligand for investigating 5-HT1A receptors in preclinical study.

8548-172, Session PSMon

Evaluation dopamine transporters and D2 receptors in hemiparkinsonian rat brain in vivo with consecutive PET scan of [18F] FPCIT and [18F]fallypride

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The quantification of dopaminergic system is of a particular interest in positron emission tomography (PET) research for the diagnosis of Parkinson's disease. The aim of this study was to investigate dopaminergic function in unilaterally lesioned 6-hydroxydopamine (6-OHDA) rats by dual PET radioligands: N-(3-[18F]fluoropropyl)-2?-carbomethoxy-3?-(4-iodophenyl)-nortropane, [18F]FPCIT (a dopamine transporter imaging radioligand) and {(S)-N-[(1-allyl-2-pyrrolidinyl) methyl]-5-(3-[18F]fluoropropyl)-2,3-dimethoxybenzamide, [18F] fallypride (a dopamine D2 receptors imaging radioligand). The PET experiments were consecutively performed in normal group or 6-OHDA unilateral lesion groups. After injection of radioligands, the PET data were acquired over 150 min in a list-mode in order to obtain time activity curves. Five weeks after unilateral lesioning of a medial forebrain bundle with 6-OHDA, brain uptake of [18F]FPCIT at 75 min was significantly decreased in the ipsilateral striatum (right side) to 1.27 ± 0.17 (n=3), representing a 72 % decrease above control and 65% contralateral striatum (intact, left side). Uptake ratio index of [18F]FPCIT in lesion striatum at 75 min was also largely decreased to 84 % or 79 % compared with control or intact striatum. On the other hand, brain uptake of [18F]fallypride was increased in ipsilateral striatum to 4.37 ± 0.73 (n=3), representing a 24 % increase above control and a 8 % intact striatum. Uptake ratio index of [18F]fallypride in lesion side at 75 min was increased to 10 % or 9% compared with control or intact striatum. From these results, in ipsilateral striatum of 6-OHDA rats, dopamine transporters were significantly down-regulated and dopamine D2 receptors were up-regulated compared by contralateral region or control group. Therefore, [18F]FPCIT-[18F]fallypride dual PET is useful imaging method to evaluate dopaminergic system for discriminate Parkinson's disease. Moreover, our result suggests that this protocol has potential for early diagnosis Parkinson's disease from various Parkinson syndromes.

8548-174, Session PSMon

The effect of rhBMP-2 coated injectable TCP/HA/CMC material in the rat tibial defect model

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This study would test the hypothesis that use of rhBMP-2 coated TCP/HA/CMC scaffolds could enhance bone regeneration in Rat's tibia defect model. Thirty six male Sprague-Dawley rats were randomized into three groups of 12 rats each (Group I: TCP/HA/CMC, Group II: TCP/HA/CMC+rhBMP-2(0.1mg/ml), Group III: TCP/HA/CMC+rhBMP-2(0.5mg/ml)). 10mm sized bony defect was made at the tibia and fixed with external fixators with K-wires. And materials were inserted at the defect site. Evaluation was done with X-rays, micro-CT, histology and real time PCR at the time of 2wks, 6wks, 8wks after the operation. All group II and III rat tibias exhibited bridging callus formation 8 weeks after operation, whereas group I tibias demonstrated non-bridging callus formation. None of the group I showed callus in the central zone of the defect. For micro-CT, bone formation and remodeling of Group III had greater values than the controls at all time-points. This study serves as preclinical evidence demonstrating the potential of combining osteoinductive rhBMP2 with our TCP/HA/CMC constructs for the repair of large bone defects in a rat's tibia.

8548-175, Session PSMon

Unilateral 6-OHDA lesion induces the down-regulation of post-synaptic serotonin 1A receptors in rat brain in vivo

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INTRODUCTION: The pathological characteristic of Parkinson disease (PD) is the degeneration of dopaminergic neuron in substantia nigra pars compacta (SNc) and subsequently, the striatum. However, PD is not solely a dopaminergic disease but the serotonergic system is also involved. Recently, it was reported that early and advanced PD patients suffer from tremor, depression and visual hallucinations. Therefore, it

is important to evaluate the dopaminergic system as well as serotonin system to understand the PD. So far, the most functional imaging studies focus on the pre-synaptic serotonin receptor to evaluate the integrity of serotonergic system.

OBJECTIVES: The purpose of this research is to investigate the changes the serotonin 1A (5-HT1A) receptor density using [18F] MEFWAY which is a highly specific radioligand for post-synaptic 5-HT1A receptors.

METHOD: The 6-hydroxydopamine (6-OHDA) unilaterally lesioned male Sprague-Dawley (SD) rats and control male SD rats were used for in vivo imaging of microPET. Each rat was anesthetized with 2.0 % isoflurane in oxygen and placed in the gantry with its head centered in the field of view. A catheter was inserted into the tail vein and fluconazole was injected at an infusion rate for 1 h. Radioactivity (13.1-19.6 MBq) was promptly injected over 1 min to the catheter and dynamic PET scans (Siemens, Inveon PET/CT) were performed for 120 min. PET data were reconstructed in user-defined time frames in length (10 sec x 6 frames, 30 sec x 8 frames, 300 sex x 5 frames, 1800 sec x 5 frames) by a 2-dimentional order-subset expectation maximization (OSEM) algorithm (4 iterations and 16 subsets). Regions of interests are hippocampus, frontal cortex, cerebellum and skull. Non-displaceable binding potential (BPND), commonly used as an indication of receptor density, is the ratio of the peak values of specific binding curve to the non-specific binding curve at the time of the peak. The cerebellum was used as the reference region because it contains very few 5-HT1A receptors in the rats..

RESULT: Time activity curves showed that hippocampal uptake in 6-OHDA lesioned rat was 35% lower than in the control group. Moreover, radioactivity uptake in lesioned side was quite similar to the intact one. At this time, the differences of cerebellar uptakes between the 6-OHDA rats and the control group were negligible. The highest specific binding to non-specific binding ratio was obtained at 75 min after the injection of radioligand. The BPND from the 6-OHDA rats was 32% lower than from the control group.

CONCLUSION: We conclude that degeneration of dopaminergic system induced the down-regulation of post-synaptic 5-HT1A receptors in the rat brain in that BPND of the 6-OHDA rats had lower value compared with the control group.

8548-176, Session PSMon

Blood qualitative imaging using terahertz technique

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Terahertz (THz) electromagnetic wave has many advantages in the study of biology and medical science, because the conformational modes of the bio-molecules and water lie in the THz frequency range. The THz imaging enables the diagnosis of cancer or burns by measuring the differences in the contents and components of body fluids in tissues. The study of body fluids and circulation system using THz wave is necessary to enhance the reliability of the diagnosis. Herein, we showed a correlation between RBC concentration and the absorbance of THz signals in vessel model using the THz imaging technique. The blood samples were collected from the tail veins of three Sprague–Dawley rats, and blood constituents such as RBCs and plasma were extracted by centrifugation. The artificial blood vessel model consisted of a polyurethane resin tube on the z-cut quartz window. The optical constants of whole blood and its constituents were determined using THz time-domain spectroscopy and the THz images were obtained by reflection mode imaging system. The ratios of the optical constants of blood and its components were similar with those of their natural volume fractions. The concentration of RBCs in whole blood was directly proportional to the THz absorbance. It was confirmed in vessel model. These results showed that THz technique can be used as the non-invasive method for detecting blood diseases as well as a novel angiography.

8548-179, Session PSMon

Hyaluronic acid induced nanostructures in a thermogel for chondrocytes 3D culture

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Hyaluronic acid is the component of extracellular matrix of articular cartilage. To investigate the effect of the HA in the tissue engineering application, we cultured chondrocytes in a 3D matrix of polypeptide thermogel. Cryo-TEM image of the gel showed that the incorporation of the HA in the polypeptide thermal gel induced the nanobundle formation in the hydrogel which can mimics the natural extracellular matrix of the articular cartilage. Compared with the thermogel without HA, the HA incorporated thermogel decreased the gel modulus, however cell proliferation and biomarker expression such as sulfated glucoaminoglycan and type II collagen for articular cartilage were significantly improved by using the HA as an excipient of the thermogel during the 3D culture. This finding suggests that HA, even though it is a hydrophilic polymer, not only provides the chondrocytes with compatible microenvironment through recruiting the nanofibrous structures but also involves the biomolecules expression of sGAG and collagen in the extracellular matrix for articular cartilage formation.

8548-180, Session PSMon

Naked eye analysis of DNA microarrays using daunorubicin-conjugated gold nanoparticles

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We introduce a naked eye analysis of DNA microarrays using daunorubicin conjugated to gold nanoparticles (DNR-AuNPs). The double-stranded DNA (ds-DNA) formed by the hybridization of single-stranded probe DNA, and the complementary target DNA on the array of chips can combine to form DNR-AuNPs because the daunorubicin (DNA intercalator) intercalates specifically into the ds-DNA. The DNA arrays can be analyzed with the naked eye or with an optical scanner following the enhancement of the DNR-AuNPs. This method can detect the synthetic target DNA at concentrations as low as 10 pM in an array format comparable to that of the fluorescence detection method. Moreover, we successfully confirmed this scanometric assay method using a hemagglutinin-subtyping DNA array designed for the identification of the H1N1 novel swine-origin and H1N1 seasonal influenza A virus.

8548-181, Session PSMon

Therapeutic application of gold nanoparticles to retinal neovascularization in retinopathy of prematurity

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The pathological angiogenesis in the retina is the major cause of vision loss at all ages. In particular, retinopathy of prematurity (ROP) is a leading cause of blindness in children. This study investigated whether gold nanoparticle (GNP) could inhibit retinal neovascularization in the animal model of ROP. Intravitreal injection of GNP significantly inhibited retinal neovascularization in the mouse model of ROP. In addition, GNP effectively suppressed VEGF-induced in vitro angiogenesis of retinal microvascular endothelial cells including proliferation, migration and capillary-like networks formation. GNP blocked VEGF-induced autophosphorylation of VEGFR-2 to inhibit consequently ERK 1/2 activation. GNP never affected on the cellular viability of retinal microvascular endothelial cells and induced no retinal toxicity.

Our data suggest that GNP could be a potent inhibitor to retinal neovascularizationwithout retinal toxicity. Furthermore, GNPcould be extensively applied to variable vaso-proliferative retinopathies mediated by VEGF.

8548-182, Session PSMon

Fluorescence-labeled zinc oxide nanoparticles and their size dependent cellular uptake

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Engineered nanomaterials such as nano-sized zinc oxide (ZnO) are attracting interests since they can be utilized in drug/gene delivery system as well as in cosmetic or pharmaceutic formulations. In order to evaluate the cellular uptake and intracellular localization of ZnO nanoparticles, we partially modified the surface of ZnO nanoparticles with organic fluorescence. Both 20 and 70 nm sized ZnO nanoparticles were preliminarily modified by (3-aminopropyl)triethoxysilane (APTES) through silanization, then cyanine 5.5 dye (Cy5.5) succinimidyl was subsequently attached on the amine terminus of APTES modified ZnO through acylation (Cy5.5@ZnO). It was successfully demonstrated that the surface of ZnO nanoparticles were sequentially modified with APTES and Cy5.5 dye without significant transformation in crystalline structures, according to the powder X-ray diffraction (PXRD) patterns and Fourier transform infrared spectroscopy (FT-IR). The photo luminescence spectroscopy (PL) results showed that the fluorescence of Cy5.5 well preserved after the surface modification reactions. The colloidal properties such as surface charge, hydrodynamic radius and particle size were determined not to be seriously affected after Cy5.5 modification. The cellular uptake of Cy5.5-APTES@ZnO was assessed with fluorescent assisted cell sorting and fluorescence microscopy, showing that the smaller nanoparticles enter cells more than the larger ones. It was also verified that the ZnO nanoparticles, regardless of the size, are taken up by the cells via clathrin-mediated endocytosis.

8548-183, Session PSMon

Color DNA core-inorganic shell hybrid for nano-forensics

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Nanoscale Bio Core@Inorganic Shell hybrid, which consists of rational color DNA molecules core with a size of ≈100 nm and spherical inorganic nanoshell of reassembled metal hydroxide nanosheets with a wall thickness of ≈10 nm, was prepared via a soft-chemical lattice engineering route. The color DNA encapsulation and its release, due to the pH-dependent solubility of inorganic nanoshell, play a crucial role in maximizing the stability of base sequence-manipulated and probes-functionalized DNA with designed forensics information. Thus prepared color DNA@Inorganic nanohybrid was applied to the Nano-forensics system, as a newly adopted integrative concept combining nano-chemistry and biochip-based molecular sensing. These achievements have further inspired to design a molecular information system comprised of four distinct procedures: encoding, encrypting, decrypting, and decoding, which is converged biological DNA code with information theory. We were able to show that the nanohybrids can be used as origin traceability of agricultural product by demonstrating blind test to discriminate the origin of mixed item. Therefore, informational code system based on DNA@Inorganic nanohybrids is expected to be useful for molecular barcodes, item level tagging, security label sensing, track-and-tracing, and authentication systems.

8548-185, Session PSMon

Titanium implants enabled with Vancomycin delivery for inhibition of infection

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Infection involved with bone fixation devices, mostly made of Titanium (Ti), has been reported as one of the major complications, which eventually leads to implant loosening or severe inflammation. The infection is caused mainly by bacterial adhesion on the implant surface that acts as a substrate for bacterial colonization. To resolve this problem, we pursued to develop Ti implants enabled with local delivery of an antimicrobial drug, vancomycin. To prove this proof-of-principle, a coin-shaped Ti sample was coated with poly (lactic-co-glycolic acids) (PLGA) loaded with the drug, where the drug release could be tailored to effectively prevent bacterial colonization on the Ti surface. In this work, the surface of Ti samples was coated by dropping several drops of 10 μl PLGA and drug solution. To control the drug release pattern, the weight percent of the drug was varied to 37.5 %, 15 % and 7.5 % (w/w) PLGA/vancomycin. The work is in progress to examine the in vitro drug release profile and anti-bacterial activity of the differently-coated Ti samples.

8548-186, Session PSMon

Preparation and characterization of various sized graphene oxide by ultrasonication and second oxidation

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Because of its extraordinary electronic, thermal, mechanical properties, Graphene and its derivatives have attracted enormous interest. Graphene oxide (GO) is one of the derivatives of graphene with many oxygen-containing functional groups such as hydroxyl and epoxide groups on its basal plane and carboxylic groups at its edges.[1] GO has emerged as a potential candidate for biosensor platform, drug carrier and new type of bioimaging agent because of its water solubility and biocompatibility.[2,3] However, information of its properties dependent on size is not sufficiently available for practical applications. Herein, we performed synthesis and characterization of GO in various diameter. GO was synthesized by modified Hummers method. Each GO-dispersion was obtained by simply adjusting sonication time and by separating with filtration. Graphene quantum dot (GQD), quantum sized GO, was derived by second oxidation with concentrated nitric acid. Graphene quantum dot (GQD), nano-graphene oxide (NGO), submicro-graphene oxide (SGO), and micro graphene oxide (MGO) are four classes of GO with average diameter 10, 50, 300 nm, and 1 ?m, respectively. Dynamic light scattering (DLS) and atomic force microscope (AFM) were used to characterize the size and thickness of GO sheets. Infrared (IR) spectroscopy, Element analysis (EA) and X-ray photoelectron spectroscopy (XPS) were performed to evaluate structural and chemical properties. Furthermore, UV/vis absorption and Photoluminescence (PL) spectra were obtained to investigate optical properties of GOs. Results suggest that NGO, SGO and MGO exhibited similar chemical and optical properties. GQD, however, showed changes in chemical property such as increase in oxygen contents and optical property such as strong blue photoluminescence.

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8548-187, Session PSMon

Nanoscale magnetism control for optimizedhysteresis loss and its application of magnetic hyperthermia

Nanoscale magnetism tuning approach could be beneficial not only for the biological application such as magnetic hyperthermia but also for other applications ranges from the design of magnetic recording system to spintronics, magnetic resonance imaging (MRI) and drug delivery system. With the aim of controlling nanoscale magnetism, we demonstrate an approach encompassing concepts of surface and exchange anisotropy while reflecting size, shape, and structural hybridization of nanoparticles. We show that Zn0.4Fe2.6O4 cube has higher magnetization value than sphere due to its reduced surface anisotropy which is strongly related to spin canting on the surface of nanoparticles. From the size control of this cube nanoparticle ranging from 20 to 140 nm, we find out the optimal region (ca. 60 nm) in which the domain structure is changed from single- to multi-domain and the coercive force becomes maximized. Furthermore, hybridization of cube nanoparticle into core-shell (CS) structure by means of hard-soft exchange coupled system brings about a 14-fold increase in the coercivity. The core-shell nanoparticle, designed to have a minimized surface anisotropy, reduced spin disordering and additional of exchange anisotropy, possesses maximized magnetisms in terms of magnetization and coercivity. From the perspective of energy transformation, the maximized hysteresis loss achieved by CS-cube nanoparticle leads to drastically enhanced specific loss power, 10600 W/g, which is the largest value reported to date. Such CS-cube can be useful especially for magnetic hyperthermia. We demonstrate the superior efficacy of in vitro hyperthermia treatment of CS-cube for treatments of drug resistant colon cancer cell, (DLD-1-ADR) compared to regular cube nanparticles and Feridex

8548-188, Session PSMon

Surface charge modification of graphene oxide nanoparticles utilizing ammonia

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In this study, we performed a preparation and surface modification of graphene oxide (GO) for functional nanoparticles in drug delivery application. GO was successfully synthesized by chemical oxidation of natural graphite (GR) using Hummers-offeman method, and further modified with ammonia to produce amine-modified GO (GN). The effective oxidation from GR to GO was revealed by the powder X-ray diffraction patterns, Fourier transform infrared (FT-IR) and Raman spectra. From transmission electron microscopy, GO were determined to have sheet-like morphology. The characteristic bonds in GN were characterized by FT-IR and X-ray photoelectron spectroscopies (XPS). FT-IR spectrum of GN showed characteristic absorption bands for -NH2 asymmetric stretching vibration, -NH2 bending vibration, and C-N stretching vibration at 3180, 1592, and 1400cm-1, respectively and XPS spectrum confirmed the existence of bonds between GO and primary amine groups. Zeta potential of GO and GN showed that the surface charge was altered from negative to slightly positive values upon amine modification.

8548-189, Session PSMon

Plasmonic photothermic angioplasty with composite nanoparticles and stem cells as the new revolution in interventional cardiology

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BACKGROUND: Some modern angioplasty techniques generally just affect the geometry of the plaque and have some inherent clinical and technical limitations. Our previous bench-to-bedside studies confirmed high efficacy and safety of nanomedicine-based approach for the management of atherosclerosis.

METHODS: A total of 120 patients 45-65 years old with PCI (percutaneous intervention) and CABG (coronary artery bypass surgery) indications were assigned to the three groups (40 patients into the group with PCI indications and nanointervention but without stenting, 40 - cardiac surgery group with nanointervention, and 40 - with PCI indications to sirolimus stenting control). Patients with PCI indications underwent delivery of nanoparticles (NPs) inside of induced pluripotent stem cells (iPS) or CD73+CD105+ mesenchymal stem cells (MSCs) in medium via catheter-based percutaneous intra- and transmural injection into the plaque and artery. CABG patients run the delivery with bioengineered on-artery patch on the basis of bovine scaffold and iPS or MSCs (with NPs) by MICS (mini-invasive) cardiac surgery. We have used a modified method for the preparation of 90-100 nm versatile NPs with iron-silica core and gold-polymeric shell as described by Lee (2008) and Deng H (2005). Studied 10 mm pull-back of proximal left anterior descending arteries was observed by 40-45 MHz near-infrared spectroscopy (NIRS) and virtual histology intravascular ultrasound (IVUS-VH).

RESULTS: A change of the total vessel volume - TVV (mm3) immediately after the laser irradiation/ in 24 weeks in groups were -18.9/ -46.2%, -10.8/ -33.6% and -1.1/ -2.2% ($p<0.01$) respectively, total plaque volume (TPV) was changed from 233 to 229/209, 236 to 230/221, and 238 to 222/219 mm3 ($p<0.01$), total lumen volume (TLV) - 304 to 305/318, 303 to 305/ 311, 305 to 317/ 315 mm3 ($p<0.05$) from baseline to immediately/ at week 24 in groups respectively. Restenosis confirmed in 3 (7.5%) patients of stenting group only. An impact over mineral deposits and calcium necrotic core was predominated in PCI group (-33.4% vs -22.1% and +3.7% respectively, $p<0.005$). Anti-inflammative and anti-apoptotic effects, signs of neovascularization and restoration of artery function were predominated in subsets with progenitor cells ($p<0.01$). Coronary flow-mediated vasodilation was observed after hyperemia and injection of nitroglycerine (+10.2 and +16.6%, +8.2 and +9.6%, +8.1 and +9.8% in groups respectively, $p<0.05$). Mean hazard ratio between PCI group and stenting control if compare with CABG and stenting control achieved 1.05 (CI 95%: 0.95-1.16, $p<0.05$) and 1.03 (CI 95%: 0.93-1.09, $p<0.05$) with favor of nanomedicine-related approaches.

CONCLUSION: Plasmonics using multifunctional (imaging and therapy) nanoparticles is being the high-effective and safe alternative to stenting and CABG for angioplasty especially in combination with stem cells promising the rejuvenation of arteries and revolutionizing current strategy in patients with coronary artery disease.

8548-190, Session PSMon

Exchange-coupled magnetic nanoparticles with high thermal energy transfer capability

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Thermal energy is emerging as an important means of triggering functions for various applications in biomedical systems. Magnetic nanoparticles are attracting considerable interest for their ability to mediate the conversion of electromagnetic energy into heat. However poor conversion efficiencies of magnetic nanoparticle have hindered practical applications so far. We modulate the magnetism of nanoparticles to obtain the significant enhancement of magnetic heat induction through facile fabrication of nanoparticle in terms of size, shape, composition and structure. Especially, with a magnetically coupled system, we can obtain the magnetic nanoparticle with high specific loss power value which is an order of magnitude larger than conventional iron-oxide nanoparticles. We successfully apply these magnetic nanoparticles in an antitumor study and find that the therapeutic efficacy of these nanoparticles is superior to that of a commercialized anticancer drug.

8548-192, Session PSMon

Active targeting and safety profile of PEG-modified adenovirus conjugatedwith Herceptin

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PEGylation of adenovirus (Ad) increases plasma retention and reduces immunogenicity, but decreases the accessibility of virus particles to target cells. We tested whether PEGylated Ad conjugated to Herceptin (Ad-PEG-HER) can be used to treat Her2/neu-positive cells in vitro and in vivo to demonstrate the therapeutic feasibility of this Ad formulation. Ad-PEG-HER transduced Her2/neu-overexpressing cancer cells through a specific interaction between Herceptin and Her2/neu. Ad-PEG-HER treatment resulted in higher plasma retention and lower neutralizing antibody and IL-6 production than naked Ad. This formulation was extended to generate a Her2/neu-targeted, PEGylated oncolytic Ad (DWP418-PEG-HER). DWP418-PEG-HER specifically killed Her2/neu-positive cells and performed better than non-targeted and naked Ad in vivo. DWP418-PEG-HER showed a 1010-fold increase in the liver to tumor biodistribution compared with naked Ad. Immunohistochemical staining confirmed accumulation of Ad E1A in tumors. These data suggest that targeted gene therapy with the PEGylated Ad conjugated with Herceptin might shed a light on its therapeutic application for metastatic cancer in the future.

8548-193, Session PSMon

Cellular responses of osteoblast on the acid and thermally treated collagen fibrils

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Type I collagen is a major extracellular matrix component and its hierarchical structure plays an important role in the regulation of cellular behavior. In order to study the effect of structure, surface chemistry, and mechanical properties change of collagen fibril on the cellular response, various collagen structures were prepared by different degrees of acidic and thermal treatment of native collagen fibrils. First, to study the microstructure and morphology of collagen, atomic force microscopy (AFM) was used due to its high spatial resolution and surface morphology specificity. Second, we applied time-of-flight secondary ion mass spectrometry (ToF-SIMS) to study the surface chemistry changes of collagen fibrils by utilizing the capability of providing molecular surface chemical information. Third, to observe the changes in the mechanical properties during acidic and thermal treatment of collagen fibrils, contact-resonance force microscopy (CR-FM) was applied because of its ability to provide not only nanoscale spatial resolution but also quantitative information about the mechanical properties. It was demonstrated that the change of microstructure, surface chemistry, and mechanical property of collagen induced by acidic and thermal treatment could be observed in molecular level using AFM, ToF-SIMS, and CR-FM. The structural, chemical, and mechanical properties of acid and thermally treated collagen fibrils could be correlated with the cellular responses such as cell morphology, cytoskeleton organization, and viability visualized using a confocal laser scanning microscope.

8548-194, Session PSMon

Release kinetic study of ferulic acid intercalated layered double hydroxide

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We investigated the release kinetics of intercalated molecules from the inorganic layered double hydroxides (LDHs) nanoparticles. The model compound, 3-(4-hydroxy-3-methoxyphenyl)-2-propenoic acid (ferulic acid: FA), a well known antioxidant species, was succesfully intercalated into the LDHs gallery space through four reaction routes of coprecipitation, reconstruction, ion exchange and exfoliation-reassembly. Thus obtained intercalates are determined to have approximately 21 ~ 37 wt% of ferulic acid in LDH nanoparticles, from inductively coupled plasma-atomic emission spectroscopy, elemental analysis, and high performance liquid chromatography. In order to study the FA release behaviors based on simple diffusion and ion exchange, the time-dependent release profiles were obtained in both deionized water and saline (0.9% NaCl solution). The release pattern of FA with respect to time was fitted to well known release kinetic models such as lst order, parabolic diffusion, elovich equation, and power fuction. The release behavior of FA are deteremined to be highly influenced by the type of intercalation method, showing parabolic for coprecipiated, Elovich for reconstructed and ion-exchanged, and Power function for exfoliated-reassembled intercalates. On the other hand, the type of release media do not significantly affect the release kinetic, but influence the kinetic parameters corresponding to the desorption constant.

8548-195, Session PSMon

Enhancing transversal relaxation for magnetite nanoparticles in MR imaging using Gd3+-chelated mesoporous silica shells

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A new magnetic nanoparticle was synthesized in the form of Gd^{3+}-chelated Fe_3O_4@SiO_2. The Fe_3O_4 nanoparticle was octahedron-structured, was highly magnetic (94 emu/g), and was the core of an encapsulating mesoporous silica shell. DOTA-NHS molecules were anchored to the interior channels of the porous silica to chelate Gd^{3+} ions. Because there were Gd^{3+} ions within the silica shell, the transverse relaxivity increased 7-fold from 97 s^{-1} mM^{-1} of Fe_3O_4 to 681 s^{-1} mM^{-1} of Gd^{3+}-chelated Fe_3O_4@SiO_2 nanoparticles with r^2/r^1 = 486. The large transversal relaxivity of the Gd^{3+}-chelated Fe_3O_4@SiO_2 nanoparticles had an effective magnetic resonance imaging effect and clearly imaged lymph nodes. Physiological studies of liver, spleen, kidney, and lung tissue in mice infused with these new nanoparticles showed no damage and no cytotoxicity in Kupffer cells, which indicated that Gd^{3+}-chelated Fe_3O_4@SiO_2 nanoparticles are biocompatible.

8548-196, Session PSMon

Montmorillonite-Sildenafil nanohybrid for taste masking and pharmacokinetic studies

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We attempted to prepare a sildenafil-montmorillonite (SDN-MMT)

hybrid for taste-masking of sildenafil (SDN). To further improve the efficiency of taste-masking and also enhance the release rate of the drug, the hybrid was coated with basic polymer, polyvinyl acetal diethylaminoacetate (AEA). The PXRD and IR data showed that sildenafil was intercalated in the interlayer space of MMT with double layer without any structural change of drug molecule. The AEA coated SDN-MMT exhibited drug release much suppressed at the neutral pH (% release rate = 4.70 ± 0.53), suggesting a potential for drug taste masking at the buccal cavity. We also performed the in vitro drug release experiments in a simulated gastric fluid (pH 1.2). According to the result, the sildenafil molecules in the AEA coated hybrid were released out for about 90% after 120min, which was determined to be lower than Viagra® by about 10%. From the pharmaceutic study, however, the AUC0-∞ and Cmax were determined to be larger for the AEA coated hybrid than for the Viagra®. It is, therefore, concluded that the intercalation reaction can be a promising way of developing new drug delivery system.

8548-197, Session PSMon

Au@SiO_2@Gd@PEG nanoparticles as a MRI/CT bimodal contrast agent

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MRI and CT imaging modalities have been used to compensate for the weakness of each modality, a dual contrast agent that works for both MRI and CT simultaneously would be useful in the diagnosis of various diseases. Herein, we report the synthesis and characterization of Au@SiO_2@Gd nanonoparticles coated with poly(ethylene glycol) and their investigation as CT/MRI imaging contrast agents. We show the well-dispersed spherical particles respectively. The 1/T1 (r1) and 1/T2 (r2) were then estimated to be 11.1 and 13.7 mM-1s-1 from the slopes of the 1/T1 and 1/T2 plots versus Gd(III) ion concentration. Also, We show CT phantom images and HU scales of our NPs, Omniscan and Ultravist. Au@SiO_2@Gd@PEG NPs show high r1 and r2 relaxivities. Also, this system shows high ability for HU scale of CT. Herein, Au@SiO_2@Gd@PEG NPs may be a new entry into multifunctional bioimaging agents.

8548-199, Session PSMon

A colorimetric detection of dopa decarboxylase activity using gold nanoparticles

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L-Dopa decarboxylase (DDC) is related to a number of diseases, including several cancers and Parkinson's disease. Therefore, a sensitive assay to report DDC activity will be valuable for biomedical applications.

We have developed a colorimetric DDC detection system using gold nanoparticles (AuNPs). This approach is based on that DDC catalyzes the decarboxylation of L-3,4-dihydroxyphenylalanine (dopa) to dopamine. When dopa mixed with AuNPs, AuNPs were well dispersed and have red color. AuNPs capped by dopamine aggregated immediately and the color of gold solution turned red to blue. We detect DDC activity with naked eye using AuNPs aggregation. In addition of dopa, DDC catalyzed dopa converted to dopamine. When AuNPs add in the mixture of DDC and dopa, AuNPs became aggregation and the color of solution changed red to blue. We have characterized by the UV-Vis absorption spectra peak of AuNP solution. As the concentration of DDC increases, the absorption peak intensity at 650nm enlarges. We confirmed dispersion or aggregation of AuNPs by transmission electron microscopy.

Traditional techniques, including high performance liquid chromatography (HPLC) and radiochemical assay, are either time-consuming, needing expensive instruments, or not simple. Our technique is simple and convenient method using colorimetric assay for detection of enzyme activity.

8548-200, Session PSMon

Quantum dots induce charge-specific amyloid-like fibrillation of insulin at physiological conditions

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Proteinopathies are diseases characterized by the accumulation of the organized aggregates of misfolded or unfolded protein. These aggregates are toxic due to their implication in the membrane oxidative damage, ion and metal dyshomeostasis, aberrant signal transduction and mitochondrial dysfunction, the processes provoking cell death; they are the result of an organized polymerization (so-called amyloid behaviour) of proteins or peptides. The neurodegenerative diseases, like Alzheimer's or Parkinson disease and diabetes have been identified as proteinopathies.

The existing data on the effects of nanoparticles (NPs) on peptide assembly are controversial. Overall, the presence of NPs has typically promoted aggregation of peptides, which was explained in terms of a condensation-ordering mechanism. Since the fibrillation occurs by nucleation-dependent kinetics, the increased local concentration of peptides in the vicinity of NPs as a result of electrostatic attraction greatly accelerates the fibril formation. At the same time, some polymeric NPs (40 nm in diameter) have been found to slow down the rate of peptides fibrillation by depleting the amount of free monomeric peptides, although the fibril formation still could not be prevented.

Here, we demonstrate that the CdSe/ZnS quantum dots (QDs) covered by PEG derivates with controlled surface charges may promote the multistage fibrillation of human insulin protein in vitro at the physiological condition. Circular dichroism (CD) protein structure analysis, Congo red specific CD measurement, thioflavin T fluorescence assay and dynamic light scattering technique have been used for comparative analysis of the of insulin structure remodelling in the presence of QDs. We show that the strongly negatively or positively charged PEGylated QDs do not affect the fibrillation of insulin protein whereas the slightly negative or neutral QDs strongly increase the rate of the amyloid-like fibrils formation.

We have finally shown that the QD effect on the rate of insulin fibrilisaiton depends not only on the QDs charge but also on the surface curvature of QDs and thus on the size of the charged surface able to interact with a protein molecule.

8548-201, Session PSMon

Telemetry and power delivery schemes for brain implantable microsystems

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No abstract available

8548-202, Session PSMon

Barium sulfate layer coating on bioabsorbable bone fixation plate for x-ray imaging

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Fracture fixation system of biodegradability has attracted a great deal of attention due to no need of secondary removal surgery mostly needed for metallic fixation devices. However, radiolucency of bioabsorbable fixation system often poses limitation on inability of postoperative examination. To resolve this, we developed an X-ray visible layer composed of a radio-opaque marker, barium sulfate, and attached the layer to the fixation plate to allow X-ray imaging for diagnosis in this work. Barium sulfate (BF) has already been used as a radio-opaque additive in clinical fields, such as in vertebroplasty cement, endodontic sealer, and so on. To prepare a radiopaque layer, a fine powder of BF was mixed with a binder material, poly (lactic-co-glycolic acid) (PLGA), which was then cased into the mold to give a layer of pre-determined shape. Subsequently, the layer was attached on a bioabsorbable fixation plate (Inion, Finland), already in clinical use. Due to biodegradation of a binder material, PLGA, BF particles would get freed from the layer in a tailored manner, which could control the longevity of X-ray visibility as well as the biocompatibility of the layer itself. The preliminary results exhibited that the plate attached with a radiopaque layer could be discerned by X-ray up to 28 days when immersed in pH 7.4 phosphate buffered saline at 37 ºC.

8548-203, Session PSMon

Transdermal controlled-delivery application of flurbiprofen-layered double hydroxide nanohybrid

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A novel drug-inorganic nanohybrids with sustained release property was successfully synthesized by immobilizing the flurbiprofen(FB), an anti-inflammatory drug for the arthritis, into layered double hydroxide (LDH) via coprecipitaion reaction. According to the powder X-ray diffraction pattern, the basal spacing of the flurbiprofen-LDH nanohybrid is determined to be 19.6 Å, which is in good agreement with the result of cross-section transmission electron microscopy analysis. Based on fourier transform infrared spectroscopic analysis, flurbiprofen is incorporated in LDH interlayers with deprotonated carboxylate form, and electrostatically bound to the interlayer surface of cationic LDH layers. The chemical composition of the flurbiprofen-LDH nanohybrid is determined as [Zn0.68Al0.33(OH)2][FB0.25]Cl0.10 • 1.06H_2O by elemental analysis, thermo-gravimetric analysis, and HPLC analysis. According to the SEM, TEM and dynamic light scattering analyses, the flurbiprofen-LDH nanohybrid has hexagonal platelet morphology with average particle size of ≃80 nm. Furthermore, in vitro release test shows a biphasic release of flurbiprofen out of the LDH lattice consisting of an initial bursting followed by a slow and sustained release. The possible role of inorganic lattice as a transdermal drug delivery carrier has been shown by demonstrating Franz diffusion cell experiments, using the mouse full skin.

8548-204, Session PSMon

Linearized oncolytic adenoviral plasmid DNA delivered by bioreducible polymers

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As an effort to overcome limits of adenovirus (Ad) as a systemic delivery vector for cancer therapy, we developed a novel system using oncolytic Ad plasmid DNA with two bioreducible polymers: arginine-grafted bioreducible poly(disulfide amine)polymer (ABP) and PEG5k-conjugated ABP (ABP5k) in expectation of oncolytic effect caused by progeny viral production followed by replication. The linearized Ad DNAs for active viral replication polyplexed with each polymer were able to replicate only in human cancer cells and produce progeny viruses. The non-immunogenic polymers delivering the DNAs markedly elicited to evade the innate and adaptive immune response. The biodistribution ratio of the polyplexes administered systemically was approximately 99% decreased in liver when compared with naked Ad. Moreover, tumor-to-liver ratio of the Ad DNA delivered by ABP or ABP5k was significantly elevated at 229- or 419-fold greater than that of naked Ad, respectively. The ABP5k improved the chance of the DNA to localizewithin tumor versus liverwith 1.8-fold increased ratio. In conclusion, the innovative and simple system for delivering oncolytic Ad plasmid DNA with the bioreducible polymers, skipping time-consuming steps such as generation and characterization of oncolytic Ad vectors, can be utilized as an alternative approach for cancer therapy.

8548-205, Session PSMon

Crystal structure evaluation of ZnO nanoparticles in various physiological pH conditions

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In order to investigate the surface behavior and possible phase transformation of zinc oxide (ZnO) nanoparticles in the physiological condition, we have evaluated their pH-dependent crystal structural change of ZnO nanoparticles. First, surface charge of ZnO nanoparticles with 20 and 70nm size were modified by L-serine and sodium citrate for positive and negative charge, respectively. Their original crystal structures were identified by X-ray diffraction patterns. Surface charge modified ZnO nanoparticles then were dispersed in aqueous solutions with different pH; pH 7.4, 1.2 and 6.8 to simulate saliva, gastric and small intestine environment, respectively. The crystal structure of each ZnO nanoparticles recovered from the aqueous solution was measured by X-ray diffraction (XRD) and further analyzed with Scherrer's equation and Rietveld refinement. The partial structure change of ZnO nanoparticles from zinc oxide (Wurtzite) to zinc hydroxide was observed in pH 6.8 and 7.4 condition after 1day incubation. Atomic absorption spectroscopy was employed for the quantitative analysis of the Zn2+ release from the ZnO nanoparticles. In the gastric condition, 15~30wt% of Zn^{2+} ion was released from ZnO solids, however less than 0.5wt% of Zn^{2+} was dissolved in saliva and intestine condition. By scanning electronic spectroscopic images, morphology and size were confirmed resulting from structure change of ZnO nanoparticles in detail.

8548-206, Session PSMon

Dose dependent cytotoxicity of gold nanoparticles in the cortex and neural progenitor cell

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Gold nanoparticles are utilized in the diagnostic and therapeutic tools to detect and treat human disease. We investigated whether GNPs induced apoptosis in the brain and neural progenitor cells, the TUNEL assay was used. We observed GNP-induced death response in human neural cell. HPCs were markedly damaged following the administration of GNPs dose of 200μM and 2mM, while HPCs treated with a low dose of GNPs (20μM) a slight increased relative to that of the control. In the case of the brain, numerous TUNEL-positive cells densely distributed surrounding GNPs after 7 days of injections, whereas TUNEL-positive cells rarely observed at the cerebral cortex of mostly treated groups when transplantation become 3 months. In this study, we observed that apoptosis increased in the brain and cultivated cell following GNP concentration. The result demonstrated that large GNPs (< 100nm) were toxic effect in neural progenitor cells or brain and cytotoxicity increased as the concentration of GNP increased.

8548-207, Session PSMon

Multispectral optoacoustic tomography (MSOT): a novel imaging modality for tracking nanoparticles in subcutaneous and orthotopic tumor models

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Cancer is a disease of aberrant tissue growth. Determining accurate progression in malignancies is of significant importance for understanding heterogeneous growth patterns and irregular nature of malignant tumors. Multispectral Optoacoustic Tomography (MSOT) is a powerful novel imaging modality that decomposes the spectral response of tissue chromophores in vivo, with high resolution and at depths of up to several centimeters. It provides the possibility to separate endogenous chromophores of interest such as oxy-/deoxy-hemoglobin as well as extrinsically administered photo-absorbing agents including nanoparticles and fluorescent dyes.

Of particular focus in this study was the examination of the delivery of labeled macrophages and targeted nanoparticles to the tumor area, studying the differences in tissue oxygenation, compound deposition and uptake into orthotopically and subcutaneously implanted tumors. In addition, we compared the performance of MSOT to an integrated Fluorescent Molecular Tomography (FMT) / X-ray CT system. For the subcutaneous model, HT29 human colon adenocarcinoma cells were injected subcutaneously in the hind limb of CD1 nude mice. For the syngeneic orthotopic model, Balb/c mice were injected with 4T1 mouse mammary tumor cells into the mammary fat pad.

Our results show the superior performance of MSOT over conventional optical imaging. A particular strength of MSOT is the ability to visualize with high spatial resolution the spectral signatures of different intrinsic and extrinsic reporters in deep tissue in vivo. This imaging strategy can be applied for monitoring tumor progression and the evaluation of appropriate treatment regimens based on changes in probe uptake and oxygenation status.

8548-209, Session PSMon

Evaluation of hybrid scaffolds including CMC/Bio-C/BMP-2 materials for regeneration of rat tibial defect using polymer deposition system

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The purpose of this study was to investigate the bone regeneration capability of a tube type polycaprolactone (PCL) scaffold fabricated using a polymer deposition system (PDS) and evaluate the biocompatibility of bone graft materials such as carboxymethyl cellulose (CMC), Bio-C (HA (30%)/TCP (70%)), and bone morphogenetic protein-2(BMP-2). The fabrication of a rapid prototyping based tube type PCL scaffold by the PDS requires a combination of several devices, including a heater, pressure dispenser, and motion controller. The system can manufacture a polymer with high precision using a 200-μm nozzle. The three groups considered in this study were PCL tube scaffold + CMC/Bio-C (Group I), PCL tube scaffold + CMC/Bio-C/BMP-2(0.1 mg/g) (Group II), and PCL tube scaffold + CMC/Bio-C/BMP-2 (0.5 mg/g) (Group III). We used scanning electron microscopy to observe the surface of the fabricated scaffolds. The functional recovery and bone regeneration potentials were estimated by performing an in-vivo animal experiment using a rat tibial defect model. Then, the effect of the groups (I, II, and III) on tibial defects in rats was examined by observing X-ray and -CT images at 4 or 8 weeks and by carrying out histological analyses (H&E staining, Von kossa staining, and trichrome staining) for bone regeneration. In this study, scaffolds fabricated by the PDS, had a diameter of 2.0 mm and a height of 8.0 mm. Moreover, we confirmed that Group III exhibited better biomedical characteristics for bone formation than the other groups. The evaluation of in-vivo experimental results suggested that the co-fabrication of the PCL tube scaffold with CMC/Bio-C/BMP-2(0.5 mg/g) result in sustained bone regeneration, which in turn improved the biocompatibility of the bone graft material.

8548-211, Session PSMon

Evaluation of the accuracy of the CyberKnife Xsight spine tracking system

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The Xsight integrates with the CyberKnife radiosurgery system to eliminate the need for implantation of radiographic markers or fiducials prior to spinal radiosurgery. It locates and tracks spinal lesions relative to spinal osseous landmarks.

The accuracy of the spinal radiosurgical procedure was assessed with an anthropomorphic head and cervical spine phantom. Using this device, all tracking modalities provided by the CyberKnife system can be simulated: fiducial tracking, 6D skull tracking and Xsight tracking for spinal targets. Dose planning was based on 1.0 mm thick computed tomography slices in which an inverse treatment planning technique was used. The end-to-end test was conducted 10 times. The total targeting error is calculated as the length of the distance vector.

RESULTS: The total targeting error of the 6D skull tracking system and fiducial tracking system were 0.53 mm and 0.74 mm. And total targeting error of the Xsight spine tracking system was measured to be 0.53 mm.

CONCLUSION: The Xsight spine tracking system is practically important because it is accurate and eliminates the use of implanted fiducials. Fiducial-free spinal radiosurgery has a significant advantage for spinal radiosurgery in terms of time, cost of treatment, and quality of the life of the patient.

8548-212, Session PSMon

Application of lidocaine-montmorillonite nanohybrid to transdermal drug delivery system

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Montmorillonite (MMT), a layered aluminosilicate, has been used clinically for a long time due to its chemical stability, biocompatibility and high cation exchange capacity. In this study, we have intercalated lidocaine (2-(diethylamino)-N-(2, 6-dimethylphenyl) acetamide, a local anesthetic drug) into MMT through the conventional ion-exchange reaction, and eventually applied the lidocaine-MMT nanohybrid to a transdermal delivery system. According to X-ray diffraction analysis and FT-IR spectra, lidocaine molecules were stabilized in the interlayer space of MMT with electrostatic interaction. From the HPLC and thermogravimetry (TG) analyses, the lidocaine content in lidocaine-MMT nanohybrid was determined to be around 15 wt%. The in-vitro release experiments show that the incorporated lidocaine molecules in MMT layers were sustainedly released due to the intrinsic diffusion pathway in two dimensional lattices through the ion-exchange reaction. The transdermal drug delivery property of the lidocaine-MMT nanohybrid was also tested with Franz-diffusion cell using the hairless mouse skin. Therefore, drug-MMT nanohybrid is effective in transdermal drug delivery system such as patch and biodegradable microneedle requiring both sustained release and enhanced transdermal property.

8548-213, Session PSMon

Surgical sutures enabled with post-surgical pain relief

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Postoperative pain is an unavoidable for the patients after surgery. To relieve the pain, therefore, a pain-relief drug is often orally administrated, which, however, may be limited in low drug bioavailability at the site of action. To resolve this, we prepared surgical sutures enabled with local delivery of a pain-relief drug, ibuprofen. The suture was modified by winding and attaching a biodegradable nanofibrous sheet as a drug carrier on top of the surface, which was separately fabricated by electrospinning a biodegradable polymer, poly (lactic-co-glycolic acid) (PLGA) loaded with ibuprofen. As a result, the drug could be released in a sustained manner for 3 days from the resulting suture in a simulated biological fluid. To further sustain drug release, we also prepared a multi-layered drug-delivery sheet, which was composed of a drug-loaded sheet sandwiched with a sheet of PLGA only, serving as an additional diffusion barrier of the drug. The suture attached with this multi-layered sheet, therefore, could release the drug for a more prolonged period of time, i.e., for up to 6 days. As we examined the in vivo pain-relief efficacy of the drug-delivery sutures, the animal model showed that the sutures could effectively relieve the pain during the period of drug release, even until complete wound healing. Therefore, we conclude that a drug-delivery suture prepared in this work has a promising potential for post-surgery pain relief.

8548-214, Session PSMon

Biosensor for simultaneous detection of Pb^{2+} and Hg^{2+}

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Heavy metal ions, especially, lead or mercury can be accumulated in the human body and able to cause serious and permanent damage. Although it has recently tried to develop functional DNA-based sensors for the detection of heavy metal ions, many of the functional DNAs are vulnerable to hydrolysis by nuclease in human blood and interfered to other ions such as K+, Na+, and so on. Therefore, we have chosen DNA sequence that could react selectively to Pb^{2+} or Hg^{2+}. In addition, We applied selected DNA sequence to gold nanoparticles (AuNPs) for the multiple and stable detection of the metal ions in human serum sample owing to its superior fluorescence quenching efficiency compared with any other organic quenchers in broad wavelength regions and a stabilization effect caused high local salt concentration around the AuNPs of immobilized DNA on AuNPs against to nucleases. We expect that our method will provide an effective tool for the detection of multiple metal ions in body fluids and will form the basis for the future development of new functional DNAs for the detection of other metal ions.

8548-215, Session PSMon

Viral genome DNA/lipoplexes elicit in situ oncolytic viral replication and potent antitumor efficacy via systemic delivery

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Adenovirus (Ad) as cancer molecular therapeutics has been extensively exploited with modification of Ad genetic information, and administration methods in vivo for effective delivery. However, delivery efficacy in vivo has been limited due to Ad envelopment by pre-existing neutralizing antibody, the liver uptake, and hepatotoxicity of Ad. In this study, as an alternative approach of cancer virotherapy, oncolytic viral DNA delivery via lipid envelopment was investigated for orthotopic lung cancer gene therapy. For synergistic therapeutic effect, multifunctional oncolytic Ad DNA expressing TRAIL as a model of therapeutic protein was generated. Lipid hybrid vectors encapsulating oncolytic Ad DNA, pmT-d19/stTR+DOTAP/DOPE was prepared to compose of cationic liposome and TRAIL-expressing oncolytic adenoviral DNA. The diameter of Ad DNA/lipid hybrid vector were characterized, resulting in 152.9 ± 6.3 for pmT-d19/stTR+DOTAP/DOPE and, at the optimal DNA: lipid ratio of 1: 6. TRAIL-expressing oncolytic Ad DNA/lipid hybrid vector (pmT-d19/stTR+DOTAP/DOPE) administered intravenously, showed highly effective antitumor effect in vivo, compared with naked oncolytic Ad or naked viral DNA on A549 orthotopic lung cancer. Furthermore, biodistribution analyzed by quantitative-PCR and histological analysis showed that preferential viral replication was occurred in tumor tissues. Moreover, the viral genome tumor-to-liver ratio was significantly elevated in pmT-d19/stTR+DOTAP/DOPE-treated mice, which was 934- and 27-fold greater than the mT-d19/stTR- and pmT-d19/stTR-treated mice, respectively. These results demonstrate that systemic delivery of oncolytic viral genome DNA with liposomes is a powerful alternative to naked Ad, overcoming the limited clinical applicability of conventional Ads and enabling effective treatment of disseminated metastatic tumors.

8548-216, Session PSMon

Synthesis of colloidal metal-oxide nanoparticles and their resistive switching characteristics

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The metal-oxide nanoparticles have been investigated mostly as medium for medical diagnostics using their optical and magnetic properties as well as for the electronic devices with their unique electrical properties such as resistive switching for logic and memory devices. It has been reported that the thin layers of NiO, TiO_2, $BaTiO_3$, and other metal-oxides exhibit the resistive switching between high and low resistance states, originating from either formation/rupture of conducting filaments, modulated Schottky barrier height at the interface, or altered internal states changing the resistivity. All of these phenomena associate nanoscale redistribution of charges, dopants, and local phase transition; therefore it is rational to employ nanoparticles as switching element. In this study, the nanoparticles of Fe_2O_3, NiO, $BaTiO_3$, Pt-Fe_2O_3 core-shell nanoparticles in diameter of ~ 10 nm were synthesized as colloids through chemical synthesis. In particular the core-shell structure of Pt-Fe_2O_3 nanoparticles could be synthesized by one-step process through preferential oxidation of Fe and consequent Pt pileup. These nanoparticles could be self-assembled as continuous layer through dip-coating process. The nanoparticle assemblies exhibited the multimode resistive switchings; (1) threshold switching with hysteresis of transition from high to low resistance at high voltage and inverse transition at low voltage, (2) bistable unipolar and bipolar switching with transition between high and low resistance states at the same and opposite polarities, and (3) memristive switching with gradually changing and retained resistance. In this presentation, we will discuss the synthesis and resistive switching characteristics of metal-oxide nanoparticles and evaluate the potential biomedical applications.

8548-217, Session PSMon

The TEM study on the in vivo localization of orally administered ZnO nanoparticles in rats

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These days, zinc oxide (ZnO) nanoparticles are widely used in medical and cosmetical industry. In spite of various application of nanosized ZnO, the toxicity of ZnO nanoparticles has not received attention much. In order to study the possible toxicity or accumulation of ZnO nanoparticles in biological system, we have studied the in vivo localization of ZnO (20nm, 70nm) in rat after oral administration. Organ samples such as kidney and liver and excreta (urine and feces) were obtained from Sprague Dawley® (SD) rats after 2000mg/kg of ZnO were orally administrated. We examined the localization and concentration of ZnO in each organ, through TEM images and EDS. The TEM images of liver and kidney from ZnO treated rats showed almost similar images of untreated ones, and we could not observe significant almost of Zn in the organs. On the other hand, the EDS amount of the feces from ZnO treated rats showed Zn concentration (20~30 wt%) fairly high. These results imply that the most of the orally administrated ZnO nanoparticles can be excreted through feces and it is thought that the ZnO nanoparticles are not significantly accumulated in organs like liver and kidney.

8548-218, Session PSMon

Active targeting of RGD-conjugated bioreducible polymer for delivery of oncolytic adenovirus expressing shRNA against IL-8 mRNA

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Even though oncolytic adenovirus (Ad) has been highlighted in the field of cancer gene therapy, transductional targeting and immune privilege still remain difficult challenges. The recent reports have noted the increasing tendency of adenoviral surface shielding with polymer to overcome the limits of its practical application. We previously reported the potential of the biodegradable polymer, poly(CBA-DAH) (CD) as a promising candidate for efficient gene delivery. To endow the selective-targeting moiety of tumor vasculature to CD, cRGDfC well-known as a ligand for cell-surface integrins on tumor endothelium was conjugated to CD using hetero-bifunctional cross-linker SM (PEG)n. The cytopathic effects of oncolytic Ad coated with the polymers were much more enhanced dose-dependently when compared with that of naked Ad in cancer cells selectively. Above all, the most potent oncolytic effect was assessed with the treatment of Ad/CD-PEG500-RGD in all cancer cells. The enhanced cytopathic effect of Ad/RGD-conjugated polymer was specifically inhibited by blocking antibodies to integrins, but not by blocking antibody to CAR. HT1080 cells treated with Ad/CD-PEG500-RGD showed strong induction of apoptosis and suppression of IL-8 and VEGF expression as well. These results suggest that RGD-conjugated bioreducible polymer might be used to deliver oncolytic Ad safely and efficiently for tumor therapy.

8548-219, Session PSMon

L4H: a lab-in-a-box approach for heart monitoring based on a high-throughput holographic homocysteine blood screening

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Many traditional medical tests require expensive and bulky equipment as well as the culturing of the cells and thus take between a couple of hours to a couple of days to complete. The global transition from analog to digital techniques is also having an impact on medicine and is fast leading to the engineering of most medical techniques. Lab technicians now adopt digital diagnostic techniques that will enable faster and more accurate analysis at a fraction of the traditional costs. Cardio-Vascular-Diseases (CVDs) are a leading cause of deaths around the world and Digital Holographic Microscopy (DHM) presents a good opportunity in this area and is emerging as a leading approach for diagnostic screening and analysis. This paper presents a low cost and high speed DHM approach that predicts the propensity for heart disease based on the presence of elevated serum levels of homocysteine. Sets of blood holograms are subjected to a wavelet transformation prior to the reconstruction and analysis steps. This transform increases the level of feature discrimination and provides a space-frequency analysis, rather than the traditional frequency-only analysis available with the Fourier transform. The output of this transform was then be subjected to a series of statistical analysis in order to extract comparative metrics for comparing the three holograms. The results have been used to develop a set of risk predictor metrics that can give an accurate estimation of the propensity of a patient for developing a CVD, based on the presence of Homocysteine in his blood sample.

8548-220, Session PSMon

Electrooxidation of saccharides at platinum electrode

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The peak position of oxidation current under EDL and oxide formation region are almost similar regardless of kinds of saccharides. This proposes that the C1 of glucose moiety might be also involved in the oxidation of sucrose. However, C1 of glucose moiety is linked to the C5 of fructose moiety in sucrose form, there is no reactive group such as hydroxyl group. Therefore, it is difficult to understand the sucrose oxidation as hemiacetal carbon based mechanism of glucose oxidation. Other positions, e.g. C2-C6, of saccharide molecule would relate to sucrose oxidation.

8548-221, Session PSMon

Development of hybrid nanoparticles for multimodal imaging and accurate diagnosis

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A variety of biomedical imaging modalities including magnetic resonance imaging (MRI), positron emission tomography (PET), and computed X-ray tomography (CT) are utilized to diagnosis various of diseases. However, each imaging modality not only has its own advantages but also disadvantages, and a single modality does not possess all of the required capabilities for comprehensive imaging. Therefore, by combining various imaging modalities which can be complementary to each other, the accuracy of diagnosis can be greatly enhanced.

Magnetic nanoparticles can serve as a platform material by hybridizing with other functional moieties including fluorescence tags, radionuclides, and other imaging components. As a result, hybrid nanoparticles can endow variety of imaging modalities with enhanced sensitivity, spatial resolution, and diagnostic accuracy. Here, we report several hybrid nanoparticles for multi modal imaging such as, PET-MRI, MRI-Optical, and T1/T2 dual mode MR imaging. The finding suggests that developed hybrid nanoparticles can be potentially applied to the imaging of wide range of biological targets with enhanced diagnostic accuracy.

8548-222, Session PSMon

Biodegradable fixation plates of layered metal hydroxides/polymer composites for x-ray diagnosis

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Biodegradable polymer plates can be clinically used as an alternative to metal plates (e.g., titanium) for internal fixation, which, however, are not visible with X-ray for post-operative diagnostics. In this study, therefore, we prepared biodegradable plates with X-ray visibility by physically mixing radiopaque inorganic metal hydroxides materials such as MgAl-LDH, ZnAl-LDH, CaFe-LDH, and Zinc basic salts with a biodegradable binder material, poly (lactic-co-glycolic acid) (PLGA). The radiopacity increases with the attenuation coefficients of metals composed of inorganic layered materials. The radiopacity also increases as the thickness of biodegradable fixation plate increases from 1.0 mm to 2.0 mm. When the fixation plate was applied to the simulated body fluid solution, the radiopacity gradually decreases due to the decreased density of layered materials in the fixation plate by swelling and degradation of PLGA regardless of the chemical composition of inorganic layered materials and thickness of layer. According to the in-vitro biodegradation test, a discernible image of the radiopaque plate could be obtained by X-ray for up to around 2 months. Therefore, the biodegradable radiopaque fixation plate, prepared in this work, have a high potential as a fixation device with X-ray visibility

8548-223, Session PSMon

Multimodal nonlinear optical microscopy for nanomaterial and biomedical imaging

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Nonlinear optical (NLO) microscopy has been developed as a powerful measurement tool for studies of complex biological tissues and nanomaterials because the strong intrinsic NLO signals are susceptible to the specific molecule or structure. Multimodal NLO microscopy combining with two-photon fluorescence (TPF), second-harmonic generation (SHG), and coherent anti-Stokes Raman scattering (CARS) has allowed not only investigation of nanomaterials such as gold nanorods (NRs), semiconducting nanowires (NWs) and carbon nanotubes, but also biological issue concerning lipid metabolism, cardiovascular disease, cancer development, and so on. We developed the platform of multimodal NLO microscopy coupling with a wavelength-tunable CARS, TPF, and SHG. A picosecond laser (80 MHz, 7 ps, picoEmerald, High Q Laser) was used to generate a CARS signal with integrated a stoke beam (1064 nm) and a tunable pump beam (700~950 nm). A femtosecond laser (80 MHz, 75 fs, Chameleon Vision-S, Coherent) used for TPF and SHG imaging. All laser beams were combined and delivered into an inverted microscope (FV1000MPE/IX81, Olympus). A 60x water immersion objective lens (1.2 NA) was used to focus the beams into the sample. The two forward signals (CARS and SHG) were collected by an air condenser and detected by two external PMT detectors, respectively. The backward signal (TPF) was collected by the objective lens and detected by the other external PMT detector. Our multimodal NLO microscopy can simultaneously provide the specific molecules and dynamic structure imaging. We expect that the many applications in nanomaterial and biomedical issues will be found by using our multimodal NLO microscopy.

8548-225, Session PSMon

Subdiffraction-limited imaging based on surface plasmon enhanced random activation of nanoscale antennas

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Recently, optical microscopy at a subdiffraction-limited imaging resolution has drawn tremendous attention. Super-resolution imaging has enabled the detection of bio-molecular events in cellular environments with unprecedented accuracy. An interesting approach to improve imaging resolution is nano-antenna based surface plasmon enhanced imaging, where nanoscale antennas excite highly localized near-fields below diffraction limit to be applied for cell imaging. In this regard, we proposed use of silver nano-islands as random nano-antennas for surface plasmon enhanced randomly activated (SUPRA) microscopy.

In this study, we report demonstration of nano-island based SUPRA imaging for imaging live cells and molecular events. Nano-islands were synthesized by high temperature annealing with varying thickness of silver films. For comparison, periodic metal nano-antenna structures based on nano-gratings and nano-posts were also fabricated. Near-field distribution by nano-islands was calculated using rigorous

coupled-wave analysis to understand the effects of film thickness and island parameters, such as island size and separation. Near-field scanning optical microscopy was used to acquire impulse response for image reconstruction.

Experimental results confirm imaging of cellular processes on the order of 100 nm below diffraction limit. SUPRA microscopy is expected to be useful as a convenient way of achieving far-field imaging of local events using plasmon enhanced metal nano-antennas based on random nanopatterns.

8548-226, Session PSMon

Smart-memory behaviours of biodegradable polymers for biomedical implants

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The aim of this study is to investigate biodegradable polymers with shape-memory property through a polymer-blend method and to characterize their shape-switching in the body temperature (37 °C). In this study, some biodegradable polymers were dissolved in chloroform and blend films were prepared with various ratios of polymers by solution casting. These blended samples were characterized by differential scanning calorimetry (DSC), dynamic mechanical analysis (DMA), and thermal gravimetric analysis (TGA). To measure the shape-memory effect, the films were cut into rectangular strips and then incubated at 37 °C for 10 min. After applying physical force to fix the temporary shape at desired temperature for 10 min, the samples were unloaded to zero stress and then held at 37 °C. Finally, the shape recovery of the samples was observed.

8548-227, Session PSMon

Bioreducible polymer-conjugated oncolytic adenovirus for hepatoma-specific therapy via systemic administration

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Systemic administration of adenovirus (Ad) vectors is complicated by host immune responses and viral accumulation in the liver, resulting in a short circulatory virus half-life, low efficacy, and host side effects. Ad surface modification is thus required to enhance safety and therapeutic efficacy. An arginine-grafted bioreducible polymer (ABP) was chemically conjugated to the Ad surface, generating Ad-DE1/GFP-ABP. A hepatocellular carcinoma [HCC]-selective oncolytic Ad complex, YKL-1001-ABP, was also generated. Transduction efficiency of Ad-DE1/GFP-ABP was enhanced compared to naked Ad-DE1/GFP. YKL-1001-ABP elicited an enhanced and specific killing effect in liver cancer cells (Huh7 and HepG2) expressing a-fetoprotein (AFP). Compared with naked Ad, systemic administration of ABP-conjugated Ad resulted in reduced liver toxicity and interleukin (IL)-6 production in vitro and in vivo. Ad-DE1/GFP-ABP was more resistant to the neutralizing effects of human serum compared to naked Ad-DE1/GFP. ABP conjugation extended blood circulation time 45-fold and reduced anti-Ad Ab neutralization. Moreover, systemic administration of YKL-1001-ABP markedly suppressed growth of Huh7 hepatocellular carcinoma. These results demonstrate that chemical conjugation of ABP to the Ad surface improves safety and efficacy, indicating that ABP-conjugated Ad is a potentially useful cancer therapeutic agent to target cancer via systemic administration.

8548-228, Session PSMon

The effect of bone morphogenic protein-2-coated tri-calcium phosphate/hydroxyapatite on new bone formation in a rat model of tibial and femoral distraction osteogenesis

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The purpose of this study was to evaluate the effect of single insertions of bone morphogenic protein-2 (BMP-2), delivered by tri-calcium phosphate (TCP)/hydroxyapatite (HA), administered at osteotomy sites, on the rate of new bone formation during DO in a rat model. Seventy-two male Sprague-Dawley rats were randomized into two groups for tibial and femoral model. And each group was also devided by three groups (Group I: control, Group II: only TCP/HA, Group III: rhBMP-2-coated TCP/HA). Materials were inserted into the medullary canal at the tibial and femoral osteotomy site at the end of the lengthening period with 10mm distraction. At two different time-points [at 4 weeks and 8 weeks after cessation of distraction], the progress of bone formation was determined with micro-CT, histology and real-time PCR. All group III exhibited bridging callus formation 8 weeks after cessation of distraction, whereas group II demonstrated non-bridging callus formation. None of the group I showed callus in the central zone of the distraction gap. For micro-CT, bone formation and remodeling of the distraction regeneration with beta-TCP/HA coated with rhBMP-2 had greater values than the control groups at all time-points. Application of rhBMP-2, at the end of the rapid distraction period, as a single bolus significantly increased the osteogenic process, while beta-TCP/HA behaved effectively as a sustained delivery system for this osteoinductive protein.

8548-229, Session PSMon

Dynamic multispectral optoacoustic tomography (MSOT) imaging of nanoparticle tumor perfusion kinetics

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A wide range of nanoparticles differing in size, shape and surface characteristics are available for therapeutic and diagnostic applications in oncology. To ensure optimal accumulation of nanoparticles in solid tumors, it is crucial to obtain quantitative data for their design. We employed a sensitive and specific imaging modality, termed Multispectral Optoacoustic Tomography (MSOT), to dynamically evaluate tumor accumulation kinetics of well-characterized nanoparticles.

Optoacoustic imaging is based on the generation of ultrasound waves induced by the absorption of light pulses in tissue. During MSOT imaging, an object is illuminated using a near-infrared (NIR) laser at multiple wavelengths to then spectrally resolve distinct absorbers over background tissue. This results in the simultaneous visualization of anatomical, functional and molecular contrast with a spatial and temporal resolution typical for ultrasound imaging. To determine the influence of nanoparticle surface characteristics on tumor perfusion kinetics, liposomes with different charges (zwitterionic, positive and negative) and different degrees of PEGylation were formulated. Using MSOT we then evaluated the tumor accumulation properties of each nanoparticle formulation.

In summary, MSOT offers a new and unique imaging modality that (1) has a resolution ten-fold higher than nuclear and optical imaging, (2) allows for real-time imaging with molecular specificity through several centimeters of tissue and (3) is safe (i.e. no ionizing radiation) and cost-efficient. We used this modality to quantitatively determine the

influence of surface charge and PEGylation on tumor perfusion kinetics of nanoparticles. These parameters can be utilized for the rational design of nanoparticles for oncology applications.

8548-230, Session PSMon

Nanohybrid system for taste masking and enhanced bioavailability of aripiprazole

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Poor aqueous solubility and unpleasant taste of aripiprazole (APZ) have been recurring problems, due to its low bioavailability and low patients' compliance, respectively. In this study, we have attempted to encapsulate drug molecules in the montmorillonite (MMT) clay to form organic-inorganic hybrids, for both taste masking and solubility enhancement of APZ (i.e., APZ-MMT). To further improve the efficacy of taste masking and solubility of the drug, the APZ-MMT was also coated with a cationic polymer, polyvinylacetal diethylaminoacetate (AEA). In vitro dissolution tests at neutral pH showed that the amount of drug released from the AEA coated APZ-MMT was greatly suppressed (< 1%) for the first 3 min, suggesting that AEA coated APZ-MMT is a potential formulation for taste masking of APZ. Notably, in a simulated gastric juice at pH 1.2, the total percentage of APZ released in the first 2 h increased up to 95% for the AEA coated APZ-MMT. Furthermore, this in vitro release profile was also similar to that of Abilify®, a medication currently available on the market. In vivo experiments using Sprague-Dawley rats were also performed to compare the pharmacokinetics of AEA coated APZ-MMT and Abilify®. The AEA coated APZ-MMT exhibited about 20% higher systemic exposure of APZ and its metabolite, dehydro-APZ, as compared with Abilify®. It can, therefore, be concluded that a new MMT-based nanovehicle, coated with a cationic polymer, could be a promising delivery system for both taste masking and enhanced bioavailability of APZ.

8548-231, Session PSMon

Control of cellular signaling via magnetic nanoparticles

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The ability to regulate cellular activities in a controlled manner is one of the most challenging issues in field ranging from cell biology to biomedicine. In contrast to conventional biochemical ligands, magnetic nanoparticles have the potential of becoming useful tools for controlling cell signaling pathways in a space and time selective fashion. Because these particles can be coupled with magnetic field to produce enough force to initiate the actuation of biological objects, this magnetic stimulation system can switch the cellular activity on and off. In addition, the nanoscale dimensions of nanoparticles make them beneficial for probing cellular sensory structures and functions at the molecular level and for inducing specific cellular activation process. In this study, we demonstrate that magnetic triggering of membrane receptor clustering-mediated cellular signaling is possible in cellular system.

8548-234, Session PSMon

Synthesis of iron oxide nanotubes and their applications in neuroscience and drug delivery

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The treatment of the diseases in the nervous system has been a formidable challenge in medicine. In this regard, the ability to differentiate cells into neurons is a field of hot pursuit. This paper discusses the biocompatibility of hematite nanotubes with PC12 cells and the use of hematite nanotubes to deliver nerve growth factor (NGF) for the differentiation and growth of PC12 cells as neurons. The dispersed hematite nanotubes used in this work were synthesized by template-assisted thermal decomposition method, followed by dissolving the template, and their morphology and magnetic properties were characterized by electron microscopes (SEM and TEM) and vibration sampling magnetometer, respectively. The hematite nanotubes had a diameter around 200 nm and an average length of about 10 & #61549;m, and they had a low coercivity (about 10 Oe) at room temperature. The biocompatibility of the hematite nanotubes was studied by culturing PC12 cells in the presence of the hematite nanotubes, and the NGF required for the differentiation of PC12 cells into neurons was coupled to the nanotubes. Neurite (axon and dendrite) outgrowth, formation of morphological connections, and close contacts between PC12 cells and hematite nanotubes unequivocally confirmed the biocompatibility of hematite nanotubes. The efficiency of hematite nanotubes to bind with NGF and the ability of the NGF-incorporated hematite nanotubes to release the bound NGF were also investigated. It is found that NGF-incorporated hematite nanotubes enabled the differentiation of PC12 cells into neurons, and the filopodia extending from growth cones were in close proximity to the NGF-incorporated hematite nanotubes, at times appearing to extend toward or into them. These observations indicate that hematite nanotubes could be used as a vehicle for NGF delivery. The approaches toward potential treatments using iron oxide nanotubes for neurodegenerative disorders and injuries to the nervous system are discussed in the final part of this paper.

8548-235, Session PSMon

Metabolomic study by using a web-based platform for analysis of large-scale TOF-SIMS data

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Time-of-flight secondary ion mass spectrometry (TOF-SIMS) has been a useful tool to profile secondary ions from the near surface region of specimens with its high molecular specificity and submicron spatial resolution. However, the TOF-SIMS analysis of even a moderately large size of samples has been hampered due to the lack of tools for automatically analyzing the huge amount of TOF-SIMS data. Here, we present a computational platform to automatically identify and align peaks, find discriminatory ions, build a classifier, and construct networks describing differential metabolic pathways. To demonstrate the utility of the platform, we analyzed 43 datasets generated from seven gastric cancer and eight normal tissues using TOF-SIMS. A total of 87,138 ions were detected from the 43 datasets by TOF-SIMS. We selected and then aligned 1,286 ions. Among them, we found the 66

ions discriminating gastric cancer tissues from normal ones. Using these 66 ions, we then built a partial least square-discriminant analysis (PLS-DA) model resulting in a misclassification error rate of 0.024. Finally, network analysis of the 66 ions showed disregulation of amino acid metabolism in the gastric cancer tissues. The results show that the proposed framework was effective in analyzing TOF-SIMS data from a moderately large size of samples, resulting in discrimination of gastric cancer tissues from normal tissues and identification of biomarker candidates associated with the amino acid metabolism.[1]

[1] Yun SJ, Park JW, CHoi IJ, Kang B, Kim HK, Moon DW, Lee TG, Hwang D. TOFSIMS-P: A web-based platform for analysis of large-scale TOF-SIMS data. (2011) Anal. Chem. 83(24) 9298-305

8548-236, Session PSMon

An evaluation of PLGA(polylactic-co-glycolic acid) plate and screw system for fixation of mandible fracture in rabbit model

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In this work, we investigated the efficacy and safety of recently-developed modifiable bioabsorbable plates and screws (Glotech, Korea), which are made of PLGA (polylactic-co-glycolic acids). In vitro extract test and bacterial reverse mutation test revealed that neither cytotoxicity nor genotoxicity was observed with the plates and screws tested in this work. In vivo mandible fracture model in rabbit was introduced to evaluate the in vivo efficacy and biocompatibility of the PLGA-based plates and screws. At 4, 6, 8 and 10 weeks after implantation, tissue specimens were taken from the implanted sites of the rabbits and histological analysis was performed for each of the specimens. After 4 weeks, the plate was covered by connective tissues and severe chronic active inflammation in soft tissue was observed. After 6 weeks, the inflammation decreased and some of the specimens exhibited new bone formation around the periostium. After 8 and 10 weeks, new bone formation was observed with all samples, where almost no severe inflammation was involved, implying the healing of the fracture. Given these, it can be suggested that biodegradable plate and screw system that we evaluated in this work be effective for treatment of mandible fracture, one of the regions under a high load-bearing condition. The adjustment process and long-term follow-up study is in progress for clinical application of the plate and screw system introduced in this work.

8548-237, Session PSMon

Gentamicin and bone morphogenic protein-2 (BMP-2)-delivering heparinized-titanium implant with enhanced antibacterial activity and osteointegration

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Insufficient bonding of implants to bone tissues and bacterial infections lead to the failure of titanium (Ti)-based orthopedic and dental implants. The aim of this study is to develop novel Ti implants that enhance osteoblast functions, while simultaneously decreasing bacterial infections. First, the surface of pristine Ti was functionalized with heparin-dopamine by mimicking a mussel adhesion mechanism. Gentamicin sulfate (GS) and/or bone morphogenic protein-2 (BMP-2) was then sequentially immobilized to the heparinized-Ti (Hep-Ti) surface. The compositions of pristine Ti and Hep-Ti with or without gentamicin and/or BMP-2 were characterized by X-ray photoelectron spectroscopy (XPS) and the growth of Staphylococcus aureus on the substrates was assayed. Osteoblast functions of all Ti substrates were investigated by cell proliferation assays, alkaline phosphate (ALP) activity, and calcium deposition. The results showed that the growth of bacteria on GS/Hep-Ti and GS/BMP-2/Hep-Ti was significantly lower compared to that on the pristine Ti and BMP-2/Hep-Ti. In addition, BMP-2/Hep-Ti and GS/BMP-2/Hep-Ti significantly enhanced ALP activity and calcium mineral deposition of osteoblast cells. Taken together, GS/BMP-2/Hep-Ti could achieve the dual functions of excellent antibacterial activity and osteoblast function promotion. Therefore, dual drug (antibiotics and osteoinductive protein)-eluting Ti substrates such as GS/BMP-2/Hep-Ti are a promising material for the enhanced osteointegration and implant longevity in orthopedics and dentistry.

8548-239, Session PSMon

Starting with silver acorn structure, followed by galvanic replacement reaction to form gold snow man structure for singlet oxygen inducting photodynamic and fluorescent activities

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Crosslinked Poly(styrene-alt-maleic acid) acorn nanoparticles with silver at the base was synthesized by hydrothermal process. Silver has been replaced with gold, prominently over the polymer by sacrificial galvanic exchange to get Au-PSMA janus nanoparticles. The Au-PSMA janus structure can be controlled to either snowman or dumbbell structure with relation to reaction time. Accounting the distinct gold and PSMA domain, snowman structure was selected for further study.

This snowman-like, organic and gold domain acts as single platform to bring photosensitiser (TBO) and the reactive oxygen sensor (Amino Phenyl Flourescin - APF) together, respectively. We successfully conjugated TBO to PSMA with the amide bond, while APF to gold domain with thiol linker. This composite Au-PSMA janus nanoparticles with TBO and APF expressed the integrated function to photo-sensitize and photo-sensitization induced fluorescence.

8548-240, Session PSMon

Development of intelligent theragonostic bacteria-based biomedical microrobot

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This paper proposed a new concept on the development of intelligent biomedical microrobot using flagellated bacteria Salmonella typhimurium contained-various properties such as micro-actuators, micro-sensors, treatment and diagnosis of solid tumors. We developed a bacteria based-microrobot using attenuated Salmonella typhimurium for medical applications. For motility enhancement of the microrobot, the bacteria could be selectively attached on microbead surfaces using the submerged property of microbeads on agarose gel. Firstly, we fabricated the bacteria based-microrobot using the polystyrene (PS) microbeads treated with antibacterial adherent factors, such as O_2 plasma and bovine serum albumin (BSA). The selective bacteria attached-PS microbead groups using O_2 plasma and BSA could show higher motility than untreated-whole bacteria attached-PS microbead groups. Secondly, we suggested a new bacteria based-microrobot using biocompatible materials, poly-ethylene-glycol (PEG). For the regulation of the bacterial selective attachment, we adopted a bacteria

adhesion material, Poly-L-Lysine (PLL). Similar with the previous results of PS microbeads, the bacteria selective attached-PEG microbead group through the PLL selective coating could show the enhanced motility than PLL uncoated- and PLL whole coated-PEG microbead groups. As the results, we expected that the proposed methodologies for the fabrication of bacteria based-microrobots could be applied to the development of a potential applicable biomedical microrobot for human body.

8548-241, Session PSMon

Fabrication and characterization of micropatterns with plasma-polymerized polyethylene glycol thin film modified by plasma treatment

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Surface treatment by using induced plasma is well-known technique as reproducible and accurate modification of surface morphology or chemical composition of the samples. In this work, we modified plasma polymerized polyethylene glycol (PP-PEG) thin film with a simple plasma treatment to change the non-fouling surface property to a fouling one for proteins and cells using the plasma enhanced chemical vapor deposition (PECVD) method. Plasma-treated surfaces were characterized with various methods such as atomic force microscopy (AFM), scanning electron microscopy (SEM), water contact angle (WCA), X-ray photoelectron spectroscopy (XPS) and time-of-flight secondary ion mass spectroscopy (TOF-SIMS). In addition, we successfully fabricated micro-patterned PP-PEG surface by simple plasma treatment through a metal shadow mask, and investigated protein adsorption and cell attachment on the micro-patterned surface. As a result, protein and cells adhered only onto the plasma-treated areas and not onto the bare PP-PEG areas. These results show that plasma treatment on a PP-PEG surface together with the metal shadow mask would be a simple yet effective method of fabricating a micro-pattern of proteins and cells for various biomedical applications.

8548-242, Session PSMon

Magnetic nano-probes for detecting ASGPr-expressed hepatoma using MR imaging

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Magnetic resonance (MR) imaging has played an important role in the diagnosis of cancer because detail anatomical images with high contrast and spatial resolution can be obtained non-invasively. In recent, MR imaging contrast agents based on high crystalline magnetic nanoparticles have attracted because biomarker-specific magnetic nanoparticles can monitor pharmacokinetic effect at specific site. Thus, we fabricated manganese ferrite nanoparticles (MFNPs) by the thermal decomposition method and they are conjugated with lactobionic acid (LBA) as a targeting moiety for specific MR imaging of hepatocellular carcinoma (HCC). LBA can be bound to asialoglycoprotein receptors (ASGPr) that are expressed on HepG2, human HCC cell line. Therefore, ASGPr-expressed HepG2 cells were selected as the target cell line and ASGPr-deficient MCF7 cells as a control expreiment. Cytotoxicity of LBA conjugated MFNPs (LBA-MFNPs) was not significant for both cell lines. The targeting ability of LBA-MFNPs was investigated using flow cytometry, MR imaging, dark field microscopy, Prussian blue staining, and transmission electron microscopy. Therefore, we confirmed that LBA-MFNPs were successfully attached to ASGPr-expressed HepG2 cells. In conclusion, we expect that results of this work will be a promising strategy for cancer diagnosis based on MR imaging.

We fabricated manganese ferrite nanoparticles (MFNPs) that are conjugated with lactobionic acid (LBA) as a targeting moiety. LBA conjugated MFNPs (LBA-MFNPs) have a high affinity to asialoglycoprotein receptors (ASGPr) that are expressed on HepG2, human hepatocellular carcinoma (HCC) cell line. Cytotoxicity of LBA-MFNPs was not significant for HepG2 cells. The targeted MR imaging ability of LBA-MFNPs was assessed by macroscopic and microscopic studies. Finally, we indicated that LBA-MFNPs have a high specific affinity to ASGPr-expressed HCC. In conclusion, we expect that our results will be a promising strategy for cancer diagnosis via MR imaging.

8548-243, Session PSMon

Bionanocomposites based on layered double hydroxides as drug delivery systems

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Bionanocomposites are nanostructured biohybrid materials in which a biopolymer is assembled to a nanosized inorganic solid. They constitute a growing field of research not only as ecological materials, but also for other applications including biomedicine, such in tissue engineering or drug delivery systems (DDS). Layered double hydroxides (LDHs) have been profited to incorporate a large variety of anionic guest species for uses as DDS although their high sensitivity to pH in many cases may provoke the rapid release of the intercalated species. Hence, LDHs coated with a protective polymeric matrix is an interesting way to reach a better control in DDS applications. Our alternative consists in the use of bionanocomposites in which LDH-drug hybrid systems are either combined to biopolymers of different hydrophilic character or to biopolymers provided of special functionalities that may favor the specific action in a part of the gastro-intestinal tract. In this communication we will show two types of LDH-based bionanocomposites for DDS applications: i) a LDH intercalated with Ibuprofen, as drug model, assembled to mixtures of the polysaccharide alginate and the hydrophobic protein zein; ii) 5-aminosalicylic acid, inflammatory drug for treatment of ulcerative colitis, intercalated in a LDH-chitosan bionanocomposite modified with tiol groups and assembled to pectin acting as a second gastroresistant biopolymer. In both approaches, the synergistic properties afforded by each component of the bionanocomposite result in DDS resistant to pH changes, being possible the drug release in a controlled manner or even acting only in the focus of the disease, minimizing side effects.

8548-503, Session PLEN3

TBD-Plenary 3

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No Abstract Available

8548-17, Session 4a

Magnetic/optic or magnetic/acoustic bifunctional iron oxide-based objects for bioimaging *(Keynote Presentation)*

Geneviève Pourroy, Institut de Physique et Chimie des Matériaux de Strasbourg (France)

No Abstract Available

8548-18, Session 4a

NIR nanoplatform for molecular imaging and photodynamic therapy of cancer

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In recent years upconversion nanoparticles (UCNPs) capable of converting NIR- to visible photons under normal condition has been drawing considerable attention in biological and medical fields. These novel nanoplatforms, excitable by economic cw diode lasers, have excellent signal-to-noise ratio when imaging owing to the absence of auto-fluorescence and reduction of light scattering. UCNPs have also high photostability and allow for deep penetration in bio-tissues.

Constructing such a qualified nanoplatform is a challenge because inherent upconversion efficiency is extremely low under clinical conditions. We have, in recent years, been focusing on the construction and optimization of biofunctionalized upconversion nanaoplatforms.

In this presentation our effort in developing a highly efficient NIR active nanoplatform for cancer diagnosis and therapy will be introduced. In brief, $NaYF_4$ nanoparticles codoped with Yb^{3+} and Er^{3+} are coated with a $NaYF_4$ shell to enhance the upconversion efficiency. Different from popular electrostatic approaches of loading photosensitizing molecules on the nanoplatform which often suffer from desorption and/or leakage, covalent binding approach is followed to load stably photosensitizing molecules in our study. In-vitro and in-vivo experimental results of simultaneous imaging and photodynamic therapy based on these nanoplatforms will be introduced and discussed.

8548-19, Session 4a

Multispectral optoacoustic tomography as a novel tool for whole-body investigation of nanoparticle biodistribution

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Multispectral Optoacoustic Tomography (MSOT) is a powerful novel imaging modality that decomposes the spectral response of intrinsic tissue chromophores in vivo, with high resolution and at depths of up to several centimeters. In addition, extrinsic absorbers of interest, such as photo-absorbing organic dyes and nanoparticles, can also be multispectrally resolved in tissue. A particular strength of MSOT over other imaging modalities is the ability to extract anatomical, functional and molecular information from a single scan.

In this work, the ability of MSOT to track nanoparticle whole-body biodistribution and pharmacokinetics is demonstrated. Liposomes containing near-infrared (NIR) fluorescent dye were injected intravenously into mice and the accumulation and clearance of the nanoparticles over time were observed by MSOT. Regions of interest included liver, spleen, kidneys, brain, heart and vasculature. The acquisition of data at 10 Hz allowed the visualization of the fast uptake kinetics, while longitudinal data acquisition allowed the determination of the differential pharmacokinetic properties of each compound. Liposomal derivatives containing polyethylene glycol (PEG) were discriminated from those preparations without PEG based on the blood clearance rate as assessed by MSOT. Further, MSOT was used to visualize the organ specificity of various derivatives. MSOT data showed an excellent correlation with ex vivo fluorescence studies.

With the ability to visualize and quantify fast kinetics and organ specificity of injected NIR-absorbing agents of interest, MSOT is poised to become an invaluable tool in the drug discovery process by enabling whole-body in vivo visualization of drug biodistribution.

8548-70, Session 4b

Nanotechnology for brain tumor diagnosis and treatment *(Keynote Presentation)*

Taeghwan Hyeon, Seoul National Univ. (Korea, Republic of)

We developed a generalized synthetic procedure, called as “heat-up process,” to produce uniform-sized nanocrystals of many transition metals and oxides without a size selection process. We were able to synthesize uniform magnetite nanocrystals as much as 1 kilogram-scale from thermolysis of Fe-oleate complex.

Extremely small 3 nm-sized iron oxide nanoparticles (ESION) were used for high resolution imaging of blood vessels of < 0.2 mm. Ferrimagnetic iron oxide nanoparticles (FION) of > 20 nm exhibit extremely large magnetization and coercivity. The cells labeled with FIONs showed enormous T2 contrast enhancement that enabled visualization of single cells. After transplantation of syngeneic islets, the diabetic rats became euglycemic, and the transplanted islets were monitored up to 150 days. Very recently, theoretically predicted maximum of r2 relaxivity was achieved by optimizing the overall size of FIONs. 22 nm FIONs exhibited excellent colloidal stability and were accumulated at the tumor after intravenous administration. In addition, we reported on the fabrication of (1) monodisperse magnetite nanoparticles immobilized with uniform pore-sized mesoporous silica spheres for simultaneous MRI, fluorescence imaging, and drug delivery, (2) Fe_3O_4/TaO_x core/shell nanoparticles for simultaneous MRI and CT imaging and (3) hollow magnetite nanocapsules and used them for both the MRI contrast agent and magnetic guided drug delivery vehicle.

As a new type of multimodal imaging probe for luminescence imaging and T1 MRI, $NaGdF_4$:Yb,Er@$NaGdF_4$ core/shell upconverting nanoparticles (UCNPs) were developed. UCNPs emit visible light under NIR excitation. The increased penetration depth of excitation light, excellent photostability, and absence of autofluorescence of UCNPs make them particularly suitable for in vivo imaging and long-term tracking of cells

8548-72, Session 4b

Carbon nanotubes-polymer nanoparticles inks for healthcare textile

Pratyush Rai, Jungmin Lee, Gyanesh N. Mathur, Vijay K. Varadan, Univ. of Arkansas (United States)

Healthcare textiles are ambient health monitoring systems that can contribute towards medical aid as well as general fitness of the populace. These are textile based products that have sensor systems mounted on them or are electrically functionalized to act as sensors. While embedded sensor chipsets and connection wires have been shown as working prototypes of this concept, there is a need for seamless integration of sensor technologies without hindering the inherent properties of the textile. Screen printing or stamping with electrically conductive inks have been demonstrated as technologies for fabricating electronics on flexible substrates. They are applicable to textile manufacturing as well. Printing technology allows for fabrication of nanocomposite based electronics elements in a bottom-up fashion. This has advantages such as low material consumption, high speed fabrication and low temperature processing. In this research, Multi-Wall Carbon Nanotubes (MWCNTs) and polyaniline nanoparticles (PANP)

core shell based nanocomposites were synthesized and formulated into colloidal ink. Printed MWCNTs-PANP traces were electrically characterized and compared with traces made with those made by other composites such as Silver, Silver-Copper, and Carbon Black. As a proof of concept, a textile based single lead ECG system enabled by the MWCNTs-PANP traces has been demonstrated.

8548-120, Session 4c

Label-free cell assay based on spectral domain optical coherence phase contrast microscopy

SuHo Ryu, Chulmin Joo, Yonsei University (Korea, Republic of)

Label-Free cell monitoring systems have gained importance in vast field such as medicine and cell biology in recent years. Examining cellular responses to various chemicals and drugs is of significance to understand cellular behaviors in various environments and assessing the effect of drugs to target cells.

Conventional label-free cellular assay technologies examine minute changes of refractive index (RI) or optical path length near the cell-substrate, as it is highly relevant to cell viability, toxicity, and dynamic mass redistribution. Those methods typically employ nanostructured sensor surface to improve the RI limit of detection and sensitivity at the surface. Despite their high sensitivity and demonstrated capability of high-throughput cell assay, they require their sophisticated nano-structured sensor surface, which accompanies the increase in terms of cost and manufacturing complexity.

Here we present novel use of spectral-domain optical coherence phase microscopy (SD-OCPM) to label-free cell assay. SD-OCPM is based on common-path spectral-domain optical coherence tomography and demonstrated its capability in measuring cellular dynamics and molecular bindings at sub-nanometer path-length sensitivity. Based on coherence gating, it can measure RI changes near the surface without any modification of sensor surfaces. We utilized this unique capability to examine the interactions at the cell-substrate to monitor cellular response to various chemicals and drugs. Our preliminary experiments with human breast cancer cells (MCF-7) upon trypsin treatment successfully demonstrated SD-OCPM measurement of cell detachment from the surface.

In this talk, we will briefly describe principle of operation and implementation of our method, and present experimental results with various cell lines and chemicals.

8548-121, Session 4c

Controlled self assembly of nanoparticles in microfluidics and its applications *(Invited Paper)*

Jungyul Park, Sogang University (Korea, Republic of)

Self-assembly of nanoparticles with controlled size, shape, and position is essential for fabricating a large-scale integrated microfluidic system. However, so far, the existing methods for in-situ formation of nanoparticles in the microchannel have only been achieved through the uncontrolled evaporation-induced self-assembly. Ozin and co-workers have employed evaporation-induced self-assembly to grow colloidal crystals in the microchannels using solvent assisted micromolding in capillaries (MIMIC). But, it is still difficult to form the crystallization of nanoparticles with the desired size and position in the middle of microchannels. Here, we report a novel method for in-situ geometrically controlled self-assembly of colloidal crystals within microchannel using properly adjusting capillary pressure and evaporation. We demonstrated two applications using the integrated microfluidic system with the self-assembled nanoparticles. First, a direct sea water desalination using the ion concentration polarization (ICP) is demonstrated. Second, a robust microfluidic platform for stable generation of multiple chemical gradients is proposed. Applications of the proposed integrated system can extended more, because ICP has the potential as a powerful tool for sorting ions or molecules, biomolecule concentration etc., and stable chemotaxis generation can be used to study angiogenesis, embryonic development, wound healing, and cancer metastasis.

8548-20, Session 5a

Ceramic-based nanomaterials for over-1000-nm (OTN) NIR biomedical imaging *(Keynote Presentation)*

Kohei Soga, Tokyo Univ. of Science (Japan)

Near infrared (NIR) wavelength region in 800-2000 nm has been called “biological window” where the both tails of scattering and infrared absorption decrease to form a valley in optical loss spectra of biological objects. Recent efforts to extend the wavelength for florescence biomedical imaging (FBI) have been limited only up to 1000 nm by the use of Si-CCD. InGaAs CCD has become commercial in the past several years to image in 900-1700 nm wavelength region, which enables the imaging in the over-1000-nm (OTN) NIR wavelength region. Organic phosphors are used as the fluorescent agent for the FBI to date. However, normally organic dyes cannot emit efficient fluorescence in the OTN NIR region. Rare-earth doped ceramic nanophorsphors (RED-CNP), on the other hand, can be a candidate for the phosphors in the OTN-NIR region. As a Nd:YAG laser (1064-nm emission with 800-nm excitation) or an Er-doped silica optical fiber amplifier (1550-nm emission with 980-nm excitation), rare-earth doped ceramics can emit efficient NIR fluorescence under NIR excitation. The authors have developed the OTN-NIR FBI materials and systems both for cellular and in vivo FBI by using the RED-CNP. The advantages of the OTN-NIR FBI as a next generation FBI is not only the low loss of biological objects, but the solution for the most of the problems of the currently used FBI, such as color fading, autofluorescence and photo toxicity. This paper will review the past several years’ development of the OTN-NIR FBI materials and systems both for biotechnologies and medical applications.

8548-21, Session 5a

The fluorescent Gd-based silicate nanoagents, expressing enhanced T2 lowering effect at high magnetic strength

Yi Hsin Chien, Chih-Chia Huang, National Cheng Kung Univ. (Taiwan); U-Ser Jeng, Hwo Shuenn Sheu, National Synchrotron Radiation Research Ctr. (Taiwan); Chia-Hao Su, Chang Gung Memorial Hospital (Taiwan); Chen-Sheng Yeh, National Cheng Kung Univ. (Taiwan)

Silicates have attracted growing interest because their structural richness makes them applicable to fundamental physical and chemical studies in addition to diverse material applications, allowing them to serve as adsorbents, catalysts and sensors and, when combined with metal elements, as a mechanism for hydrogen storage. Recently, attention has gradually shifted to their role in biomedical materials. This report describes the creation of a series of fluorescent Gd-based silicate nanoparticles, i.e. Gd silicate:FITC, Gd silicate:FITC@$mSiO_2$ ($mSiO_2$: mesoporous silica shell), and Gd^{3+} chelated Gd silicate:FITC@$mSiO_2$ (Gd^{3+}-DOTA chelated on the $mSiO_2$). Those three silicate nanoparticles containing Gd exhibited dual effect, expressing T1-brightened and T2-lowering effects in lower field (3T). Most interestingly, the silicate nanoparticles exhibited significantly large r2 relaxivity under high magnetic strength. The transverse relaxivity (r2) values were enlarged to 4-5 times, with r1 showing a slight decrease, as field increased from 3T to 7T. Considering that the silicate nanoparticles present effectively reduced T2 contrast, the

MRI effects in vitro and in vivo with a 9.4T animal micro MRI system were performed and compared with the MRI effects using Gd-DOTA and commercial Resovist® agents. Because the as-prepared silicate nanoparticles have encapsulated FITC fluorophore, they provide additional advantage to act as a platform for the development of a cellular imaging vector.

8548-22, Session 5a

Bi-photon imaging and diagnostics with the ultra-small diagnostic probes engineered from semiconductor nanocrystals and single-domain antibodies

Hilal Hafian, Univ. de Reims Champagne-Ardenne (France); Alyona Sukhanova, Trinity College Dublin (Ireland) and Moscow Engineering Physics Institute (Russian Federation); Patrick Chames, Daniel Baty, INSERM (France); Michel Pluot, Jacques H. M. Cohen, Univ. de Reims Champagne-Ardenne (France); Igor R. Nabiev, Trinity College Dublin (Ireland) and National Research Nuclear Univ. MEPhI (Russian Federation); Jean-Marc Millot, Univ. de Reims Champagne-Ardenne (France)

Semiconductor fluorescent quantum dots (QDs) have just demonstrated their numerous advantages over organic dyes in bioimaging and diagnostics. One of the particularities of QDs is their very large cross-section of bi-photon absorption The common approach to biodetection with QD is to use the monoclonal antibodies (mAbs) for targeting. The mAbs-QD conjugates have a large size, which limits the number of ligands that can be linked to the surface of a QD, impedes intratumoral distribution due to interstitial tumor pressure and limits their intracellular and intratissue penetration. Additionally, it is difficult to couple mAbs with QDs in an oriented manner. Very recently we have engineered ultrasmall diagnostic nanoprobes based on highly oriented conjugates of QDs with the single-domain antibodies (sdAbs) against different breast and prostate cancers biomarkers. With a molecular weight of only 13 kDa (12-fold smaller than the full-size mAbs) and extreme stability and capability to refolding, sdAbs represent the smallest functional Ab-fragments capable of binding their antigens with affinities comparable to conventional Abs.

Here, we demonstrate, for the first time, bi-photon immunohistochemical imaging and diagnostics of breast cancer biomarkers with the sdAbs-QD conjugates. We have found the optimal excitation conditions for imaging of the clinical tissue samples after the biopsies with sdAb-QD ultrasmall nanoprobes and have also shown significant improvement in sensitivity of breast cancer biomarkers detection which was determined by the absence of samples autofluorescence upon the application of the bi-photon diagnostic setup.

8548-23, Session 5a

Synthesis and MRI application of extremely small-sized iron oxide nanoparticles

Byung H. Kim, Taeghwan Hyeon, Seoul National Univ. (Korea, Republic of)

Uniform Extremely small iron oxide nanoparticles of < 4 nm were synthesized by thermal decomposition of iron-oleate complex. These nanoparticles exhibited very low magnetization derived from their small magnetic moment and spin-canting effect. The hydrophobic as-synthesized nanoparticles can be easily transferred to aqueous media by capping with poly(ethylene glycol)-derivatized phosphine oxide (POPEG) ligand, and the resulting hydrophilic nanoparticles showed no significant cytotoxicity. They exhibited good T1 effect derived from weak magnetism and high concentration of surface iron ions with five unpaired electrons. In in vivo blood pool magnetic resonance imaging, iron oxide nanoparticles showed long term imaging than commercial gadolinium complex. These results indicate the potential of ultra small iron oxide nanoparticles to serve as T1 magnetic resonance imaging contrast agents in clinical settings.

8548-24, Session 5a

Simultaneous clearance kinetics analysis of different optical markers using multispectral optoacoustic tomography

Stefan Morscher, iThera Medical GmbH (Germany) and Technische Univ. München (Germany); Jing Claussen, Wouter H. Driessen, Neal C. Burton, iThera Medical GmbH (Germany); Daniel Razansky, Vasilis Ntziachristos, Helmholtz Zentrum München GmbH (Germany) and Technische Univ. München (Germany)

Overall low tissue absorbance promotes imaging in the near-infrared (NIR) range, especially for deep tissue in vivo imaging. Here, conventional optical imaging suffers from low spatial resolution and long acquisition times, while Multispectral Optoacoustic Tomography (MSOT) offers real-time imaging of optical contrast, with high spatial and temporal resolution. Individual absorbers in tissue can be revealed using images acquired at multiple excitation wavelengths, enabling a rich portfolio of biomedical applications with clinical settings readily within reach.

Fast image acquisition permits the collection of a multispectral data set of a single, cross-sectional slice within seconds. Multispectral unmixing simultaneously reveals the biodistribution of several absorbers with distinct spectral absorption profiles, both tissue intrinsic (e.g. hemoglobin) and extrinsic, without the necessity of a baseline scan.

Herein we present a non-invasive in vivo study of mouse organ functionality, where gold nanoparticles synthesized in our lab were co-injected i.v. with a fluorescent agent packaged in liposomes. Imaging was performed continuously at selected areas in kidneys, liver and spleen, allowing successful tracking of the distribution of the injected substances over time in multiple organs. Monitoring of selected regions of interest shows distinct pharmacokinetic behavior for each probe in excellent accordance with ex vivo fluorescence imaging.

These results prove MSOT as a powerful imaging modality that has the potential of revolutionizing the field of biomedical imaging, enabling a large variety of applications in monitoring therapeutic efficacy and assisting drug development. A key strength emphasized here lies in tracking multiple injected substances within one measurement.

8548-25, Session 5a

Semiconductor quantum dots affect fluidity of purple membrane from Halobacterium salinarum through disruption of bacteriorhodopsin trimer organization.

Nicolas Bouchonville, Michael Molinari, Michel Troyon, Univ. de Reims Champagne-Ardenne (France); Alyona Sukhanova, Igor R Nabiev, Trinity College Dublin (Ireland) and Moscow Engineering Physics Institute (Russian Federation)

Bacteriorhodopsin (bR) is a unique protein of purple membranes (PMs) extracted from the bacterium Halobacterium salinarum. Tight trimers of this photochromic protein form a highly ordered 2D hexagonal crystalline lattice within the PMs. Due to strong excitonic interactions between the bR chromophores (retinals) in the protein trimers, PMs exhibit a strong circular dichroism (CD) activity in the region of the retinal absorption band, which allows monitoring the regularity and stability of the bR trimer organization within the membrane.

In this study, the effects of semiconductor quantum dots (QDs) on the bR intramembrane organization and the time course of bR

monomerization under the action of detergents have been analyzed. The results show that the interaction with QDs does not influence the bR structural organization but considerably accelerates the monomerization of the protein by detergents. These data have been confirmed by the results of atomic force microscopy (AFM) followed by Fourier transform analysis, which have shown that interactions with QDs cause an eightfold acceleration of bR monomerization with Triton.

The data show that interactions of nanoparticles with biological membranes may modulate the membrane fluidity and the structural organization and function of integral proteins embedded in these membranes.

8548-161, Session 5a

Nanoscale surface modification to achieve improved osseointegration and controlled drug delivery *(Keynote Presentation)*

Sankara Narayanan, Min Ho Lee, Chonbuk National Univ. (Korea, Republic of)

The clinical success of implants is largely determined by their ability to interact with biological fluids and tissues, to promote an early osseointegration and to offer a controlled drug delivery. The rate and quality of osseointegration as well as the tissue-implant interactions are related to the surface properties, particularly surface topography, surface chemistry and wettability. Surface modification is a viable approach to impart these desirable characteristics. In recent years, nanoscale surface modification methods assume significance and they are targeted towards the development of smart implant materials with tunable surface properties to respond according to the implantation site environment. The present paper will address the importance of nanoscale surface modification methods such as surface mechanical attrition treatment (SMAT) and electrochemical oxidation to achieve improved osseointegration and controlled drug delivery. SMAT is based on surface severe plastic deformation by controlled peening using spherical balls while electrochemical oxidation involves the formation of self-organized nanotubular arrays. The effect of SMAT on the change in surface roughness, contact angle, surface free energy and apatite growth on CP-Ti and the electrochemical fabrication of TiO_2 nanotubes for controlled drug delivery will be addressed.

8548-73, Session 5b

Histology-directed MALDI mass spectrometry for the diagnostic pathology *(Keynote Presentation)*

In-Hoo Kim M.D., Hark Kyun Kim M.D., National Cancer Ctr. (Korea, Republic of)

With the advent of targeted agents, it has become clinically important to distinguish histologic types of non-small cell lung cancers (NSCLCs) using biopsy samples. We investigated whether direct tissue matrix-assisted laser desorption/ionization (MALDI) mass spectrometry (MS) analysis on lipid may classify histology of NSCLCs. Twenty-one pairs of frozen, resected NSCLCs were analyzed using histology-directed, MALDI MS. 2,5-dihydroxybenzoic acid/?-cyano-4-hydroxycinnamic acid were manually deposited on areas of each tissue section enriched in epithelial cells to identify lipid profiles, and mass spectra were acquired using a MALDI-time of flight instrument. Squamous cell carcinomas and adenocarcinomas, two major histologic types of NSCLC, were found to have different lipid profiles. Discriminatory lipids correctly classified the histology of 80.4% of independent NSCLC surgical tissue samples (41 out of 51) in validation set, suggesting that lipid profiles can classify NSCLCs according to the histologic type.

We also found that protein and lipid MALDI MS profiles can classify 30 breast cancers according to the intrinsic subtypes. Immunohistochemistry-defined, luminal, HER2+, and triple-negative tumors demonstrated different protein and lipid profiles, as evidenced by cross validation P values < 0.01. Discriminatory proteins and lipids classified tumors according to the intrinsic subtype with median prediction accuracies of 80.0-81.3% in 100 random test sets.

Potential advantages of this label-free approach may include small tissue requirement, relatively rapid procedure, and low reagent cost. Day-to-day variation of this technology is also acceptable, with the Pearson correlation of 0.95. Taken together, these results suggest the possible clinical utility of histology-directed, lipid and protein MALDI MS.

8548-74, Session 5b

In situ fluorescence optical detection for structured illumination imaging of 3D cell-based assays

Jong-Ryul Choi, Donghyun Kim, Yonsei Univ. (Korea, Republic of)

In this study, we introduce the development of in situ fluorescence optical detection system with structured illumination for 3D cell cultures. Fluorescence optical measurement is a general approach to analyze various cellular dynamics and behaviors and conventional widefield fluorescence microscopy has been employed in cell-based studies of 2D cultured cells. On the other hand, widefield fluorescence microscopy is difficult to be applied to study cell-based studies of 3D cultured cells in an extracellular matrix because axial sectioning of widefield microscopy is limited by diffraction limit determined by Rayleigh criteria.

To acquire optical information with higher axial resolution, we applied a structured illumination microscopic technique to in situ fluorescence optical detection system (ISFODS). The structured illumination microscopic technique provides highly improved axial scanning resolution using the modulation and the isolation of in-focus and out-of-focus fluorescence signals. In comparison with confocal fluorescence microscopy based ISFODS, ISFODS using the structured illumination microscopic technique needs less image acquisition time to obtain sectioned optical images.

To generate structured illumination with grid patterns, a digital micromirror device (DMD) is applied in the ISFODS as a spatial light modulator. To confirm the improvement of axial resolution in optical fluorescence images, we measured 2D distributed fluorescent microbeads (ϕ = 10 μm) on a glass plate and determined axial point-spread functions (PSF) in widefield and structured illumination modes. Also, to study the feasibility of applications in 3D cell cultures, we measured 3D distributed fluorescent microbeads in a 1-mm alginate gel matrix.

8548-75, Session 5b

Nanoscale antenna-based surface plasmon resonance detection of colocalized molecular interactions

Youngjin Oh, Yonghwi Kim, Wonju Lee, Donghyun Kim, Yonsei Univ. (Korea, Republic of)

Surface plasmon (SP) refers to a electron concentration wave that is formed between metal and dielectric interface. SP resonance (SPR) has been applied to sensing bio-molecular interactions because it allows real-time monitoring on a quantitative basis. However, traditional SPR detection suffers from moderate limit of detection. For this reason, many approaches have been taken to enhance the sensing capability. In this presentation, we investigate nanoscale optical antennas for localization of near-fields and excitation of extremely small locally amplified hot spots in order to demonstrate SPR sensitivity enhancement. For colocalization of target molecules, we use angled dielectric shadow evaporation method, whereby small nanogaps are created at the hot spots. Near-field distribution produced by nanoscale antennas (NAs) was calculated using rigorous coupled-wave analysis (RCWA). An angle scanning SPR set-up was custom-built for

experiments. The concept was experimentally tested by detecting DNA hybridization. In addition, to confirm the correlation between nanogap associated with NAs and sensitivity enhancement, we measured the effect of gap size on the detection sensitivity. Experimental results indicate that sensitivity provided by NA-based colocalization was at least two orders magnitude enhanced compared to that of conventional thin-film based SPR detection. These results may open a new approach to bio-molecular and drug analysis based on SPR.

8548-76, Session 5b

Hybrid nanobio-devices based on carbon nanostructures and biomolecules *(Keynote Presentation)*

Seunghun Hong, Seoul National Univ. (Korea, Republic of)

Recently, various new nanostructures (e.g. nanoparticles, carbon nanotubes, protein motors, graphene etc) have been utilized as a component for advanced functional devices. However, a major stumbling block holding back their practical applications is a difficulty in massive assembly of such devices. In this talk, we will first present a strategy to mass-produce nanostructure-based hybrid devices, where molecular patterns on solid substrates are utilized to direct the adsorption and alignment of nanostructures to form a desired device structures. Then, we will discuss how this simple strategy can be utilized to fabricate various new hybrid nanobio-devices for bio- and medical applications such as taste receptor protein-based bioelectronic tongues, canine olfactory receptor-based artificial noses, and carbon nanostructure-based substrates for stem cell control.

8548-77, Session 5b

Bio-microinstrumentation technology: discrete components to modular systems *(Keynote Presentation)*

Bonnie L. Gray, Simon Fraser Univ. (Canada)

The Microinstrumentation Lab at Simon Fraser University (SFU) takes a bottom-up approach to the development of biomedical micro- and nano-devices and modular systems with integrated interconnect technology. A major focus of our research is the development and application of novel nanomaterials to discrete components, combined with generically applicable integration and interconnection standards. In this overview, we present a sample of these technologies, along with key developments in an ever-expanding group of collaborative applications in biology and biomedicine, including: cell research platforms to study mechanisms of disease; flexible electro-enzymatic and impedance-based biomedical sensors and microfluidics; and highly parallel microfluidics for biological cell monitoring and multi-sample manipulation.

8548-122, Session 5c

Drug eluting biodegradable polymeric stents *(Keynote Presentation)*

Suong-Hyu Hyon, Kyoto Institute of Technology (Japan)

Localized drug delivery from drug-eluting stents has been accepted as one of the most promising treatment methods for preventing restenosis after stenting. However, thrombosis, inflammation, and restenosis are still major problems for the utility of cardiovascular prostheses such as vascular grafts and stents. Epigallocatechin-3-O-gallate (EGCG), a major polyphenolic constituent of green tea, has been shown to have anti-thrombotic, anti-inflammatory and anti-proliferative activities. It was hypothesized that controlled release of EGCG from biodegradable poly(lactide-co-?-caprolactone, PLCL) stent coatings would suppress migration and invasion of vascular smooth muscle cells (VSMCs) as well as platelet-mediated thrombosis.

EGCG-releasing PLCL (E-PLCL) was prepared by blending PLCL with 5% EGCG. The surface morphology, roughness and melting temperature of PLCL were not changed despite EGCG addition. EGCG did, however, EGCG appreciably increase the hydrophilicity of PLCL. EGCG was found to be uniformly dispersed throughout E-PLCL without direct chemical interactions with PLCL. E-PLCL displayed diffusion controlled release of EGCG release for periods up to 34 days. E-PLCL significantly suppressed the migration and invasion of VSMCs as well as the adhesion and activation of platelets. E-PLCL coatings were able to smooth the surface of bare stents with neither cracks nor webbings after balloon-expansion. The structural integrity of coatings was sufficient to resist delamination or destruction during 90% dilatation. These results suggest that EGCG-releasing polymers can be effectively applied for fabricating an EGCG-eluting vascular stent to prevent in-stent restenosis and thrombosis.

8548-123, Session 5c

Development and characterization of biodegradable drug-eluting stents *(Invited Paper)*

Dong-Wook Han, Pusan National University (Korea, Republic of); Suong-Hyu Hyon, Kyoto Institute of Technology (Japan)

Biodegradable polymers, including poly(lactic acid), poly(glycolic acid), poly-?-caprolactone, etc. have been used to develop various cardiovascular prostheses, such as artificial vessels and stent struts or coatings. However, implant-associated thrombosis, inflammation and restenosis are still major problems for the utility of these devices. Epigallocatechin gallate (EGCG), the predominant catechin from tea, is well-known to exert anti-thrombotic, anti-inflammatory and antioxidative activities. In this study, it was hypothesized that EGCG eluted from biodegradable poly(lactide-co-?-caprolactone, PLCL) for stent application would differentially affect the behaviors of vascular smooth muscle cells (VSMCs) versus vascular endothelial cells (VECs). EGCG-eluting PLCL (E-PLCL) were prepared by blending PLCL with EGCG. The surface morphology and melting temperature of PLCL were not changed despite EGCG addition, while its hydrophilicity was appreciably increased by EGCG. EGCG was uniformly dispersed into E-PLCL and sustainedly released for over 30 d by controlled diffusion rather than PLCL degradation. Moreover, EGCG did not affect tensile strength at break, but significantly increased Elastic modulus of PLCL. The proliferation and migration of VSMCs were completely suppressed by EGCG, whereas the migration of VECs was not adversely affected. The underlying mechanism for this EGCG-mediated selective inhibition of VSMC migration was partly elucidated at the molecular levels. In conclusion, it is suggested that E-PLCL can be potentially applied for fabricating an EGCG-eluting vascular stent, namely an EGCG-eluting polymeric stent, or even an EGCG-releasing polymer-coated metal stent, to prevent thrombosis, inflammation and in-stent restenosis.

8548-124, Session 5c

Effective suppression of post-angioplasty restenosis with an Akt1 siRNA-embedded coronary stent in an experimental rabbit stent model *(Invited Paper)*

In-Kyu Park, Hui-Lian Che, Chonnam National University Medical School (Korea, Republic of); Haeshin Lee, KAIST (Korea, Republic of); Won Jong Kim, Pohang University of Science and Technology (Korea, Republic of); Youngkeun Ahn, Myung-Ho Jeong, Chonnam National University Hospital (Korea, Republic of)

Restenosis is the formation of blockages occurring at the site of angioplasty or stent placement. In order to avoid such blockages, the suppression of smooth muscle cells near the implanted stent

is required. The Akt1 protein is known to be responsible for cellular proliferation, and specific inhibition of Akt1 gene expression results in the retardation of cell growth. To take advantage of these benefits, we developed a new delivery technique for Akt1 siRNA nanoparticles from a hyaluronic acid (HA)-coated stent surface. For this purpose, the disulfide cross-linked low molecular polyethyleneimine (PEI) (ssPEI) was used as a gene delivery carrier because disulfide bonds are stable in an oxidative extracellular environment but degrade rapidly in reductive intracellular environments. Akt1 siRNA/ssPEI nanoparticles (ASNs) were immobilized on the HA-coated stent surface and exhibited stable binding and localization, followed by time-dependent sustained release for intracellular uptake. Transfection efficiency was quantified using a luciferase assay; the transgene expression of Akt1 suppression through the delivered Akt1 siRNA was measured using RT-PCR and western blot, demonstrating higher gene silencing efficiency when compared to other carriers. ASN coated on HA stents were deployed in the balloon-injured external iliac artery in rabbits in vivo. It was shown that the Akt1 released from the stent suppressed the growth of the smooth muscle at the peri-stent implantation area, resulting in the prevention of restenosis in the post-implantation phase.

8548-126, Session 5c

Controlled release behaviours of sirolimus by solvent effects for drug-eluting stents

Yoon Ki Joung, Korea Institute of Science and Technology (Korea, Republic of)

Biodegradable poly(lactide-co-glycolide) (PLGA) with sirolimus (SRL) was coated instead of non-degradable polymer on stainless steel (SUS 316L) spring by ultrasonic spray method to prevent restenosis and late thrombosis of vascular stents. SRL, an immune inhibitor, exhibits the effect of decreasing the thickness of intima in the wounded blood vessel model. The molecular interaction among PLGA, organic solvent, and SRL affected surface roughness, particle size, and loading amount of SRL during coating process. As organic solvents influenced the conformational arrangement of polymer chain and the SRL aggregation, the glass transition temperature (Tg) of PLGA matrix became significantly low due to the plasticizer effect. The release pattern depended on the size of aggregated particle as a result of in vitro drug release. This study would have great potential for biomedical and pharmaceutical applications for controlled drug release including drug-eluting stent (DES).

8548-134, Session 5c

Several different approaches in biomedical micro/nano robotics *(Keynote Presentation)*

Jong-Oh Park, Chonnam National Univ. (Korea, Republic of)

Micro/Nano robotics can be defined as robotic technologies where robot body size is lower than of millimeter up to nanometer. Micro/nano robot is regarded as noble solution rather than general solution. Based on such characteristic micro/nano robot is appropriate in human body. Therefore micro/nano robot can be categorized in general as biomedical robot. Solutions of biomedical micro/nano robot will be different from others, for instance, it might be mechanical or pneumatic solution, or electromechanical, MEMS/nanotechnological or biological depending upon the robot body size, application target and robot functionality.

We have been involved in several different sized robots, from cm, mm, μm and even up to nm size. The application target is digestive organ, blood vessel, or tumor tissue. The robot functionality will be diagnosis, drug delivery, tissue biopsy and some therapeutic functions. Depending upon the combination of several aspects the working principle will be different.

General approach in colon like as conventional colonoscope will be satisfied with pure mechanical, or in more specific way with pneumatic approach. Instead of wired colonoscopic robot, if wireless robot required, then electromechanical approach will be appropriate, because the available size of robot is considerably enough to integrate several required functionality into such dimension with available technologies. But with the time it might be necessary to apply MEMS technology.

In the field of blood vessel, if diagnostic function as well as biopsy required, then MEMS technology including mechanical approach will be appropriate. Pure MEMS technology is not enough to fulfill any medical function due to relatively too small dimension in comparison with the tissue dimension.

In case of nanorobotic dimension, currently available and practical approach will be microbiological, because artificial fabrication would not work in proper way.

Another viewpoint to differentiate from others is what kind of major technologies will be applied. Based on such viewpoint, the smaller the robot size the more different technologies will be applied.

In this paper several examples will be explained with different approaches and different application targets.

8548-135, Session 5c

Targeted delivery of anticancer agents for personalized cancer medicine *(Keynote Presentation)*

Tae-You Kim, Seoul National Univ. (Korea, Republic of)

Chemotherapy represents a mainstay in the treatment of metastatic cancer. Although its efficacy has been demonstrated in most types of tumor, chemotherapy has two critical drawbacks: toxicity and non-selectivity. Most anti-cancer drugs affect on proliferating normal cells such as digestive mucosa, hair follicles, and blood cells, resulting in various systemic toxicities. And delivery of chemotherapy is hampered by the presence of bio-barriers such as reticulo-endothelial systems, high interstitial pressure and abnormal blood flow in tumor. Therefore, in order to overcome these obstacles of chemotherapy, two strategies have been investigated. First is the development of molecular targeted therapy. Molecular targeted agents are highly effective in cancers which carry characteristic genetic alterations in specific type of tumors. For example, 25% of breast cancer has activation of Her2 signaling, and trastuzumab, a humanized monoclonal antibody for Her2, is highly effective in Her2 positive breast cancer. Currently, more than 20 targeted agents are actively used in clinic. These include gefitinib for EGFR mutant lung cancer, and imatinib for c-kit positive gastrointestinal stromal tumors. Second is the development of nano-delivery systems using liposomes, polymeric micelles, and conjugates. This novel delivery enables the delivery of chemotherapeutics by protecting from degradation, prolonged circulation times, and increased tumor accumulation. Previously, we have developed Genexol-PM, which is a paclitaxel formulated with a polymeric micelle. Compared to conventional paclitaxel, genexol-PM permits the delivery of a higher paclitaxel dose and the achievement of higher paclitaxel dose without additional toxicity, indicating the efficacy of nano-delivery of anticancer agents. Interestingly, combination of above two strategies, which is a nano-delivery of targeted agent, is tested in breast cancer. T-DM1 is a novel targeted drug delivery of trastuzumab-DM1. T-DM1 first binds to Her2 positive cancer cells and then cytotoxic DM1 is activated by cytosomal degradation and induces cell killing. T-DM1 shows significant survival prolongation compared to other Her2 inhibitors in trastuzumab-resistant breast cancer. These suggest that design of nano-delivery of targeted agents is feasible and effective for cancer therapy.

8548-26, Session 6a

Biomimetic micro/nanosystem using microfluidic approach *(Keynote Presentation)*

Jianhua Qin, Dalian Institute of Chemical Physics (China)

Adaptation of micro or nanoscale technologies to lab-on-chip format is offering a attractive platform for the constructing biomimetic micro/nano system that connected to healthcare and medical diagnosis. In this talk, I will present the unique microfluidic approach that can be applied for a range of bioprocessing and bioengineering applications. By incorporating unique structures, the functional series of micro/nano devices will be presented to mimic complex tumor environment involving the interaction between cell-cell, cell-extracellular, and cell-molecules from molecular-level to tissue levels. This will be benefit for medical diagnosis and target cancer therapy.

8548-27, Session 6a

Microfluidic tissue engineering for efficient proliferation and differentiation of animal cells *(Invited Paper)*

Sungsu Park, Ewha Womans University (Korea, Republic of)

Microfluidic cell culture system (uFCCS) has been used to grow and differentiate various types of cells including progenitor cells, stem cells and cancer cells because it makes it possible to tailor the cellular microenvironment in a controllable and reproducible manner. The complexity of the cellular microenvironment can be easily mimicked in a microchannel through incorporating well-defined architectures, patterning extracellular matrix (ECM) biopolymer in a defined area, carefully controlling cell density and flow, etc. uFCCS has been used for 2-dimensional (2D) and 3-dimensional (3D) cell culture as well as co-culture. We demonstrated that uFCCS is highly useful for culturing certain cell types such as hepatocytes that need to be embedded with either neighboring cells or ECM to form 3D constructs. uFCCS was made of PDMS (polydimethlyl siloxane) and contained a compartment zone surrounded by micropillar (30 um X 20 um) with a gap (30 um) between pillars by soft lithography. Recently, we reported that neurospheres originated from human adipose tissue-derived stem cells (hATSCs) were induced to form neurons in uFCCS. Currently, we have been developing uFCCS where tumor cells experience two different stresses such as starvation and anti-cancer drug, hoping that we can understand underlying mechanisms of cancer adaptation against anti-cancer drugs such as doxorubicin. These results suggest that microfluidic tissue engineering enable researchers to mimic a certain cell niche required for efficient growth and differentiation of various types of cells.

8548-28, Session 6a

Microfluidic 3 dimensional cell culture assay *(Invited Paper)*

Seok Chung, Korea University (Korea, Republic of)

A simple but robust microfluidic assay for three-dimensional and heterotypic cell culture has been developed by hydrogel incorporating PDMS device. Using this assay, well-defined biochemical and biophysical stimuli can be applied to multiple cell types interacting each other, thereby replicating many aspects of the in vivo microenvironment in organs and many diseases. Capabilities exist for time-dependent manipulation of flows and chemical gradients as well as high-resolution real-time imaging for observing spatial-temporal single cell behavior, cell-cell communication, cell-matrix interactions and cell population dynamics. These assays can be used to study various aspects of cells; survival, proliferation, migration, morphogenesis and differentiation under controlled conditions. Applications include the study of previously unexplored cellular interactions, and have already provided new insights into how biochemical and biophysical factors regulate interactions between populations of different cell types.

8548-106, Session 6a

Bio-inspired, smart, multiscale interfacial materials *(Keynote Presentation)*

Lei Jiang, Institute of Chemistry (China)

Learning from nature, we revealed that a super-hydrophobic surface needs the cooperation of micro- and nanostructures. Considering the arrangement of the micro- and nanostructures, the surface structures of the water-strider's legs were studied in detail. Accordingly, a series of super-hydrophobic surfaces have been fabricated. Under certain circumstances, a surface wettability can switch between superhydrophilicity and superhydrophobicity, Most recently, we developed a superoleophobic and controllable adhesive water/solid interface which opens up a new strategy to control self-cleaning properties in water. To expand the "switching" concept of the smart 2D surface, we also did a lot of interesting work in 1D system. For example, we discovered the water collection ability of capture silk of the cribellate spider Uloborus walckenaerius and then prepared artificial spider silk which will have great applications in water collection. In addition, we developed the novel biomimetic ion channel systems with a variety of intelligent properties, which were controlled by our designed biomolecules or smart polymers responding to the single external stimulus, provided an artificial counterpart of switchable protein-made nanochannels. These intelligent nanochannels could be used in energy-conversion system, such as photoelectric conversion system inspired by rhodopsin from retina or bR, and concentration-gradient-driven nanofluidic power source that mimic the function of the electric eels.

8548-78, Session 6b

Nanotechnology for brain tumor diagnosis and treatment *(Keynote Presentation)*

Miqin Zhang, Univ. of Washington (United States)

Treating malignant brain tumors remains a formidable challenge due to the difficulty in differentiating between tumors and healthy brain tissue, intrinsic cellular resistance of tumors to drugs, and the blood brain barrier (BBB) preventing the passage of drugs and contrast agents. Targeted delivery of contrast agents and therapeutic payloads using nanoparticles is a promising approach that may overcome these barriers. Our research aims to develop multifunctional nanoparticle systems that can serve as imaging markers, targeting agents, and drug delivery vehicles for non-invasive diagnosis, treatment, and therapy-response monitoring of brain cancers. In the past few years, we have developed several multifunctional nanoparticle systems that demonstrate an ability to specifically target brain tumors across the BBB, and exhibit innocuous toxicity profiles and sustained retention in tumors, as established through uptake assays, in vivo magnetic resonance and biophotonic imaging, and histological and biodistribution analyses. A typical multifunctional nanoparticle system in our design comprises a superparamagnetic iron oxide core that enables magnetic resonance imaging, a biodegradable polymeric shell that stabilizes the nanoparticle and provides functional groups for biomolecule conjugation, and a targeting ligand for specific binding of target cells. My talk will focus on our recent research in development of nanoparticle systems, including design and characterization of these nanoparticle systems for MR imaging, chemotherapy and DNA delivery.

8548-79, Session 6b

Macrophages homing to metastatic lymph nodes can be monitored with ultrasensitive ferromagnetic iron-oxide nanocubes and a 1.5T clinical MR scanner

Seung Hong Choi M.D., Seoul National University Hospital (Korea, Republic of)

Due to the ability of macrophages to specifically home to tumors their potential use as a delivery vehicle for cancer therapeutics has been suggested. Tracking the delivery and engraftment of macrophages into human tumors with a 1.5T clinical MR scanner requires the development of sensitive contrast agents for cell labeling. Thus, we used PEG-phospholipid encapsulated ferromagnetic iron-oxide nanocubes (FIONs) with r2 value of 324 mM-1s-1. We used in vivo MRI in combination with histology to demonstrate and monitor the capacity of metastatic cancer cells in lymph nodes (LNs) to attract intravenously administrated macrophages in a mouse model.

The FIONs did not affect the viability or functions, including phagocytosis and migration, of the labeled macrophages. Using T2* GRE MR imaging of mice with main tumors or metastatic LNs, hypointensities from the FION-labeled macrophages were detected within both areas the day after the intravenous administration of the labeled macrophages. This is the first study to utilize labeled macrophages, which could be monitored non-invasively using a 1.5T clinical MR scanner, for targeting both main tumors and LN metastasis. Overall, the use of macrophages may have many future applications in the clinic for vectorizing therapeutic agents towards main tumors as well as LN metastasis.

8548-80, Session 6b

Optical biodetection and diagnotics strategies with SERS

Ramon A. Alvarez-Puebla, Univ. de Vigo (Spain)

Surface-enhanced Raman scattering (SERS) spectroscopy is one of the most powerful analytical techniques for identification of molecular species, with the potential to reach single-molecule detection under ambient conditions. Here a brief introduction and discussion of both recent advances and limitations of SERS in the context of diagnosis

and biodetection, ranging from direct sensing to the use of encoded nanoparticles, in particular focusing on ultradetection of relevant bioanalytes, rapid diagnosis of diseases, marking of organelles within individual cells, and non-invasive tagging of anomalous tissues in living animals will be presented.

8548-81, Session 6b

Comparison study of [F-18]WAY derivatives for imaging brain 5-HT1A receptors in vivo

Jae Yong Choi, Gangnam Severance Hospital (Korea, Republic of); Chul Hoon Kim, Department of Pharmacology, Yonsei University College of Medicine (Korea, Republic of); Tae Joo Jeon, Minkyung Lee, Youngbeom Seo, Young Hoon Ryu, Gangnam Severance Hospital (Korea, Republic of)

INTRODUCTION: The serotonin 1A receptors (5-HT1A) in the central nervous systems are strongly implicated in psychiatric disorders such as depression, schizophrenia and Alzheimer's disease. Thus, a number of [F-18]WAY derivatives are developed for measuring 5-HT1A receptor densities in the brain. Among these radioligands, [18F]FCWAY, [18F] MPPF, and [18F]MEFWAY have been reported as useful PET agents for imaging 5-HT1A receptors. However, there have been few reports on the comparative study of these radioligands.

OBJECTIVES: The purpose of this research is to compare the uptakes of [F-18]WAY derivatives in rat brains and to find optimal candidate for preclinical study.

METHOD: For in vivo experiment, male Sprague-Dawley rat was anesthetized with 2.0 % isoflurane in oxygen and placed in the gantry with its head centered in the field of view. A catheter was inserted into the tail vein and fluconazole was injected at an infusion rate for 1 h. Radioactivity (13.1-19.6 MBq) was promptly injected over 1 min to the catheter and dynamic PET scans (Siemens, Inveon PET/CT) were performed for 120 min. Control rats were injected with [18F] FCWAY, [18F]MEFWAY or [18F]MPPF alone with no treatment. Regions of interests are hippocampus, frontal cortex, cerebellum and skull. Fluconazole, antifungal drug was tested the ability for defluorination of the radioligands.

RESULT: PET experiments indicated that authentic [18F]FCWAY revealed extensive skull uptake due to defluorination, while [18F]MPPF showed little defluorination. (skull uptake : [18F]FCWAY > [18F]MEFWAY >>[18F]MPPF). This skull uptake was efficiently reduced by fluconazole. Moreover, [18F]MPPF revealed fast uptake and short lasting time in the brain. This data supported that [18F]MPPF had moderate affinity to 5-HT1A receptor. In fluconazole pretreatment group (60mg/kg intravenously), the brain uptake of [18F]FCWAY was the highest while radioactivity in receptor-rich regions is two times higher than that of receptor-poor areas.

CONCLUSION: We conclude that defluorination of [18F]FCWAY or [18F] MEFWAY in rat brain was almost completely blocked by fluconazole, probably through the inhibition of CYP2E1. In the comparative study of PET images, inhibitor treated [18F]FCWAY was the highest brain uptake. We suggest that fluconazole-treated [18F]FCWAY may serve as an optimal radioligand for investigating 5-HT1A receptors in rat models of neuropsychiatric disorders.

8548-127, Session 6c

Role of metallic stents in benign esophageal stricture *(Keynote Presentation)*

Chan Sup Shim M.D., Konkuk Univ. Medical Ctr. (Korea, Republic of)

Simple esophageal strictures, which are focal, straight, and large in diameter, usually require 1 - 3 dilation sessions to relieve symptoms. However, complex strictures, which are long, tortuous, or associated with a severely compromised luminal diameter, are usually more difficult to treat with conventional bougie or balloon dilation techniques, and often have high recurrence rates.

Although the permanent placement of self-expandable metal stents (SEMS) has been used to manage refractory benign esophageal strictures, this procedure is associated with additional problems, such as stricture from tissue hyperplasia, stent migration, and fistula formation. Thus, several new types of stents have been developed, including temporary SEMS, self-expandable plastic stents (SEPS), and biodegradable stents. The use of these new products has produced varied results. Temporary SEMS that have been used to relieve benign esophageal conditions have caused granulation tissue at both ends of the stent because of contact between the mucosa and the exposed metal components of the stent, thus hindering stent removal. We examined the tissue response to two new types of SEMS, a flange-type and a straight-type, each coated with a silicone membrane on the outside of the metal mesh. These two SEMS were evaluated individually and compared with a conventional control stent in animal experiments. Although the newly designed stents resulted in reduced tissue hyperplasia, and were thus more easily separated from the esophageal tissue, some degree of tissue hyperplasia did occur.

We suggest that newly designed DES (drug-eluting stents) may provide an alternative tool to manage refractory benign esophageal stricture.`

8548-128, Session 6c

Stenting for cerebral aneurysm: application of nanotechniques *(Keynote Presentation)*

Dong Ik Kim M.D., Yonsei Univ. (Korea, Republic of)

Intracranial aneurysms are abnormal dilatations of the intracranial arteries. Rupture of an aneurysm results in immediate death in 10-15% of patients with more than 50% of the survivors having serious disability. The goal of treatment in aneurysms is to prevent bleeding of unruptured or rebleeding of ruptured aneurysms. The standard of treatment has been microsurgical clipping of the aneurysm after craniectomy. However, endovascular therapy has recently become an alternative treatment option. The International Subarachnoid Aneurysm Trial (ISAT) has shown that the outcome in terms of survival free of disability at 1 year is significantly better with endovascular coiling compared to clipping. Recent advances in endovascular tools and techniques have allowed greater success in treatment of difficult aneurysms. Stents as an adjunctive or the main treatment tool has greatly improved the treatment results of wide neck and giant aneurysms. Stents may induce multiple effects in the treatment of aneurysms. They provide a mechanical barrier for coil embolization of wide neck aneurysms, hemodynamic dissociation of flow between the parent artery and the aneurysm sac, and provide a scaffold for biological remodeling by endothelialization. Recent development of low porosity flow diverting stents has allowed treatment of giant aneurysms by exploiting the hemodynamic uncoupling effect of the stent. However, the use of stents may cause stenosis of the parent artery and the mandatory use of aggressive antithrombotic medication may increase the risk of drug related hemorrhage. Since nanotechnology has come to occupy a key position in most of research and commercial area, the surface layer of the stent that interacts with tissues and biofluids can be readily adjusted at the molecular level through a diverse range of nano-coating techniques. Current challenges include the requirement for more biocompatible and stable layer formation, the need to minimize potential long-term complications, and the development of simple and cost effective methods. Modification and development of the stents in terms of maximizing the treatment effects with improvement of the safety issues is necessary.

8548-129, Session 6c

Multi-layered Pluronic micelle as a drug reservoir for controlled release on drug eluting stent

Jong Hoon Choi, Ki Dong Park, Ajou University (Korea, Republic of)

The treatment of coronary artery diseases have been innovated through the introduction of drug eluting stent (DES). However DES still has several limitations such as stent restenosis and thrombosis. To overcome these limitations, many researchers have attempted to functionalize the coating layer on the stent. In this study, novel coating technique to form the multilayered micelle on the stent, which is facilitated to control the release of incorporated drugs by modulating the layer composition condition was developed and investigated. To prepare the muti-micelle coated stent, the Paclitaxel (PTX) loaded Tetronic conjugated with tyramine and catechol group (PTTD) micelle was coated by simple dipping method, and then PTX loaded PTX loaded Tetronic conjugated with tyramine (PTTA) micelle was coated via enzymatic reaction. Surface morphology of multi-PTTA coated nitinol stent showed that the PTTA was coated homogeneously on the nitinol stent without fragment. Loading amount of PTX on the surface of nitinol stent was measured to be about 1.2 ?g/mm2 by HPLC, which is almost similar amount with commercialized DES such as Taxus and Cypher. In vitro PTX release profile indicated that the release amount of PTX from the stent was controllable from 20 to 100% per 2 weeks as changing the number of PTTA layer. Anti-proliferative assay demonstrated that released PTX was inhibited completely the growth of smooth muscle cells. Obtained results demonstrated that the multi-PTTA coated nitinol stent is great candidate to treat coronary artery diseases, which inhibit the growth of SMC and prevent the thrombosis.

8548-30, Session 7a

Automated microfluidic analysis and screening based on DropLab *(Keynote Presentation)*

Qun Fang, Wen-Bin Du, Shu-Qing Gu, Ying Zhu, Zhejiang Univ. (China); Meng Sun, Zhejiang Univ. (United States); Yun-xia Zhang, Hangzhou (China)

Currently, droplet-based microfluidics is undergoing fast progress. It holds great potentials in high throughput screening by minimizing biological and chemical assay in picoliter to nanoliter droplets.

In 2010, we developed DropLab, an automated platform for performing chemical and biological reactions and screenings in nanoliter-scale droplet array [1]. The droplet assembling strategy was used to produce multi-component droplets in the nanoliter to picoliter range under control of computer program with high controllability on the size and composition of each droplet. The DropLab system was applied in enzyme inhibition assays, protein crystallization screening and identification of trace reducible carbohydrates. Compared with the conventional systems, the sample and reagent consumptions were reduced 1000 to 100,000 fold.

Recently, on the basis of DropLab, we developed an automated and multifunctional platform for single cell analysis [2]. Multiple manipulations including precise picoliter-scale droplet generation, high-efficiency single-cell encapsulation, sequential reactions, and multi-step solid-phase extractions could be automatically achieved in the platform. We applied the platform in high-efficiency single-cell encapsulation, enzyme activity assay at the single cell level, and single cell DNA purification based on solid-phase extraction.

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8548-31, Session 7a

Reproducible preparation of up-scaled polyplexes at extremely low N/P ratio using 3D microfluidic with enhanced vortex mixing

Kyoung-Ik Min, Pohang Univ. of Science and Technology (Korea, Republic of)

Polyplexes are well known as efficient non-viral gene delivery systems due to the low cost and flexibility in gene therapy applications. A typical method of preparing polyplexes is mixing positively charged polymer with negatively charged DNA in bulk solution to form the complex particles by electrostatic interaction. Such inhomogeneous mixing in the solution usually may lead to poor reproducibility in terms of the particle size, surface charge, and even in transfection efficiency. Therefore, it has been highly demanded to develop a new approach for producing well defined and competent particles at much lower N/P (charge ratio of nitrogens in polymer to phosphates in DNA) ratios to obtain homogeneous nanocomplexes and to reduce polymer-mediated toxicity. Here we present the microfluidic approach to prepare the quality-controlled polyplexes under extremely low N/P ratios using 3D polyimide film microreactor. The multi-layered film microfluidic device fabricated by laser ablation are designed with 10 sets of 50 um diameter hole arrays at junction of up/down stream along the microchannel (W 300 x H 125 um, L 80 cm) for enhancing vortex mixing. The polyethylenimine and PAMAM dendrimer (G4) are used at various N/P ratios, and the morphology of formed nanocomplex is investigated by AFM, DLS and SEM, and in-vitro stability, cytotoxicity and transfection efficiency are also evaluated.

8548-32, Session 7a

Topical release of photo-thermal responsive liposome in vivo monitored by fluorescence measurement

Kuo-Chih Liao, National Chung Hsing Univ. (Taiwan)

The research is aimed to provide a pinpointed heating strategy for stimulating topical release of a photo-thermal resposive liposome by application of gold nanoparticles (Au NPs), and a non-invasive method with fluorescence self-quench phenomenon in monitoring the photo-thermal responsive topical release of liposome in vivo. In this study, photo-thermal responsive liposome will be fabricated by incorporation of hydrophobic gold nanoparticles (Au NPs) in a temperature-responsive liposome. The photothermal effects of gold nanoparticles can efficiently generate heat enhanced by surface plasma resonance in the presence of electromagnetic radiation. The NIR fluorophore (such as diglucosamid-SIDAG) in self-quench concentration will be encapsulated in the photo-thermal responsive liposome to simulate the drug payload releasing under the stimulation of electromagnetic radiation. The percentage of triggered release can be monitored by the florescence restoration of SIDAG after being released from liposome and diluted to eliminate the self-quench situation.

8548-33, Session 7a

Biological and photodynamic activity of new cationic porphyrins

Aram G. Gyulkhandanyan, Anna Gyulkhandanyan, Institute of Biochemistry (Armenia); Robert K. Ghazaryan, Yerevan State Medical Univ. (Armenia); Marina Paronyan, Institute of Biotechnology (Armenia); Grigor V. Gyulkhandanyan, Institute of Biochemistry (Armenia)

We synthesized a set of water-soluble cationic porphyrins (PSs) with different peripheral functional groups and metalloporphyrins with different central metal atoms that were found be good candidates for PDT and photodynamic inactivation of microorganisms. Cancer cell сulture (monolayer and suspension) equally well destroyed by cytotoxic or phototoxic action of new cationic porphyrins with charge +3 and +4. By photodynamic effect on culture of suspension cells K-562 (chronic myelogenous leukemia lymphoblasts) the most effective preparations are Zn-metalloporphyrins with hydrocarbon “tails” (-C12 or -C16). Photodynamic actions of metalloporphyrins are in 10-20 times more effective than the cytotoxic action the same porphyrins. It is established that in vitro for the destruction of Gram (+) and Gram (-) microorganisms in photodynamic mode cationic water-soluble synthetic metalloporphyrins, especially Zn-meso-tetra-[4-N-(2`- butyl) pyridyl] porphyrin (Zn-TBut4PyP), many times more effective than Zn-pheophytins, synthesized from the nature origin. In vivo conditions on mice established that the best therapeutic activity against various strains of the microorganism St. aureus has the synthetic metalloporphyrin Ag-TBut4PyP. For PDT among blood proteins the most important in the transport of porphyrins are serum albumin, lipoproteins, and hemoglobin. Via different methods of optical spectroscopy it was found, that long-chain fatty acids, palmitic and stearic acids, compete with cationic porphyrins for binding to the heme high-affinity site of human serum albumin (HSA). Computer simulation (docking) of cationic porphyrins into the subdomain I B of HSA revealed the amino acids that differentially interact with peripheral functional groups of PSs and thereby, could affect the affinity for HSA.

8548-34, Session 7a

Various microfluidic bioprocesses in droplets and continuous flow *(Keynote Presentation)*

Dong-Pyo Kim, Pohang Univ. of Science and Technology (Korea, Republic of)

Microfluidic device for bio-applications has received much attention because of various advantages it enables such as fast and high throughput screening with little sample amount. Firstly, we present two types of bio-performance of droplet-assisted microfluidic devices. A new transformation method for microalgae Chlamydomonas reinhardtii was developed by microfluidic droplet process that the model green encapsulated droplet was flown along the electroporation chip. The transformation efficiency via the microfluidic electroporation was more than 1000 times higher than bulk phase electroporation at the same condition. Alternative work in a microfluidic droplet process is cell-free protein synthesis. The in vitro protein synthesis reaction was carried out in silanized PDMS or PFPE channels in the following three steps; Preparation of array of oil plugs in air, formation of pre-PCR-cocktail plugs followed by PCR-amplification reaction, and protein synthesis reaction by merging the plugs of PCR products with protein synthesis machinery. When compared to the existing methods to date, through our current method, integration of PCR and protein expression can be achieved without any difficulties. Thirdly, the separation process of chiral compounds in a triple laminar flow was demonstrated in the presence of stereospecific reactive enzyme by using the organic polymer derived microchannels with organic solvent resistance and optical transparency. At the last, the integrated microbioreactor equipped with pneumatic valve system is also presented for conducting serially the culturing bacteria for secreted enzyme production, immobilizing the enzymes on the packed channel, efficient enzymatic chemical reactions in single chip. The various polymeric microchannels can be a promising tool for various microchemistry and biotechnology applications.

8548-35, Session 7a

Chitosan oligosaccharide-stabilized ferrimagnetic iron oxide anocubes for magnetically modulated cancer hyperthermia

Mihyun Park, Seoul National Univ. (Korea, Republic of) and World Class Univ. Program of Chemical Convergence for Energy & Environment (Korea, Republic of); Ki Hyun Bae, Department of Biological Sciences, Korea Advanced Institute of Science and Technology (Korea, Republic of); Taeghwan Hyeon, Seoul National Univ. (Korea, Republic of) and World Class Univ. Program of Chemical Convergence for Energy & Environment, (Korea, Republic of); Tae Gwan Park, Department of Biological Sciences, Korea Advanced Institute of Science and Technology (Korea, Republic of); CheolGi Kim, Department of Materials Science and Engineering, Chungnam National University, (Korea, Republic of)

Magnetic nanoparticles have gained significant attention as a therapeutic agent for cancer treatment. Herein, we developed chitosan oligosaccharide-stabilized ferrimagnetic iron oxide nanocubes (Chito-FIONs) as an effective heat nanomediator for cancer hyperthermia. Dynamic light scattering and transmission electron microscopic analyses revealed that Chito-FIONs were composed of multiple 30-nm-sized FIONs encapsulated by chitosan polymer shell. Multiple FIONs in an interior increased the total magnetic moments, which leads the localized accumulation under applied magnetic field. Chito-FIONs also exhibited superior magnetic heating ability with high specific loss power value (2614 W/g) compared to commercial superparamagnetic Feridex nanoparticles (83 W/g). The magnetically guided Chito-FIONs successfully eradicated target cancer cells through caspase-mediated apoptosis. Furthermore, Chito-FIONs showed excellent anti-tumor efficacy on an animal tumor model without any severe toxicity.

8548-36, Session 7a

The photodynamic activity of core-shell type Ag @ TiO_2-nanoparticles in human erythrocytes

Meena K. Mohan, Univ. of Madras (India)

Core-shell type Ag@TiO_2 nanoparticles were prepared by one pot simultaneous reduction of AgNO3 and hydrolysis of Ti (IV) isopropoxide. Their XRD patterns showed anatase form of TiO^2 and the noble metal (Ag). High resolution transmission electron microscopic measurements revealed their size below 50 nm. Ag@TiO_2-NPs showed photodynamic activity in human erythrocytes. A 0.5% hematocrit suspension was prepared in PBS and the photohemolysis was carried out using the synthesized nano-photosensitizer, irradiating the sample with light from Xenon source filtered at 445nm with 20 nm band pass filter. The mechanism of photodynamic activity was studied using scavengers such as NaN3 and GSH. In the present study the photo killing effect was correlated with the concentration of nano-photosensitizer and light dose. The photohemolysis induced by Ag@TiO_2 core shell particles reveals that the percent hemolysis increased with the increase in concentration and light dose. When the concentration is increased from 50µg/ml to150µg/ml and light dose from 7.2J/cm^2 to 21.5 J/cm^2, 100% hemolysis was achieved. The study of effect of scavengers, with GSH and sodium azide showed formation of considerable amount of superoxide anion and singlet oxygen that caused cell death. The role of scavengers showed that the photohemolysis by Ag@TiO_2 nanoparticles favour both Type-I and Type-II mechanisms among which Type-II predominates. The detailed mechanism has been discussed. The unexposed Ag@TiO_2 nanoparticles were found to be non-toxic towards red blood cells. Ag@TiO_2 nano-photosensitizer being non-toxic could be a convenient substitute for the classical photosensitizers (organic dyes).

8548-82, Session 7b

Magnetic nanoparticles for imaging and therapeutics *(Keynote Presentation)*

Jin Woo Chun, Yonsei Univ. College of Medicine (Korea, Republic of)

One of the important trends of next-generation nanomedicine is theranostics that is defined by the combination of therapeutics and diagnostics on a single platform. Magnetic nanoparticles are among one of the most essential platforms for targeted imaging, therapy, and simultaneous monitoring of therapeutic efficacy. In this talk, I will discuss magnetic nanoparticles as a core platform material for theranostics and add a variety of functionalities such as drug, targeting moiety, and gene to enhance their performance. Their unique utilization in highly accurate dual-modal MR imaging1, therapeutic hyperthermia of cancer cells2, controlled drug release3, gene delivery4, and molecular level cell signaling and cell fate control5 will be discussed.

8548-83, Session 7b

Gd chelated PANI Nanoparticles for combined MR imaging and NIR photothermal cancer therapy

Taeksu Lee, Doyeon Bang, Yonsei Univ. (Korea, Republic of); Suh Jin-Suck, Yonsei University (Korea, Republic of); Yong-min Huh, Seungjoo Haam, Yonsei Univ. (Korea, Republic of)

The ultrasensitive and selective diagnosis along with efficient therapy in earliest stage of cancer has been enormously highlighted by a better means to treat the cancer. Herein, Gd(III) chelated polyaniline nanoparticles (GPNPs) was synthesized to be served as a highly T1 enhanced contrast agents and Near-Infrared photothermal therapy probes. In addition, therapeutic antibody was conjugated on the surface of GPNPs for the targeted theragnosis. Fabricated GPNPs significantly reduced the T1 of water protons with as well as represented photothermal ability. The physicochemical properties and biocompatibilities of GNPSs were fully characterized and GPNPs exhibited excellent tumor targeting ability. Consequently, GPNPs exhibited strong potential for efficient diagnosis of cancer in MR imaging and photothermal ablation of epithelial cancer cells.

8548-84, Session 7b

Multiple monitoring of proteolytic activity using fluorescent protein-conjugated gold nanoparticles

Jinyoung Jeong, KRIBB (Korea, Republic of); Kyoungsook Park, University of Science and Technology (Korea, Republic of); Bong Hyun Chung, KRIBB (Korea, Republic of)

Since proteases is key factor in many biological processes such as immunity, development, and apoptosis, diverse techniques have been developed to measure their activities in vitro and in vivo using various nanomaterials such as quantum dot, nanoquencher-embedded mesoporous silica nanoparticles. In this work, we developed a new protease imaging probe based on fluorescent protein conjugated gold nanoparticles (AuNPs) as a nanoquencher. We designed detecting system based on fluorescent protein (FPs) which combined with caspase-cleavable motif and cystein-tagged GST in N-terminus. As-prepared fluorescent proteins were to be attached to AuNP surface through the cystein residue due to pseudo-covalent binding of Au-S. And AuNP acts as strong quencher of FPs because of its strong surface energy transfer. In this system, the quenched fluorescence of FP in normal condition was selectively to be recovered by cleavage of target sequence by caspase activity. Using this system, various caspases activation was also monitored in HeLa cells treated with staurosporine, an anticancer agent to induce apoptosis. These results showed that this new fluorescence nanoprobe was useful for monitoring of various caspases activation both in vitro and in vivo.

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8548-85, Session 7b

Biomolecule immobilization over nanoporous silica and non-siliceous materials and their application in biosensing *(Keynote Presentation)*

Ajayan Vinu, The Univ. of Queensland (Australia)

Adsorption of proteins onto the solid surface has been a topic of interest in the recent years and play a critical role in various applications including the formulation and stabilization of foam and emulsion based products in food industry, analysis and the purification of proteins, the preparation of immunoassays for medical diagnostic tests, enzymatic catalysis, drug delivery systems, and the protein based biosensors. In the first part of the talk, we demonstrate the immobilization of biomolecules in nanoporous silica and carbons in powder form. The effect of pore diameter, structure, and the surface composition of the adsorbent affecting the amount of the protein encapsulation will be demonstrated. We found that the amount of adsorption mainly depends on the solution pH, ionic strength, adsorption temperature, and the pore volume and the pore diameter

of the adsorbent. The mechanism of adsorption at different adsorption conditions over different nanoporous materials will also be discussed. The structural stability of proteins and the adsorbent before and the after the immobilization process will be demonstrated. In the second part of the talk, I will be focusing mainly on the nanoporous non-siliceous materials such as carbons, nitrides, metals, and biomolecules and their application in sensing. A simple approach for constructing highly ordered macro-nanoporous carbon, nitride, proteins and semiconductor films with controlled thickness and pore size will be demonstrated. These macroporous films have been employed as sensors for detecting various molecules including amine based compounds. For example, macro-nanoporous film has a strong selective adsorption capability towards aromatic aniline, and the selectivity can be encouragingly modulated by a simple way based on the ozone cleaning. By functionalizing the surface of the carbon film, the adsorption selectivity can be controlled and improved flexibly based on ozone cleaner. In addition, the method of the fabrication of nanoporous proteins films and their application in sensing of acidic or basic molecules and glucose will be demonstrated.

8548-87, Session 7b

3D manipulation of permanent magnetic polymer micro-robots: a new approach towards guided wireless capsule endoscopy

Ajit Khosla, Daniel D. Hilbich, Akireza Rahbar, Kyle Griffith, Bonnie L. Gray, Simon Fraser Univ. (Canada)

Wireless capsule endoscopy is a pain less process which allows direct visualization of the whole stomach, upper small bowel and colon in a non-invasive manner [1]. This technique is fast replacing the conventional probe endoscopy and has become the gold standard. However, wireless capsule endoscopy is not without drawbacks. The motion of these wireless endoscopic devices is determined by visceral peristalsis and gravity. This results in a lack of a navigation control, which makes their movements and orientations totally random, hence, limiting their clinical usage and efficiency. Another serious problem which is reported is the retention of wireless endoscopic capsule inside the body in patients. The retention of wireless endoscopic capsule rarely causes symptoms, but can potentially cause small bowel obstruction or perforation [2]. The wireless endoscopic capsule retention can be treated by surgical and non-surgical techniques [3, 4].

One of the solutions to overcome the problems associated with wireless endoscope capsules is to integrate permanent magnetic MEMS based micro-robots. These permanent magnetic micro-robots which can be controlled and guided inside the body by external coils or already existing systems such as Stereotaxis magnetic navigation epoch platform [5]. However, until recently there has been little success in developing high magnetic field strength permanent magnets for use in micro-robots for wireless endoscopy devices [6, 7]. With the recent, developments in permanent magnetic powder manufacturing technologies pioneered at Magnaquench Inc [8], it is now possible to make extremely small polymer bonded permanent micro-magnets down to a feature size on 5 µm. This polymer bonded nano-micro-magnet technology was developed at Microinstrumentation Laboratory, Simon Fraser University [9,10].

In this paper we present the concept and preliminary results of our magnetic micro-robotic navigation system for wireless endoscopy systems. Initial results indicate that we can not only control the motion of the wireless endoscope capsule but also make it turn, twist and rotate along x,y,z plane.

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8548-208, Session 7b

Luminescence/magnetic resonance imaging and photodynamic therapy based on upconverting nanoparticles

Yong Il Park, Seoul National University (Korea, Republic of); Hyung Min Kim, Korea Research Institute of Chemical Technology (Korea, Republic of); Jeong Hyun Kim, Seoul National University (Korea, Republic of); Kyung Chul Moon, Korea University (Korea, Republic of); Byeongjun Yoo, Seoul National University (Korea, Republic of); Kang Taek Lee, Korea Research Institute of Chemical Technology (Korea, Republic of); Soo-Young Yoon, Korea University (Korea, Republic of); Yung Doug Suh, Korea Research Institute of Chemical Technology (Korea, Republic of); Sung Ho Lee, Korea University (Korea, Republic of); Taeghwan Hyeon, Seoul National University (Korea, Republic of)

Recently, upconverting nanoparticles (UCNPs), which emit shorter wavelength light than excitation energy, have been proposed as next-generation luminescent probes. Because a near-infrared (NIR) laser is used as an excitation source, the penetration depth is increased and autofluorescence in biological samples is suppressed. By introducing Gd ions-doped shell to UCNPs, UCNPs could be utilized in T1 magnetic resonance (MR) imaging. Furthermore, when UCNPs are combined with photodynamic therapy (PDT) drugs, the NIR-to-visible upconversion capability of UCNPs leads to activation of photosensitizers through energy transfer, and subsequent generation of reactive oxygen species deep in the tissue.

For in vivo application of UCNPs as a diagnostic and therapeutic agent, we developed a multifunctional nanoparticle system composed of lanthanide doped UCNPs and PDT drugs. Tumors could be clearly visualized in both upconversion luminescence images and MR images, and in vivo PDT effect by systemic administration of UCNP-PDT drug nanocomposites was observed under NIR irradiation. These results indicate that UCNP-PDT drug nanocomposites can be used not only as dual-modal imaging probes for accurate diagnosis but also as PDT agents for efficient therapy.

8548-130, Session 7c

Drug-eluting stent (DES) in malignant biliary obstruction *(Keynote Presentation)*

Dong-Ki Lee, Sung Ill Jang, Gangnam Severance Hospital, Yonsei Univ. (Korea, Republic of)

In unresectable malignant bile duct obstruction, endoscopic stent insertion is the treatment of choice. However, the current stent allows only act as conduit for bile drainage without anti-tumor effect. The non-vascular DES were designed to release a cancer drug in a controlled manner and to provide both local cancer therapy and prolonged patency.

Previously, we reported our use of a metal stent covered with a paclitaxel-incorporated membrane giving an antitumor effect to prevent occlusion from tumor ingrowth. We have also developed a new generation of pclitaxel-eluting biliary stent using a membrane containing pluronic F-127 for effective drug delivery. And this functioning stent is now under clinical evaluation in human subjects. The physicochemical and compositional properties of the polymer membrane critically affect the release of the drug and scientists manipulate the polymer membrane properties to achieve a homogeneous and sustained drug release during the patency. In contrast to paclitaxel, more hydrophilic gemcitabine shows high initial burst release up to 70% of the loaded dose which makes it difficult for clinical use. Currently, in order to improve the release behavior of gemcitabine from polyurathane membrane, gemcitabine releasing system in nano-granulated states was developed.

Such a development remains remote until DES becomes common for the local treatment of tumors. Further supplementation of clinical data as well as basic research to provide a theoretical background is needed. However, DES indeed seems to be a very challenging but promising treatment method for malignant biliary obstruction. DES is expected to improve stent patency and contribute to increased survival as an added multidisciplinary treatment tool.

8548-131, Session 7c

Wire knitted Nitinol stent; thermal and surface treatment *(Keynote Presentation)*

Sung-Gwon Kang M.D., Seoul National Univ. (Korea, Republic of)

Wire knitted stent is now getting more and more popular in clinical practice. Most Gastrointestinal stents including esophageal stent, pyloric stent, colorectal stent and also biliary stent are made of Nitinol wire these days. But thermal treatment technique and polishing technique is now known very well. Thermal treatment and surface treatment are very important to make stent's physical properties and biocompatibility. Many technologies including Nanotechnology are under investigation. Thermal treatment technique sets physical properties such as radial force, expansile force, and long-term durability, and also chronic fatigue resistance. Surface treatment sets mainly biocompatibility, corrosion resistance, and also chronic fatigue resistance. Both electropolishing and mechanical polishing can be used for laser or chemical etched coronary and vascular stents. But neither of them could not be used for wire knitted stent. As the use of Gastrointestinal stent is getting popular, the biocompatibility and physical properties become important issues. We have studied proper thermal treatment technique to obtain optimal physical properties of Nitinol wire knitted stent, and mechanical and electropolishing techniques for better biocompatibilities and long-term durability.

8548-132, Session 7c

A portable and high energy efficient desalination/purification system by ion concentration polarization *(Invited Paper)*

Sung Jae Kim, Seoul National Univ. (Korea, Republic of)

The lethal threats to human health from heavy metals are associated with untreated ground water in vast number of countries in the World. Arsenic (As), cadmium (Cd) and lead (Pb) can cause serious illness such as skin cancer, kidney damage and gastrointestinal uptake. In the past few decades, a number of researches and commercial products that provide solutions to efficiently remove heavy metals have been reported. However, most of these methods were target-specific separation and required multi-step processes and expensive apparatus.

In this work, we developed a high throughput (~1mL/min) single step heavy metal purification process based on Ion Concentration Polarization (ICP) desalination mechanism. Instead of microfluidic channel networks, the plastic prototype made of plastic meshes and Nafion nanoporous membrane was built so that the manufacturability and cost efficiency were maximized. A modeled source water of Bangladeshi's ground water (As (500ppb), Cd(200ppb) and Pb (200ppb)) was filtered below the safe heavy metal concentration (As<10ppb, Cd<5ppb and Pb<15ppb). In addition, a higher concentrated source water (NaCl: 30,000TDS, seawater concentration) was also successfully desalted to fresh water level at the power efficiency of ~5Wh/L. Therefore, by assuming the flow rate of 1mL/min from 1/4inch scale system, one can expect to achieve a 100mL/min throughput from a 2.5inch portable system which is capable of desalting seawater, purifying heavy metals and disinfecting biological contaminants.

8548-138, Session 8c

Neuromodulation therapies in the field of stereotactic and functional neurosurgery *(Keynote Presentation)*

Jin Woo Chang, Yonsei Univ. College of Medicine (Korea, Republic of)

The idea of treating chronic neurological disorders with chronic stimulation began to emerge in the 1960s, but stimulation was largely used for targeting surgical lesions. In the early 1970s, the preliminary reports of using chronic deep brain stimulation (DBS) therapeutically emerged for treating patients with pain, movement disorders (tremor, Parkinson's disease, dystonia & etc), or epilepsy. As well, the clinical application of DBS for the treating movement disorders in the world has become popular in the early 2000s. Since then, DBS has become increasingly used & investigated for treating various types of chronic neurological disorders.

Currently, many different targets in selected brain regions have touted the potential benefit of DBS for other neurological disorders such as rare forms of pain, depression, dystonia, Tourette syndrome, obsessive compulsive disorder (OCD), dementia and etc. Despite the current marked clinical benefits by using DBS system for certain neurological disorders, and these realized and potential advances in treatment tools, controversy swirls around a number of clinically relevant and basic mechanistic issues. As well, the new innovative techniques of neuromodulation therapy which are based on the techniques of electrical stimulation, cell therapy, gene therapy, radiation & focused ultrasound have tried for the treatment of new diseases such as hypertension, appetite, epilepsy, hearing and etc. Its future will involve a complex interaction of improved understanding of the indications and mechanisms of action, exciting new indications, more mature assessment of outcomes, socioeconomic considerations, and fundamental technological developments.

I will address these controversial issues and emphasize the future directions & investigations for neuromodulation therapies for chronic neurologlical disorders.

8548-141, Session 8c

Flexible multichannel micro-electrodes for brain-machine interface and invasive feedback electrode for deep brain stimulation of mouse *(Keynote Presentation)*

SangHoon Lee, Korea Univ. (Korea, Republic of)

By the progress of brain-machine interface technology, the supporting

or replacement of human cognitive or sensory-motor functions tends to become in reality. Although the direct connection of brain to machine connection is still challengeable, the interfacing technology between neuron and machine has progressed rapidly, and is broadly applied in prosthesis of sensing and moving organs including ear, eye, arm, leg and etc. In addition, this technology extends its application to consumer products such as diverse haptic devices. In this paper, we introduce diverse flexible multichannel micro-electrodes which are usable in small animal (e.g.: mouse). Based on polyimide substrates, multichannel electrodes to measure evoked potentials from the skull of mouse were fabricated using MEMS technology, and they robustly measured the signals to the diverse stimulation (touch & press and sound) even from the skull.

The invasive feedback electrode for deep brain stimulation (DBS) was developed in cost-effective way. Elastic photo-resistor (SU-8) was used as substrate, and this electrode has 2 signal recording site an one stimulating site. The width of electrode is about 100 microns and the length is over 1 cm. It can penetrate the brain of mouse, and can reach to the subthalamic nucleus (STN). We characterized this electrode mechanically and electrically, and evaluated its function.

8548-244, Session 8c

Optogenetic mapping of brain circuitry *(Keynote Presentation)*

George J. Augustine, Duke Univ. (United States)

Studies of the brain promise to be revolutionized by new experimental strategies that harness the combined power of optical techniques and genetics. My talk will describe examples of such optogenetic approaches, both actuators that control neuronal activity and sensors that detect neuronal activity. Using the light-activated cation channel, channelrhodopsin-2, to map local inhibitory circuits in the cerebellum reveals organizational features that eluded more than 100 years' worth of anatomical studies. Using the fluorescent sensor for chloride ions, Clomeleon, allows imaging of the spatial and temporal dimensions of inhibitory circuits in the brain. The combined use of light to both control and monitor neural activity creates unprecedented opportunities to explore brain function, screen pharmaceutical agents, and potentially to use light to ameliorate psychiatric and neurological disorders.

8548-504, Session PLEN4

Advanced nano-bio hybrid drug delivery system : A wonder to chemotherapy?

Jin-Ho CHOY, Ewha Womans University (Korea, Republic of)

Many researches on drug delivery carriers have been restrictively focused on biomolecules and biodegradable polymers such as plasmid, polyethylene glycol and etc. However, there are still many problems unsolved, for example, low delivery efficacy, low expression rate, formation of toxic degradation products, and etc. In the present study, a novel concept of inorganic nano-vectors with targeting and drug delivery functions will be proposed to get breakthroughs in gene- and chemo-therapy [1-3].

In order to examine 2d-structured inorganic nano-material as nanocarrier for gene and drug delivery, an attempt has been made to prepare host-guest interaction mediated nanohybrid assemblies by intercalating the negatively charged anticancer drug, methotrexate (MTX), into the positively charged layered double hydroxides (LDHs). And eventually we found that the encapsulated drug molecules in the interlayer space of LDHs retained their chemical and biological integrity, and that the present inorganic-bio hybrids showed targeting and drug delivery functions

According to the in-vitro and in-vivo experiments, not only the passive targeting was realized by controlling the particle size of MTX-LDHs, thanks to an EPR effect, but also the active targeting could be demonstrated due to the clathrin-mediated endocytosis of such a nanohybrid drug [4,5]. Since the LDH nanoparticles are partially soluble in cytosol, the drug concentration in the cell increases and as a consequence, the drug efficacy is maximized.

It is, therefore, concluded that the present advanced functional drug delivery system could provide a promising integrative therapeutic action in chemo-and gene therapy.

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8548-37, Session 8a

Nanostructures from amphiphilic cyclotriphosphazenes and their applications *(Keynote Presentation)*

Youn Soo Sohn, RSTech (Korea, Republic of)

Conventional synthetic amphiphiles are mostly linear diblock or triblock copolymers composed of hydrophilic and hydrophobic segments, which rarely satisfy simultaneously all of the physicochemical properties required for practical drug delivery applications. Therefore, it is an urgent task to exploit new types of stronger amphiphiles. Recently, we have developed a new platform technology to prepare tripodal amphiphiles, represented as [N=P(X)(Y)]3, by cis-nongeminal grafting of equimolar a hydrophilic poly(ethylene glycol) (X) and a hydrophobic oligopeptide (Y) to a cyclic phosphazene template(1,2). These tripodal amphiphiles provide strong intra- and intermolecular hydrophobic interactions tuneable for self-assembly into stable polymeric micelles, polymersomes, and molecular hydrogels depending on the structure of the hydrophobic oligopeptide (Y). For example, the tripodal amphiphiles bearing linear oligopeptides with high hydrophobicity (log P >1, P = [solute]n-octanol/[solute]water) are self-assembled into stable micelles, but the tripodal amphiphiles bearing linear oligopeptides with an intermediate hydrophobicity (0< log P <1) reassemble from initially formed micelles into polymersomes. The tripodal amphiphiles grafted with branched oligopeptides instead of linear oligopeptides are self-assembled into thixotropic and thermosensitive molecular gels in aqueous solution. In particular, the polymeric micelles are suitable for polymer therapy of hydrophobic small molecular anticancer drugs such as taxanes and platinum complexes. In particular, docetaxel that is not formulated into stable micelles by conventional amphiphilic polymers could be stably encapsulated by our tripodal amphiphiles, and is now in the stage of preclinical studies. Other applications of the polymeric micelles and molecular hydrogels will be presented as well.

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8548-38, Session 8a

Medical device combination products based on custom shaped biomaterials *(Invited Paper)*

Young Bin Choy, Seoul National Univ College of Medicine (Korea, Republic of)

Medical devices have been drawing much attention in both industry

and academia to improve the efficacy and convenience in therapy. Although many of traditional medical devices have already shown their advantages to a large extent, several critical issues, such as long-term biocompatibility and patients' compliance, have been still unresolved and remained as their unmet clinical needs. Therefore, we developed novel combination products enabled with drug delivery to further improve their functionality in the biological milieu. In Biomaterials Processing & Application Laboratory (BPAL), therefore, we prepared a new-generation oral tablet designed for linear drug delivery, employing nanofibrous sheets. We also investigated drug-delivery micro-chips and -tubes to be integrated with deep brain stimulation (DBS) system. The surgical suture enabled with drug delivery could relieve the pain after wound closure. The combination products that we developed in our laboratory can benefit from accurately tailored drug delivery and enhanced targeting efficiency as we processed biomaterials with highly controlled geometry.

8548-39, Session 8a

Tetrameric far-red fluorescent protein as a scaffold to assemble an octavalent peptide nanoprobe for enhanced tumor targeting and intracellular uptake in vivo

Haiming Luo, Huazhong Univ. of Science and Technology (China)

Relatively weak tumor affinities and short retention time in vivo hinder the application of targeting peptides in tumor molecular imaging. Multivalent strategies based on various scaffolds have been utilized to improve the ability of peptide-receptor binding or extend the clearance time of peptide-based probes. Here, we use a tetrameric far-red fluorescent protein (tfRFP) as a scaffold to create a self-assembled octavalent peptide fluorescent nanoprobe (named as Octa-FNP) using a genetic engineering approach. The multi-ligand connecting, fluorophore labeling and nano-sized structure formation of Octa-FNP were performed in one step. In vitro studies showed Octa-FNP is a 10 nm fluorescent probe with excellent serum stability. Cellular uptake of Octa-FNP by human nasopharyngeal cancer 5-8F cells is 15-fold of tetravalent probe, ~80-fold of monovalent probe and ~600-fold of nulvalent tfRFP. In vivo enhanced tumor targeting and intracellular uptake of Octa-FNP were confirmed using optical imaging and western-blot analysis. It achieved extremely high contrast of Octa-FNP signal between tumor tissue and normal organs, especially seldom Octa-FNP detected in liver and spleen. Owing to easy preparation, precise structural and functional control and multivalent effect, Octa-FNP provides a powerful tool for tumor optical molecular imaging and evaluating the targeting ability of numerous peptides in vivo.

8548-88, Session 8b

Molecular isolation on the nanoscale *(Keynote Presentation)*

Joshua Edel, Imperial College London (United Kingdom)

The use of surface-enhanced Raman spectroscopy (SERS) as an analytical tool has gained increased interest in recent years due to its greater sensitivity and "fingerprinting" ability when compared to other spectroscopic techniques. This presentation will discuss approaches used to detect single, aggregated, and arrays of metallic nanoparticles in a high throughput fashion using SERS. Specifically a we report on a simple, fast, and inexpensive method to study adsorption and desorption of metallic nanoparticles at a liquid/liquid interface. These interfaces provide an ideal platform for the formation of two-dimensional monolayers of nanoparticles, as they form spontaneously, cannot be broken, and are defect-correcting, acting as 2D 'nanoparticle traps'. Such two-dimensional self-assembled nanoparticle arrays have a vast range of potential applications in displays, catalysis, plasmonic rulers, optoelectronics, sensors and detectors.

8548-89, Session 8b

Infrared eye tracker in an oculary clinical setting

Mizhanim Mohamad Shahimin, Univ. Kebangsaan Malaysia (Malaysia); Mukhzeer Mohamad Shahimin, Univ. Malaysia Perlis (Malaysia)

Infrared eye tracker is demonstrated in providing a more objective and quantitative results of the cover test measurement in eye care practices. The use of an infrared eye tracker, Tobii X120 (Tobii Technology AB, Sweden, sampling rate of 120Hz) is exploited and combined with the traditional fundamental technique in measuring eye alignment, the cover test. The eye tracker does not require the use of head gear or the chin rest as the algorithms used allows for head movements of 30 x 22 x 30 cm at a distance of 70cm. This feature in an eye tracker is also an added value as it will allow a more natural behaviour in the eye examination and be seen as a patient-friendly instrument. The objective cover test is performed using a custom made occluder that allows the infra red light to pass through, simultaneously measuring both eyes' positions at a time. The objective cover test findings from the eye tracker are compared with the subjective cover test measurements using alternating prism neutralised cover test, performed by a skilled optometrist. The statistical analysis comparing the subjective cover test to the objective cover test finding from the infrared eye tracker yielded a high correlation of 0.96. This implies that the objective cover test measurements, performed with the infrared eye tracker, showed good agreement with the cover test findings from the optometrist. Using an eye tracker would make available to the clinician a simple system for making quantitave measurements when performing the cover test in eye examination.

8548-90, Session 8b

Wireless Telemedicine Systems for Diagnosing Sleep Disorders with Zigbee Star Network Topology

Sechang Oh, Hyeokjun Kwon, Vijay K. Varadan, Univ. of Arkansas (United States)

Good sleep is critical for one's overall physical and mental health but more than 30 million people have experienced or are suffering from sleep disorder. Nevertheless, 85% of them remain undiagnosed or untreated. It can lead to a chronic disease such as diabetes, hypertension and depression. Sleep disorders are diagnosed through polysomnography, also known as a sleep study, in sleep laboratory overnight. This can perturb his ordinary sleep routine, and consequently an accurate diagnosis cannot be made. Many companies have been developing home sleep test systems to reduce the cost of sleep study and provide convenience to patients and the systems category varies as type II, type III and type IV according to types of sleep studies. However, current systems cannot be easily extended to a higher type. A patient who already had a type III system for diagnosing sleep apnea should purchase another a type II system which also has the function of a type III system to evaluate sleep stages. In this research, we propose a wireless telemedicine system for easy extension of channels by using a start network topology of Zigbee. The proposed system consists of two wireless transmitters, a receiver and a monitoring unit. One transmitter has 5 channels for EOG, EEG, EMG to evaluate sleep stages and the other transmitter has another 5 channels for ECG, Nasal flow, body position, abdominal/chest efforts, and oxygen saturation to diagnosing sleep apnea. These two transmitters build a star network with the receiver through Zigbee. The data from each transmitter in the receiver are retransmitted to the monitoring unit through Wi-Fi. By building a star network with Zigbee, channels can be easily extended. In addition, by using Wi-Fi, bio-signals can be monitored at remote places.

8548-139, Session 9c

Resting state brain network and its implication in neurodegenerative disease *(Invited Paper)*

William Seunghyun Sohn, Kwangsun Yoo, Jinho Kim, Yong Jeong, KAIST (Korea, Republic of)

Neurons are the basic units of the brain, and form network by connecting via synapses. Given that brain function is not mediated not by isolated neurons but by dynamic processes in the brain networks, approaches with the brain network perspective is becoming more important in understanding of the brain function and diseases. Brain networks span multiple spatial scales, from the microscale of individual neurons and synapses to the macroscale of cognitive systems. Furthermore, the networks are not static, they changes with time. Measurement and analysis of dynamic properties of brain network are challenging.

So far, there have been limited ways to measure the brain networks. Recently, imaging modalities such as MRI, NIRS (near-infrared spectroscopy) for human and microMRI, intrinsic optical signals for animal experiments are widely used for this purpose. In this paper, brain network mapping using resting state fMRI will be introduced. Firstly, a novel method for decomposition of functional sub-networks, localized ICA will be discussed. Second, the evidences of network functional connectivity change after motor learning. Changes of functional connectivity in neurodegenerative disease such as Alzheimer's disease and Parkinson's disease will be discussed. This finding may be helpful in understanding the disease pathophysiology and in early diagnosis. The resting functional connectivity using intrinsic functional connectivity in mouse is useful since we can take advantage of perturbation or stimulation of certain nodes of the network.

In conclusion, the study of brain connectivity will open a new era in understanding of brain and diseases thus will be an essential foundation for future research.

8548-140, Session 9c

Dynamic functional mapping of mouse brain using optogenetic tool

(Invited Paper)

JEE HYUN CHOI, Korea Institute of Science and Technology (Korea, Republic of)

1. BACKGROUND: As a way to study information processing in large-scale brain networks, the methods such as the event-related brain potential or electrical deep brain stimulation are applicable to mouse model. Such a direct electrical stimulation method, however, has several demerits including tissue damage, non-selectivity on activation or inhibition, and non-selectivity on neural type. Furthermore, the electromagnetic interference from the stimulator can contaminate the electrophysiological signals. Recently introduced technique, called optogenetic method can optically excite or inhibit neurons using light sensitive proteins such as Channelrhodopsin-2 (ChR2) or Halorhodopsin (NpHR). We use the transgenic mice, Thy1-ChR2-EYFP, of which all neurons express ChR2 proteins. We locally stimulated the brain regions with optic fiber connected laser system and the cortical responses were simultaneously measured with high density EEG using polyimide-based microelectrode (PBM) and mapped using reconstruction of measured 38 channel EEG on mouse skull.

2. METHODS: An integrated system of polyimid-based microarray with optroelectrode (optic fiber+electrode) is applied for dynamic cortical mapping in Thy1-ChR2-EYFP mouse model.The stimulation spot was identified with YFP histological iamges. The cortical images were obtained with equivalent dipole source model.

3. RESULTS: A. Characterization of transfer function of cortical response with respect to optogenetic stimulation

Multivariate regression results in the local field potential induced by the light pulse follows a Rayleigh distributions. The regression parameters, E (amplitude of local field potential) and tau (peak time) were obtained as functions of device parameters such as pulse duration and strength

B. Functionally-evoked cortical mapping by mouse EEG with respect to optogenetic stimulation

To characterize the neuronal connectivity to the cortical regions, we applied optical deep brain stimulation and observed the spatiotemporal dynamics patterns in mouse EEG. In particular, we applied the optical stimulation on the primary somatosensory cortex (S1) and hippocampus cornu ammonis (CA1) regions. The stimulation light intensity and pulse duration were 5 mW/mm2 and 20 ms, respectively.

The cortical EEG topographies evoked by light stimulation on brain regions in depth give us completely different functional connectivity information over time. In case of S1 stimulation, focal responses at the stimulated region were observed and then re-activation at the same region was monitored accompanied by contralateral responses in the parietal cortex. Additionally, the dynamic brain mapping could provide the information of response latency, which is approximately 24 ms in this case. The location of maximal response coincide with the stimulation position and the response amplitude decreases along the distance from stimulation spot in a power law, which is consistent with the photon density of light is decaying in a power law. However, the range of response is larger than the decay constant of photon density, which is less than 1 mm, which is speculated due to the volume conduction.

In case of CA3 hippocampal stimulation, the ipsilateral primary somatosensory cortex of limb region was activated first with

latency of about 24 ms and then contralateral primary somatosensory cortex of limb region was activated about 30 ms after the peak response at the ipsilateral region. It is interesting to note that the synaptic response was more anterior than the direct response to the optic stimulation. No direct activation due to volume conduction from the activated region is observed. It means that the hippocampal stimulating region is sufficiently far from the directly recordable range of EEG, hence the EEG signals are supposed to be a result from functionally connected synaptic projection.

4. CONCLUSION: We demonstrated dynamic brain mapping of functional connectivity in mouse model by applying high resolution EEG to transgenic mice with light activated neurons.

Co-localized LFP delivered a predictable model of neuronal response with respect to optical stimulation parameters.

The topographic maps obtained during optical stimulation to cortical, hippocampal, and thalamic regions showed the spatio-temporal synaptic projection toward cortex.

Independent component analysis of cortical response induced by optically evoked thalamic potential showed the signal transduction time from thalamic nuclei is distinct depending on cortical area. This suggests that the thalamic connectivity to cortex can be separable based on information transfer patterns

8548-142, Session 9c

Odorant discrimination by decoding many single units from main olfactory bulb *(Invited Paper)*

Hyung-Cheul Shin, Hallym University (Korea, Republic of)

Many previous studies on brain-machine interface (BMI) aiming to create neural prosthetic devices have been trying to decode movement-related information in real-time from motor brain areas of conscious animals. This type of BMI has a practical limitation when the number of neurons for both recording and decoding is dramatically increased. In our laboratory, we have shown a different type of BMI system, in which a small number of single units from various non-motor brain areas including somatosensory cortex, hippocampus, or prefrontal cortex of either rats or dogs were functionally substituted as neurons encoding motor information to control 1D or 2D machine

movements for various applications. These two types of BMI belong to the output BMI in comparison to the input BMI to transfer different modalities of sensory information directly to the CNS by bypassing normal afferent pathways. Both output and input BMIs will be eventually applied to disabled patients having either movement or sensory deficits. Another unique application of BMI technology is to exploit superb sensory functions of various animals adapted in unique environments and evolved in everlasting survival competitions. In this talk, I will present our recent results obtained by recording many channel single neurons from main olfactory bulb of both rats and dogs, where we aimed to test a possibility of creating a sensory neuron decoding-based BMI system for the discrimination of various odorants. We believe that this type of animal BMI will be applicable for various scent-related industries and medical fields. Supported by a grant(2012K001127) from BRC of the 21st Century Frontier Research Program, MEST, the Republic of Korea.

8548-148, Session 9c

Optogenetic tools for in vivo applications in neonatal mice *(Invited Paper)*

Jiayi Zhang, Qingpeng Yu, Nan Qin, Yupu Diao, Fudan University (China); Yue Zhang, Yangtai Guan, Lu Fan, Department of Neurology, Changhai Hospital, Second Military Medical Hospital (China)

The visual world is organized into anatomically and functionally stereotypic maps in mammalian animals. Spontaneous neural activities exist early in development and play important roles in the development of visual maps such as eye-specific segregation. We developed optogenetic tools to precisely manipulate the spatiotemporal patterns of retinal activities in vivo. Transgenic mouse lines and viral-mediated transfection methods enabled the expression of light-gated channelrhodopsin (ChR2) in retinal ganglion cells (RGCs) before the onset of vision (postnatal day 12). Whole mount retinal patch-clamp and multi-electrode array experiments verified the optical responses of RGCs, whereas in vivo calcium imaging experiments demonstrated the uniform postsynaptic light responses in superior colliculus (SC). During the chronic stimulation experiment, light-emitting diodes controled the activity patterns of each eye respectively in vivo. Anatomical organization of eye-segregation maps in SC was examined by injection of Alexa-fluorescent dyes intravitreously. We also looked at the functional features of SC neurons before the onset of vision. Our results revealed that synchronous activation of both eyes disrupted segregation, whereas asynchronous stimulation enhanced segregation. These techniques can be readily used in the development of central nervous system of neonatal rodents models.

8548-149, Session 9c

Nano-scale surface cues and in vitro neuronal growth

(Invited Paper)

Yoonkey Nam, Min Jee Jang, Kyungtae Kang, Insung S Choi, KAIST (Korea, Republic of)

Nerve cells (neurons) have been used for a convenient and effective model for basic neurobiology and it has also served as a test bed for the development of neural prosthetic devices. The characterization of neuronal growth in vitro has become an important part of neural tissue engineering. In this talk, I will present recent progresses on the investigation of nano-scale effects on neuronal growth in vitro. Hippocampal neurons from a small brain tissue dissected from E-18 (embryonic stage 18 days) Sprague-Dawley rat were used as a developing neuron model. They were seeded on substrates with carbon nanotube patterned glass substrates, anodized aluminum oxide surfaces with two different pitch sizes (60 nm, 400 nm), and silica nano bead surfaces with five different bead sizes (110, 190, 320, 480, 670 nm). These surfaces uniquely defined nano-scale surfaces with different topographical features. We observed longer neurite outgrowth and faster neuronal development on nano-scale surfaces compared to plain glass surfaces. The results from nano-scale cell culture platforms will be useful to understand nano-environments of the brain during the early neural developments. In addition, the promoted neuronal development could be further applied for neural tissue scaffolds or implantable neural interface systems.

8548-125, Session 10c

New drug-eluting stents to prevent stent thrombosis and restenosis for acute myocardial infarction: from the experience of Korean acute myocardial infarction registry *(Keynote Presentation)*

In-Ho Bae, Heart Research Ctr., Korea Ministry of Health and Welfare (Korea, Republic of); Myung Ho Jeong, Chonnam National Univ. Hospital (Korea, Republic of)

Drug-eluting stents (DES) are superior to bare metal stents (BMS) in reducing restenosis rates across a wide range of patients and lesion subsets. This study presented the investigation of one-year clinical follow-up were registered in 52 primary percutaneous coronary intervention sites in Korea, and pre-clinical results of various drug-coated stent fabricating with many other coating approaches on physiological parameters, Based on our clinical study adverse cardiac events were 17.4 % after DES implantation, which was significantly lower compared with 24.9% of BMS implanted patients. As assumption above outcome, it well repays research and development in new DES. Our research group carefully chooses abciximab, alpha-lipoic acid, heparin / dopamine, inhibitors in cell signal cascade were employed as coating drug. These drug candidates were coated on BMS surface by various methods such as TiO2 film deposited by plasma enhanced chemical vapor deposition, ultrasonic sprayer / simple-dip coating, or bio-inspired natural binding technique. In vitro and in vivo results of these new DES fabricated by our research group have showed superior outcomes compare to BMS on physiological parameters such as inflammation score, re-endothelialization, preventing neointema or thrombosis etc. These results are promising safer and more effective to overcome the limitation of DES.

Keywords: Drug-eluting stent, acute myocardial infarction, Korean Acute Myocardial Infarction Registry, Abciximab, alpha lipoic acid, anti-oxidant agent, dual-coating, thrombosis, restenosis

8548-133, Session 10c

Optical coherence tomography for ophthalmology: recent advancement in Korea *(Keynote Presentation)*

Beop-Min Kim, Korea Univ. (Korea, Republic of); Jeehyun Kim, Kyungpook National Univ. (Korea, Republic of); Hyun-Woo Jeong, Jaeryung Oh, Korea Univ. (Korea, Republic of); Seong-Woo Kim, Korea University (Korea, Republic of); Hae-Jeong Park, Yonsei University (Korea, Republic of)

Optical coherence tomography (OCT) is a unique tool that can provide cross-sectional, tomographic images of human eye, which enables accurate diagnosis of various pathologic conditions. Ophthalmologic OCT devices have been commercialized by nearly 10 companies and successfully accepted as an essential tool in eye clinics. In Korea, several research groups are investing much effort as a team to develop a top-notch ophthalmologic OCT system. Recent advances of our team include dual-depth OCT system which can image both anterior part of the eye and retina simultaneously, fast signal/image processing for

ultra-high frame rates, 3-D image segmentation for accurate diagnosis and construction of portable OCT probe. Details of these new technologies will be presented and future prospect will be discussed.

8548-136, Session 10c

Laminated, cubic, biodegradable polymer structures for bacteria-based, robotic drug delivery *(Invited Paper)*

Hyung Jung Yoo, Sangmin Lee, Jae Hyun Ahn, Seok-jun Hong, Minjae Lee, Seoul National University (Korea, Republic of); Jong-Mo Seo M.D., Seoul National Univ. Hospital (Korea, Republic of); Tae-You Kim, Seour National Univ. College of Medicine (Korea, Republic of); Sung-Jae Kim, Seoul National Univ. (Korea, Republic of); Dong-il D Cho, Seoul National University (Korea, Republic of)

Recently, bacteria-based drug delivery systems have been studied to achieve active and localized drug delivery [1]. Researchers have shown that the flagellated bacteria have chemotactic properties to tumor cells, and they can be used as energy sources for active drug delivery [2-3]. Our previous results have reported that a droplet made by a biodegradable polymer can be used in the localized drug delivery, using the flagellated bacteria [4]. We also have investigated on a surface energy modification method to control the bacterial adhesion on a biodegradable polymer surface for enhancing the directivity and motility [5].

In this paper, a bacteria-based microbot which has a laminated structure made of several layers of biodegradable polymers is proposed. The laminated structure made of biodegradable polymers is beneficial for a time-controlled and sustained drug release, since the release rate of the loaded drugs in the laminated structure is determined by the degradation rate of the biodegradable polymer [6]. The fabrication process is shown as follows. A five-level laminated polymer film is prepared, and exposed by X-ray synchrotron radiation. After the X-ray lithography on the biodegradable polymer, the exposed area is dissolved in an alkaline solution, as the main chain of the biodegradable polymer is broken by the X-ray radiation. The remained area of the polymer film has cubic structures and the length of each cubic side is 50 um. The results show that lamination of several polymeric materials is possible, and that X-ray synchrotron radiation is an excellent method of microfabricating cubic structures to develop bacteria-based microbots for targeted drug delivery.

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8548-137, Session 10c

Drug delivery microchip for potential application to chronic pain relief

Seung Ho Lee, Min Park, Chun Gwon Park, Ji Eun Lee, Seoul National Univ. College of Medicine (Korea, Republic of); Young Bin Choy, Seoul National Univ. College of Medicine (Korea, Republic of) and Seoul National Univ. (Korea, Republic of)

A great deal of interest has been focused on long-term drug delivery to maintain maximum therapeutic benefit and minimize the side effect especially for the patients suffering from chronic pain. However, sustained delivery of a small-molecule drug still poses limitation in uncontrolled, diffusion-mediated drug release, mostly due to a large initial burst followed by short-term drug release. In order to resolve this, we propose a microchip equipped with precisely designed micro-wells and -channels in this work. A microchip composed a pair of micro-channel and -well was fabricated on a PMMA plate using CO_2 laser. A channel was filled with a biocompatible polymer, PEG, as diffusion barrier and a well with a find powder of a drug to serve as drug reservoir. For the potential application to long-term pain-relief, we employed a drug, dichlorofenac sodium salt, in this work. After filling the micro-channel and well, the side of the microchip, where a micro-channel and -well were exposed, was sealed with Ideal 9144 Masking Tape. To control the drug release profile, we varied the geometric parameter of the micro-channel, i.e., the length and cross-sectional area of the channel. As a result, the onset time and period of drug release increased as the channel length increased and the cross-sectional area decreased, following the Fick’s 1st law of diffusion. The work is now in progress to design a single microchip embedded multiple pairs of micro-channels and -wells, where the channels of different lengths and cross-sectional areas were integrated, allowing both immediate onset and more prolonged drug release.

8548-40, Session 9a

Toward artificial cells: membrane protein mediated uptake and release from lipid bilayer coated nanoporous silica particles *(Keynote Presentation)*

Lennart Bergström, Stockholm Univ. (Sweden)

Transport across membranes is mediated by membrane proteins and underpin basic functions of the living cells such as energy transduction, sensory perception, cell adhesion and movement, and cell recognition. The uptake of specific ions is also an integral part of biomineralisation processes in living organisms. The use of lipid vesicles to study various types of cell membrane events in vitro is wide-spread but limited by inherent instabilities. Supporting the lipid bilayers on planar or curved (particulate) solid substrates offer enhanced stability. Porous silica spheres are particularly attractive because of their cytoskeleton-like pore structure and tuneable external and internal surface properties.

We will report a robust and versatile membrane protein based system for selective uptake and release of ions from nanoporous particles sealed with ion-tight lipid bilayers of various compositions that is driven by the addition of ATP or a chemical potential gradient. We have successfully incorporated both a passive ion channel -type peptide (gramicidin A) and a more complex primary sodium ion transporter (ATP synthase) into the supported lipid bilayers on solid nanoporous silica particles. Protein-mediated controlled release/uptake of sodium ions across the ion-tight lipid bilayer seal from or into the nanoporous silica carrier was imaged in real time using confocal laser scanning microscope and the intensity changes were quantified. ATP-driven transport of sodium ions across the supported lipid bilayer against a chemical gradient was demonstrated. We will also demonstrate how a multisubunit, transmembrane complex “molecular machine”, cytochrome c oxidase (CytcO), can be incorporated in a fully functional, reconstituted form into a supported lipid membrane supported The

enzyme CytcO is a proton pump that is driven by electron transfer from cytochrome c to oxygen, which is reduced to water.

The possibility to design durable carriers with tight lipid membranes, containing membrane proteins for selective ion uptake and release, offers new possibilities for functional studies of single or cascading membrane protein systems and could also be used as delivery vehicles and biomimetic microreactors.

8548-41, Session 9a

Biocompatible multi-interaction ligands capped nanoparticles for biomedical applications

Daishun Ling, Taeghwan Hyeon, Seoul National Univ. (Korea, Republic of)

Inspired by mussel adhesive protein, we herein report on the designed synthesis of versatile multi-interaction ligand (MIL) by combining poly(ethylene glycol), polyethylenimine and polyDOPA for ultrastable and biocompatible nanoparticles. The MIL can stabilize various nanoparticles of metals and metal oxides by various cooperative binding modes including direct binding with catechol and amine groups, micelle formation using amphiphilic branched block copolymer structure and electrostatic interaction between positively charged ligand and negatively charged nanoparticle surface. The MIL stabilized nanoparticles ofFe_3O_4, MnO, and Au exhibited extremely high stability in various harsh aqueous environments including highly acidic and basic media, highly concentrated NaCl solution, and even boiling water. The synthetic procedure is easy to scale-up, and the ligand exchange process is very simple and short. The confocal laser scanning microscopy study showed that the RITC (Rhodamine-B-Isothiocyanate)-labeled MIL-functionalizatized nanoparticles can easily transfected into MDA-MB-231 and Hela cancer cells. MTT assay revealed that cell viability was not hindered following culture with a concentration of 600 μg Fe ml-1 for both 24 h and 72 h. Trypan blue exclusion assays also showed that proliferation was not reduced in the presence of MIL-functionalizatized Fe_3O_4 nanoparticles even after 72 h. Also for the live and dead assay, no toxicity was found through fluorescence microscopy in the cells treated with various concentrations of MIL-functionalized Fe_3O_4 nanoparticles. These results demonstrated that MIL-functionalizatized nanoparticles are highly biocompatible. The in vivo mice pharmacokinetic studies showed that MIL-functionalized Fe_3O_4 nanoparticles (T1/2, MIL2 = 3.45 hr) had much longer blood circulation time than that of the previously reported iron oxide based nanoparticles. The in vivo mouse MRI results using MIL-functionalizatized Fe_3O_4 nanoparticles showed that the nanoparticles exhibited a long blood circulation time and accumulated in lymph nodes 24 h after the injection which indicated that MIL2-functionalized Fe_3O_4 nanoparticles are highly stable in blood stream. Biodistribution studies revealed relatively high accumulation of MIL-functionalized Fe_3O_4 nanoparticles in the spleen and liver, which has been commonly observed for nanoparticles in vivo. These results clearly demonstrated that the MIL-functionalized nanoparticles are highly stable in various harsh biological media for diverse biomedical applications such as high-resolution MRI and cell labeling.

8548-42, Session 9a

Printable Thermoelectric Devices and Conductive Patterns for Medical Applications

Jungmin Lee, Univ. of Arkansas (United States); Hyunjung Kim, National Institute of Aerospace (United States); Linfeng Chen, Univ. of Arkansas (United States); Sang H. Choi, NASA Langley Research Ctr. (United States); Vijay K. Varadan, Univ. of Arkansas (United States)

As concern about health increases, point-of-care diagnosis devices get attention in the medical industry. The devices enable to measure and monitor bio-signals or physiological signals with easy manner. Therefore, the devices should be portable and cost-effective. The life time of battery and production cost are the bottle neck to satisfy the requirements of point-of-care devices. These limitations can be overcome by applying printing technology because it allows high resolution, continuous process, high-speed fabrication, low material consumption and nano-sized pattern on both flexible and rigid substrates. In addition, thermoelectric generator can replace the solid battery as a power source because it uses heat source from nature and converts heat to electrical energy. In this research, we propose a printable thermoelectric generator and conductive patterns to implement more portable and cost-effective medical devices. To print thermoelectric generator and conductive pattern on substrate, development of inks is the critical parts. Thermoelectric inks are synthesized with nano-structured bismuth telluride and antimony telluride which are used as n- and p- type material, respectively. These n-and p- type inks form p-n junction. The unit cell of single p-n junction is arrayed and each unit cell is connected in series to produce more power. Each carbon and metal is used as fillers in polymer based conductive ink. The conductive patterns are printed by screen printing method.

8548-44, Session 9a

Synthesis and characterization of cellulose-functionalized 3,4-dihydroxyphenyl alanine(dopamine)/silica-gold nanomaterials by sol-gel process.

Ramesh Sivalingam, Joo-Hyung Kim, Chosun Univ. (Korea, Republic of)

To functionalize common cellulose, therefore, the present investigation focuses on cellulose hybrid composites- cellulose-silica and cellulose-functionalize dopamine-silica/gold nano-materials- by sol-gel process. The tetraethoxysilane (TEOS) and gold precursors and γ-aminopropyltriethoxysilane (γ-APS) as coupling agent were used for sol-gel crosslinking process. The chemical and morphological properties of cellulose/silica and cellulose/silica-gold nanomaterials via covalent crosslinking hybrids were characterized by FTIR, XRD, SEM, TEM and AFM analysis. The results show that cellulose-silica and cellulose-silica/gold hybrids form new macromolecular structures in the size of 20-100nm. The cellulose functionalized nanosized materials with many applications in electronics, molecular engineering, biotechnology, catalysis and sensor devices.

8548-91, Session 9b

The evolution of telemedicine and nano-technology *(Keynote Presentation)*

Dong Kyun Park M.D., Gachon Univ. Gil Medical Ctr. (Korea, Republic of)

A series of process is necessary for the patients such as they need to go to a hospital, to be diagnosed by doctors, to go through many different tests and then to be prescribed. However, when such process is unavailable, telemedicine has been substituting for that by transmitting the data measured by medical devices at home or at the hospitals, insufficient conditions in diagnosis and treatment, and yet only a medical service substitute for such series of process.

However, the telemedicine is evolving into m-Health, u-Health thanks to an epoch-making development of telecommunication technology, popularization of smartphone, development of nano technology, the conversion of paradigm from the treatment of acute diseases to the prevention and management of chronic diseases. Telemedicine system is basically divided into sensing, transmission, analysis and feedback, and transmission, analysis and feedback fields have been remarkably developed except the sensing part that developed only in

miniaturization of existing general home medical devices.

Lap on chip, lensfree on-chip micorscopy, potable tomography, implantable moniter, non-invasive biochemical monitoring have become available thanks to the development of nano technologies. Such development of telemedicine has made it possible for the patients to have their health conditions monitored at home doing in their daily routines and the data from the monitoring to be sent by wireless for real time. Telemedicine is now evolving from the medical service that having been done without any other options to essential infrastructure of basic medical service.

8548-92, Session 9b

E-Bra system for women ECG measurement with GPRS communication, Nanosensor, and motion artifact remove algorithm

Hyeokjun Kwon, Sechang Oh, Prashanth S Kumar, Vijay K. Varadan, Univ. of Arkansas (United States)

The Electrocardiogram(ECG) signal is the most important bio-signal for people who have cardiac disease. To develop the self-diagnosis system, several kinds of wireless technologies such as Zigbee and Wi-Fi are being used to send ECG data to a server. In this paper, a technology using in 2G or 3G communication, which is GPRS is suggested as a data transmission technology. In measuring ECG signal, there are several kinds of methods in attaching electrode on the body called as Lead I, II, III, etc. Several noise components occurred by different measurement situation such as experimenter's respiration, sensor's contact point movement, and the wire movement attached on sensor are included in pure ECG signal. Those motion artifacts influence to distort ECG signal, and the frequency distribution is duplicated in actual ECG signal frequency. The suggested algorithm in this paper has two kinds of main parts to extract clear ECG signal from measured original signal through an electrode. The first part is to extract motion noise signal from measured signal, and the second part is to extract clear ECG by using extracted motion noise signal and measured original signal. The paper suggests several techniques in order to extract motion noise signal such as predictability estimation theory, band pass filter, a filter including a moving weighted factor, amplitude detection, and interpolation techniques. In addition, this paper introduces an adaptive filter in order to extract clear ECG signal by using extracted baseline noise signal and measured signal from sensor.

8548-93, Session 9b

Smart garments in chronic disease management: progress and challenges *(Keynote Presentation)*

Ajit Khosla, Simon Fraser Univ. (Canada)

Global healthcare expenditures for the year 2011 exceeded $6 trillion. It has been estimated by World Health Organization (WHO) that up to 75% of healthcare spending is on chronic disease management, such as: cancer, heart disease, diabetes, obesity, hypertension etc. In order to reduce the expenditure associated with chronic disease management, there is a need to change the way healthcare monitoring is done. This can be done by making a shift from Hospital based chronic disease management to Home based chronic disease management. This will result in reducing hospital visits and thus significantly reducing the cost. Over last 10 years, there has been a big thrust on developing Smart Garments for home based chronic disease management.

This paper reviews state-of-the-art smart clothes that are embedded with nano-micro systems and sensors which can read bio-signals that are intrinsic to the body. We will also discuss the challenges involved in developing next generation smart garments for healthcare monitoring and potential solutions.

8548-94, Session 9b

Achieve the continuity of care in diabetes management via IBGMS (internet based glucose monitoring system) *(Keynote Presentation)*

Hun-Sung Kim M.D., Jae-Hyoung Cho M.D., Kun-Ho Yoon M.D., The Catholic Univ. of Korea (Korea, Republic of) and Seoul St. Mary's Hospital (Korea, Republic of)

Continuity of care in chronic diseases is a cornerstone of effective health care organization and has been associated with lower mortality, better access to care, less hospitalization and referral, fewer emergencies and better detection of adverse medical events. During last 10 years, our team has been tried to establish the bidirectional communication system called "Internet-Based Glucose Monitoring System (IBGMS)". With that, we clearly demonstrated the beneficial effects in short- and long-term periods by randomized clinical trials. Patients and medical team come to communicate via Internet or telecommunication, where patients upload their glucose data as well as personal information and then medical team send optimal feedback. Clinical evidences of long-term trial as well as short-term trial have already been made. Telecommunication based model is also introduced and expected to be more convenient and be able to applied to even countries with low-IT infra settings. However, most of all, evidences for cost effectiveness of such the system should be demonstrated to propagate to general population in real clinical practice. To establish cost-efficient model, various kinds of clinical decision supporing softwares for reducing lobor time of physicians need to be developed. Numerous sensors and devices to monitor patients' data will be available in near future and so, automatic interconnection between devices and web chart is also developed accordingly. Further investigations to show clinical outcomes of such the system should be performed, leading to opening a new paradigm of chronic disease management.

8548-95, Session 9b

Nanobiomedical device for personalized nanomedicine *(Keynote Presentation)*

HeaYeon Lee, Northeastern University (United States)

In recent years, a new paradigm of nanobiomedical devices combining miniaturization and integration has been exploited in areas such as combinational chemistry, biotechnology, engineering, proteomics and clinical diagnostics. One of the critical issues in the development of nanobiomedical system is how to differentiate signal-to-noise ratio per very small amount of signal. Developing biocompatible integrated nanosystem requires the fabrication of appropriately designed nanowell array structure for high sensitivity homogenous assays. Until now, we achieved high specific detection of DNA molecule using nanowell array structure integrated top-down and bottom-up nanotechnology. We obtained a 150-orders–of-magnitude enhancement in sensitivity of DNA chip. This nanowell array system could be applied to numerous the integrated digitizing biosensors. In this presentation, I will describe a demonstration of precious molecule recognition without nonspecific binding while maintaining the bioactivity on nanostructured space. And also, in general, lipid membranes vesicles are a biomimetic platform for various application of ligand-receptor interactions, cellular attack or signal transduction. It turned out the gently-sloped vertical nanowells were optimized structure for selective array of single liposomes without capillary resistances. With this nanowell electrode, the electrochemical responses were significantly enhanced for the binding event of streptavidin to the biotinylated functional lipid vesicles. A simple sandwich format was used for the successful detection of a specific target of obesity molecules using the nanowell electrode. A substantial decrease in peak current density was found with the addition of leptin without nonspecific binding or false signals. The developed miniaturized/integrated nanowell array-device system has shown excellent advantages over conventional instrumental systems for analysis of biomaterials in its size, cost, detection time and multiplex detection capability. It also showed high potential to apply in various nanobiomedical devices for high throughput analysis.

8548-505, Session PLEN5

Advances in neuro imaging from molecular imaging to tractograph

Zang-Hee Cho, Gachon Univ. (Korea, Republic of)

No Abstract Available

8548-46, Session 10a

Why we need to develop standard measurement techniques in nanomaterial safety research *(Keynote Presentation)*

Nam Woong Song, Korea Research Institute of Standards and Science (Korea, Republic of)

Commercialized products using nanomaterials have been already launched to the market according to the development of the nanotechnology. It is prerequisite to validate the safety of those products on the environment and human health for the prospective growth of nanoindustry. Thus the safety issue of nanomaterials becomes more and more emphasized in these days. To understand the relationship between physicochemical properties and nanotoxicity, it is required to develop reliable measurement techniques adequate for the analysis of nanomaterials in respect to toxicity test. Furthermore, it is also needed to analyze the property of nanomaterials before and after the toxicity test because their properties usually change according to the environment. However, the measurement methods for some characteristics have to be developed to give consistent, quantitative and accurate results.

In Korea Research Institute of Standards and Science (KRISS), we are seeking and developing reliable methods to identify various kinds of nanomaterial characteristics such as size, size distribution, surface charge/composition, optical and photoinduced chemical properties. We are also trying to relate the interaction behavior of nanomaterials with their physicochemical properties at cellular level. In this presentation, some examples of established techniques for nanomaterial characterization by using microscopic and spectroscopic analysis will be introduced. The need of development on each technique will be explained along with the case study results.

8548-47, Session 10a

Toxicity and toxicokinetics of inorganic nanoparticles *(Invited Paper)*

Soo-Jin Choi, Seoul Women's University (Korea, Republic of)

Along with the extensive development of nanomaterials for biological and medical applications, a growing concern about their potential toxicological effects on humans has been raised in recent years. Human body may be intentionally or unconsciously exposed to diverse types of nanoparticles by several routes due to the expanded production and use of artificial nanomaterials in a variety of fields. And it is certain that the toxicity of nanomaterials with large surface area and high reactivity may not be predictable from the known properties of bulk-sized materials. It is, therefore, highly required to understand the biological response of nanoparticles and toxicity mechanism as well. We evaluated the cellular uptake behaviors of inorganic nanoparticles such as anionic nanoclays and zinc oxide nanoparticles in cell lines and their toxicity mechanism was also investigated. Moreover, their intracellular trafficking pathway and toxicokinetics were determined in human cell as well as in animals, focusing on endo-exocytic pathway, pharmacokinetics, tissue distribution, and excretion profiles. These results will be useful for practical biological and medical applications of inorganic nanoparticles with safe and biocompatible level.

8548-48, Session 10a

Wireless glucose monitoring watch enabled by an implantable self-sustaining glucose sensor system

Pratyush Rai, Vijay K. Varadan, Univ. of Arkansas (United States)

Implantable glucose sensors can measure real time blood glucose as compared to conventional techniques involving drawing blood samples and in-vitro processing. An implantable sensor requires energy source for operation with wire in-out provision for power and sending signals. Implants capable of generation-transmission of sensory signals, with minimal or no power requirement, can solve this problem. An implantable nanosensor design has been presented here, which can passively detect glucose concentration in blood stream and transmit data to a wearable receiver-recorder system or a watch. The glucose sensitive component is a redox pair of electrodes that generates voltage proportional to glucose concentration. The bio-electrode, made of carbon nanotubes-enzyme nanocluster, has been investigated because the large surface area for taping electrical signals. Radio frequency (RF) based sensor telemetry works on LCR resonance/inductive coupling. It relies on change in the capacitive element, charged by the glucose sensor, to induce a frequency shift. A simultaneous power transmission and signal transmission is achieved by employing two separate LCR oscillating loops, one for each operation. The corresponding coupling LCR circuits are housed in the wearable receiving watch unit. The sensor system has a logarithmic response function to glucose concentration change. The signal is amplified by a logarithmic amplifier post reception. The data logged in this glucose monitoring watch can be instrumental in managing blood glucose as trigger for an insulin dispensing payload worn on person or implanted.

8548-96, Session 10b

Microwave thermal radiation effects on skin tissues

Kyo D. Song, Hargsoon Yoon, Norfolk State Univ. (United States); Uhn Lee M.D., Gachon Univ. Gil Medical Ctr. (Korea, Republic of); Sang H. Choi, NASA Langley Research Ctr. (United States)

Microwave/RF energy has been used for many therapeutic applications, such as transurethral microwave therapy (TUMT). For safe uses of RF power, it is important to know how to deliver microwave energy on focused area and control the temperature changes not to drastically increase and get too high. Graphical analysis of thermal loading factor is important to understand how to achieve effective transmission of microwave through the tissue. The loss mechanism while transmission often appears as thermal effects due to absorption of microwave, especially for materials such as human skin, muscles, and other organic parts including brain. In this paper, microwave thermal effects are investigated to measure temperatures, penetration depth through animal skins in terms of input power and various frequencies. This result will be compared with the case of human applications.

8548-97, Session 10b

Sensing of neural activity from neural tissues using a micro-spectrometer

Hargsoon Yoon, Norfolk State Univ. (United States); Yeonjoon Park, National Institute of Aerospace (United States); Kyo D. Song, Norfolk State Univ. (United States); Uhn Lee M.D., Gachon Univ. Gil Medical Ctr. (Korea, Republic of); Sang H. Choi, NASA Langley Research Ctr. (United States)

Sensing and monitoring of electrophysiological and chemical activities from single or largely populated neural cells within functional networks are essential to interpret neural processes in the brain. Development of an optical neural sensing system and real-time monitoring of neural activities in the brain are highly beneficial to analyze brain function and offer new ways to diagnose and cure neurological disorders and diseases. In this research, an optical neural sensing method is studied to measure neural signals in the brain using a micro-spectrometer which is based on a micro-scale Fresnel diffraction optics. The research for the optical neural system design and experiment results from neural cells and tissues is presented. The sensing capability and performance of the micro-spectrometer system are discussed with electrical sensing methods.

8548-98, Session 10b

Magnetic resonant coupling for power transmission

Hyunjung Kim, National Institute of Aerospace (United States); Hargsoon Yoon, Norfolk State Univ. (United States); Sang H. Choi, NASA Langley Research Ctr. (United States); Larry D. Sanford, Eastern Virginia Medical School (United States); Kyo D. Song, Norfolk State Univ. (United States)

Wireless power transfer via electromagnetic coupling has been studied for biomedical applications including medical sensors, implantable devices, etc. Delivery of data and control information can also be achieved through electronic communication devices that are integrated into wireless power transfer modules. Recently, significant improvement on wireless power transfer efficiency has been demonstrated by magnetic resonant coupling technique. Specifically this study has explored a potential application of magnetic resonant coupling for neural sensing systems. Compared to other inductive coupling methods, the magnetic resonant coupling provides a sufficient power to cover the power budget required for the wireless data communication of neural sensor. In this study, a magnetic coupling device for wireless power transmission was specifically designed for neural sensing purpose. The test results of a simple experimental set-up and a circuit model of magnetic resonant coupling modules show 15.4% of power transfer efficiency with a device volume of 3 cm^3. Delivered power, 22 mW, is considered sufficient to cover the power budget of a wireless data communication system designed for chronic neural sensing. This will allow a long term neural sensing operation and stimulation. The concerns on the sensor's positioning, sizes of source, and receiver coils including its power budget for the wireless data communication system for the neural sensing will be contemplated in the discussion.

8548-99, Session 10b

Development of a nanotechnology-based flexible neural recording probe for chronic sensing of neurodegeneration

Hargsoon Yoon, Courtney S. Smith, Kyo D. Song, Darryl W. Scott, Norfolk State Univ. (United States)

Clear understanding of neurodegeneration mechanism is essential for early intervention and novel therapeutic treatment to neurological disorders before having irreversible loss of neuronal functions. This research is focused on the development of a neural recording system which can monitor the alteration of neural function. The goal of this research is to implement a nanotechnology-enabled neural recording device for in-vivo monitoring of unit neural impulses that are implicated in the neurological disorders. This nanotechnology-based flexible neural probe for electrophysiological sensing can detect burst discharge of neuronal firing with high spatiotemporal resolution. In addition, the implementation of the flexible neural probe could alleviate the complexity of current surgical procedure requiring micro-positioning of neural probe after implantation.

8548-143, Session 11c

Micro-nano robotic manipulation and biomedical applications *(Keynote Presentation)*

Fumihito Arai, Nagoya Univ. (Japan)

Integration of the microfluidics and robotics based on MEMS and nanotechnology is unique approach for biomedical innovations. In addition to the advantage of environmental control by microfluidic chip, microrobotic technology enables physical operation to the cell with high throughput. We have studied on robotic technology on a microfluidic chip. Our concept is based on micro-nano robots or tools being put in the microchannel, where they are actuated and manipulated for works such as sensing, handling, analysis, surgery. Microfluidic systems having high-speed mcirorobots are developed and applied for biomedical innovations. In this talk, our recent research works on On-chip Robotics will be given.

i) Precise 3DOF control method of magnetically driven microtool (MMT)1),

ii) High-speed microtool actuation by making riblet surface on its bottom2),

iii) Active enrichment of influenza virus using insulated dielectrophoresis (DEP), transport of single virus to a specific cell by optical tweezrers3) and intracellular measurement.

Furthermore, technical issues and future direction will be discussed.

References

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8548-144, Session 11c

Tracing and quantification of pharmaceuticals using MR imaging and spectroscopy *(Keynote Presentation)*

Eun-Kee Jeong, The Univ. of Utah (United States)

MRI can be a powerful non-invasive imaging tool for tracing or monitoring the pharmaceuticals in in-vivo animals, for instance, substance containing a paramagnetic-ion. Although there are many challenges to perform drug-delivery research using a clinical whole-body MRI system, which include low sensitivity and limited spatial resolution due to weak gradient hardware system, there are many advantages. It is widely available and one of the greatest advantages of drug-delivery research on the whole-body MRI system includes that we will deal with the similar problems with those with human application, should the pharmaceuticals become transferable to human imaging. In this presentation, I will present several drug-delivery researches that were performed at a clinical whole-body MRI system on small animals, including mice and rabbits.

8548-2, Session 11a

Systems nanotechnology to fight cancer *(Invited Paper)*

Ji Ho Park, KAIST (Korea, Republic of)

Over the past decade, widespread progress in nanotechnology has produced an impressive array of nanodevices with powerful electromagnetic and therapeutic properties. Nonetheless, our capacity to precisely home these materials to regions of disease in vivo has

remained very limited and, despite three decades of research, ligand-targeted nanomedicines have yet to provide a benefit to patients. A fundamental limitation of current approaches to nanoparticle targeting is that they lack mechanisms of communication and amplification through which specific targeting events could assist the targeting of materials still in circulation. In this work, we developed nanosystems where a "cocktail" of two distinct nanomaterials work in concert within the bloodstream to amplify tumor targeting and improve therapy in vivo, which was inspired by examples of communication in natural targeting systems (e.g. inflammatory cell recruitment to infection). Specifically, the first activator nanoparticles initially targets tumors and, after arrival, sends signals through the biological cascades or directly to the second responder (diagnostic or therapeutic) nanoparticles to recruit them into tumors efficiently. This approach stands in contradistinction to all current nanotechnologies that utilize formulations of nearly-identical nanoparticles that perform competitive tasks without cooperation in vivo. We believe this work motivates a new paradigm of "systems nanotechnology" for biomedicine, where multi-component, interactive nanoparticle systems are engineered to improve the sensing and treatment of diseases in vivo.

8548-7, Session 11a

Microneedle patches for improved influenza vaccination *(Invited Paper)*

Yeu-Chun Kim, KAIST (Korea, Republic of)

Influenza is a vaccine-preventable disease, but remains a major health problem world-wide. Morbidity and mortality due to influenza could be reduced by development of simple and effective vaccination methods. Immunization via the skin is attractive, because, in large part, the skin is replete with antigen-presenting cells such as Langerhans and dermal dendritic cells.

Arrays of metal micron-scale needles were coated with influenza inactivated virus vaccines suitable for simple, manual application. A single dose of influenza vaccine from microneedles (MNs) generated strong antibody and cellular immune responses in mice and provided superior protection against lethal viral challenge at the main site of viral replication in the lung, as evidenced by virus clearance below the detection limit. Additionally, microneedle vaccination resulted in enhanced cellular recall responses after challenge.

Virus like particles (VLPs) and DNA vaccines are attractive cell-based vaccines and the vaccinations using MN patch coated with VLP or DNA demonstrated dose-sparing effects of influenza vaccine in comparison with intramuscular (IM) injection.

Apart from immunologic advantages, microneedles also offer potential logistic opportunities. The small size of microneedles should facilitate storage, stockpiling and transportation of influenza vaccines. Vaccination should be faster and simpler because microneedles are painless and suitable for self administration. Mass-produced microneedles would be cost-competitive with hypodermic needle and syringe.

In summary, our results suggest that influenza vaccine delivery to the skin using microneedle patches may provide a new modality to increase patient coverage and improve immunogenicity of influenza and other vaccines.

8548-8, Session 11a

Biopolymer-inorganic nanohybrid for potential biomaterials and drug delivery systems *(Invited Paper)*

Jae-Min Oh, Gyeong-Hyeon Gwak, Yonsei University (Korea, Republic of); Seung-Min Paek, Kyungpook National University (Korea, Republic of)

We have successfully prepared biopolymer-inorganic nanohybrid utilizing agarose hydrogel and two-dimensional layered metal hydroxide (LMH) nanoparticles through electrophoretic route. Agarose hydrogel of 1% concentration was prepared with Tris-Cl buffer (pH 7.4) solution, and both cationic (Ni^{2+}, Zn^{2+}, Al^{3+}, Ga^{3+} and etc.) and aionic precursors ($NaOH/NaHCO_3$) were forced into the hydrogel by electrical force to form homogeneous LMH nanoparticles. Various combination of metal precursors solutions, such as Ni^{2+}/Al^{3+}, Ni^{2+}/Ga^{3+}, and Zn^{2+} only were tested to prepare biopolymer nanohybrid containing $Ni_2Al(OH)_6(CO_3)_{0.5}$, $Ni_2Ga(OH)_6(CO3)_{0.5}$, and $Zn_5(OH)_8(CO_3)$ nanoparticles. According to the X-ray diffraction (XRD) patterns and X-ray absorption spectrum (XAS), it was exhibited that each nanohybrid contains LMH particles with nanoscopic crystal size. The infrared spectra showed characteristic absorption peaks attributed to the stretching modes of hydrogels and LMHs, exhibiting that the physicochemical properties of each substances (hydrogel and LMH nanoparticles) are not significantly affected by the electrophoretic synthesis. According to the scanning electron microscopy (SEM), it was also determined that the nanohybrid has homogeneous dispersion of LMH nanoparticles in biopolymer matrix. In order to investigate the potential of the prepared nanohybrid as drug delivery system, we incorporated polyphenol molecules by simply soaking in polyphenol solution and time-dependent release patterns of polyphenol in aqueous environment was evaluated. As a result, the homogeneous hybrids showed controlled drug release behaviors compared to the hydrogel matrix, suggesting its potential as biomaterials and drug delivery system.

8548-49, Session 11a

Preparation of Functional Surfaces by Forced Manual Assembly *(Keynote Presentation)*

Kyung Byung Yoon, Sogang Univ. (Korea, Republic of)

The existing methods to organize colloidal particles into one- (1D) and two-dimensional (2D) arrays on substrates commonly begin with the deposition or adsorption of particles from the solution to the substrates. We refer to this conventional method as 'wet self-assembly' since they depend on self-assembly in solution. In wet self-assembly, the adhered particles self-assemble into hexagonally ordered arrays with the help of solvents. However, the two key requirements for the adhered particles to undergo ordering, namely, self-assembly and solvents, have concomitantly served as the anchors that prevent further progress of the field because there are too many factors that sensitively affect the self-assembly process. Accordingly, the organization of colloidal particles into large (> cm), perfect 1D and 2D arrays based on wet self-assembly in solution has been extremely difficult. Therefore, novel methods that do not depend on self-assembly and solvents have to be developed. In relation to this, organization of dry micro silica beads into three-dimensional (3D) structures on patterned substrates was demonstrated using a microrobot. However, this method is far from being practical. Stemming from our recent finding that rubbing is a highly effective method for the organization of zeolite microparticles into monolayers on flat substrates,[1] we discovered that rubbing of dry spherical colloidal particles into the patterned nano-well arrays leads to a very fast organization of the spherical colloidal particles into large and perfect 1D and 2D arrays.[2] We refer to this method as 'dry manual assembly'

8548-50, Session 11a

Surface topography effect for plasmonic sensor development

Glen C. King, NASA Langley Research Ctr. (United States); Hyunjung Kim, Yeonjoon Park, National Institute of Aerospace (United States); Kyo D. Song, Norfolk State Univ. (United States); Sang H. Choi, NASA Langley Research Ctr. (United States)

The key interest of this study was to understand the physics of

plasmonic behavior within quantum-confined domains. Major efforts have been devoted to the design, fabrication, and patterning of metallic nanostructures with controllable sizes and shapes due to the size- and shape-dependent plasmon-derived optical properties such nanostructures possess. To experimentally observe the plasmonic behavior, a series of arrayed nanometer-sized aperture configurations was fabricated in thin silver films on a quartz substrate using a focused ion beam instrument and E-beam lithography system. Nano-scaled symmetrical features built around each aperture cause the plasmon to undergo a topography-dependent momentum change which is uniquely represented by artificially created electromagnetic dipole radiation. This study also examined exploitation of the surface plasmon polariton (SPP) phenomenon to permit phase modulation and controlled variation in intensity and spectral response of the transmitted light. The electromagnetic dipole radiation losses were determined from the changes in transmitted light between the apertures built on the plain surface and the surface with topographical features. Applying a varying electrical field to the array allows control of the transmitted light. Laser light of several wavelengths, both with and without an applied electrical field were analyzed with the near field scanning optical microscope and a spectrometer. The surface plasmon behavior in thin metal films enables possible biomedical applications such as optical biosensors that can detect target biomolecules near the film surface. SPP detection for the biomarker of Alzheimer's disease, and for chemical analysis of cerebrospinal fluid and in-situ organ health is proposed.

8548-53, Session 11a

The evaluation in vitro and in vivo of bone morphogenic protein-2 (BMP-2) immobilized PCL/PLGA scaffolds for enhanced osteoblast functions and bone formations

Young-Pil Yun, Sung Eun Kim, Hae-Ryong Song M.D., Korea Univ. College of Medicine (Korea, Republic of)

Autografts and allografts are usually used for the bone regeneration of bone defect/loss caused due to trauma, fracture, and tumor. However, these methods have limitations in their clinical application such as donor site morbidity, additional blood loss and inflammatory responses. We have developed another approach based on the principles of tissue engineering for repair and regeneration of bone loss/defect.

8548-100, Session 11b

Size control of ferrimagnetic iron oxide nanocubes to achieve optimum static dephasing regime r2 relaxivity for in vivo MRI

Youjin Lee, Nohyun Lee, Mihyun Park, Seung Hong Choi, Taeghwan Hyeon, Seoul National Univ. (Korea, Republic of)

Ferrimagnetic nanoparticles have been limited in in vivo application because the nanoparticles aggreagates due to its remanence magnetism. Uniform-sized ferromagnetic iron oxide nanocubes with similar value of bulk saturated magnetization were synthesized with several different core size, 22, 32, 42, 58 as previous reported method. Size control had minimized remanence of nanoparticles so that the remnant magnetization and coercivity of 22nm particles were ca.5 emu/g Fe and ca. 14 Oe, respectively. PEG-phospholipid encapsulation enabled spacing to prevent the aggregation. As a result, water-dispersed single core ferrimagnetic iron oxide nanocubes were successfully prepared and its r2 relaxivity was 761 $s^{-1}mM^{-1}$. It was very close to theoretical calculated value 800 $s^{-1}mM^{-1}$ in static dephasing regime. As size of nanoparticle increased, aggregation started and the relaxivity value decreased. For medical application, Cell viability was also checked and synthesized 22 nm nanoparticles showed biocompatibility up to 0.75mg Fe/ml. Also in vivo MR images were obtained after intravenous injection to a mouse. The MR signal of tumor site changed significantly. In this research, synthesized ferrimagnetic iron oxide nanocubes showed a superior T2 contrast effect and it would be able to improve the quality of early diagnosis and detection of tumor.

8548-224, Session 11b

Neurobiological linkage between stress and sleep *(Keynote Presentation)*

Larry D. Sanford, Eastern Virginia Medical School (United States)

Stress can have a significant negative impact on health and stress-induced alterations in sleep are implicated in both human sleep disorders and in psychiatric disorders in which sleep is affected. We have demonstrated that the amygdala, a region critical for regulating emotion, is a key modulator of sleep. Our current research is focused on understanding how the amygdala and stressful emotion affect sleep and on the role sleep plays in recovery from stress. We have developed animal models to examine how stressor controllability alters sleep and how stress-related memories following controllable and uncontrollable stress can produce significantly and directionally different alterations in sleep. Experiencing uncontrollable stress and reminders of uncontrollable stress can produce significant reductions in sleep, in particular rapid eye movement sleep. By comparison, experiencing controllable stress and reminders of controllable stress can produce increases in sleep. We are using these models to explore the neurobiology linking stress-related emotion and sleep and are utilizing standard and optogenetic methods to examine the processes by which stress comes to produce persisting effects on sleep. This research is relevant for sleep disorders such as insomnia and into mental disorders in which sleep is affected such as post-traumatic stress disorder (PTSD), which is typically characterized by a prominent sleep disturbance in the aftermath of exposure to a psychologically traumatic event.

8548-245, Session 11b

Nano-oncological translational research for personalized cancer treatment *(Invited Paper)*

No Abstract Available

8548-145, Session 12c

Magnetic resonance imaging using chemical exchange saturation transfer *(Keynote Presentation)*

Jaeseok Park, Korea Univ. (Korea, Republic of)

This talk is to provide basic physical principles of magnetic resonance imaging (MRI) and a relatively new molecular imaging mechanism called chemical exchange saturation transfer (CEST). In CEST, exogenous or endogenous compounds containing exchangeable protons or molecules are selectively saturated and then imaging sensitivity is indirectly reflected through the water signal in a similar way to conventional magnetization transfer. The focus of this work is on technical aspects of CEST magnetic resonance imaging with either exogenous or endogenous compounds using radio-frequency saturation, inversion, and gradient-dephasing, etc.

8548-146, Session 12c

A new medical x-ray imaging using monochromatic filter and grating interferometer *(Keynote Presentation)*

Kwon-Ha Yoon, Wonkwang Univ. School of Medicine (Korea, Republic of)

No Abstract Available