DAY 1

Scientific Tracks & Abstracts

EuroSciCon Conference on

Nanotech & Nanobiotechnology

July 12-13, 2018 Paris, France

DAY 1

July 12, 2018

Sessions

Nanobiotechnology | NanoMedicine | Nanopharmaceuticals | Nano-Chemistry | Nanodevices and Nanosensors | Advancement in Nanotechnology

Session Chair
Andreas Seifert
CIC nanoGUNE, Spain

Session Co-Chair
Jinrich Kopecek
University of Utah, USA

Session Introduction

Title: **Challenges and innovation in next generation nanoscience**
Jinrich Kopecek, University of Utah, USA

Title: **Structure and mechanism based design of nanoparticles as therapeutic candidates**
Chang-Guo Zhan, University of Kentucky, USA

Title: **Nanocarriers for nose-to-brain, non-invasive delivery of gene therapy**
Juan-Sanchez Ramos, University of South Florida, USA

Title: **Direct measurement of the local temperature increment for individual live cells**
Shengyong Xu, Peking University, China

Title: **Future of nanoscience in natural product drug discovery: applications in thymoquinone-based nanoformulations**
Hala Gali-Muhtasib, American University of Beirut, Lebanon

Title: **Advances and challenges in pharmaceutical nanotechnology**
Abraham J. Domb, The Hebrew University of Jerusalem, Israel

Title: **Antibacterial activity of gold nanorods against *Staphylococcus aureus* and *Propionibacterium acnes*: Misinterpretations and artifacts.**
Nouf Mahmoud, Al-Zaytoonah University of Jordan, Jordan

Title: **Snthesis of sub-10 nm ibuprofen drug molecular clusters via RESS processing**
Sudhir Sharma, New York University Abu Dhabi, UAE

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CHALLENGES AND INNOVATION IN NEXT GENERATION NANOSCIENCE

Jinrich Kopecek, Jiyuan Yang and Lian Li
University of Utah, USA

The address will be based on our strong belief that the future of science in general and smart biomaterials and nanomedicines in particular is in the interdisciplinary approach to hypotheses formulation and problem solving. Nanoscience moved from copying/mimicking nature's design to modify it and designing bioactive materials. Our understanding of the relationship between structure and properties reached levels needed for the design of totally new materials different from those in nature. The latter approach has the highest potential for scientific and application breakthroughs in the near future. The nanomedicine field needs new ideas, so it can continue to enhance basic scientific knowledge and translate the laboratory and animal model work into humans. One new concept is called drug-free macromolecular therapeutics (DFMT). The design of DFMT is based on molecular biorecognition, which is at the center of all biological processes. Several therapeutic systems were designed that do not contain a low molecular weight drug, but their therapeutic efficacy is based on a combination of a macromolecule with a biorecognition domain. Biological activity is a result of one or more biorecognition events. The majority of studied systems are based on the crosslinking of receptors at the cell surface of blood cancer cells. Other systems target E-selectin receptors in the vasculature or focus on the biomineralization around cancer cells mediated by receptor – ligand recognition.

Biography

Jindrich Kopecek received his PhD in Macromolecular Chemistry from the Institute of Macromolecular Chemistry (IMC) and DSc in Chemistry from the Czechoslovak Academy of Sciences (CAS), Prague, Czech Republic. He has done his Post-doctoral studies at the National Research Council of Canada. He served as Laboratory Head at IMC CAS and is currently, Distinguished Professor of Bioengineering and Distinguished Professor of Pharmaceutical Chemistry at the University of Utah. He serves on Editorial Boards of 14 international scientific journals. He is an elected member of the US National Academy of Engineering. His research interests are focused on biorecognition of macromolecules, bioconjugate chemistry, drug delivery systems, and self-assembled biomaterials. Hydrogels from his laboratory have been in clinical use and HPMA copolymer - anticancer drug conjugates in clinical trials. His Hirsch index is 87; his publications have been cited 26,900 times.

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STRUCTURE AND MECHANISM-BASED DESIGN OF NANOPARTICLES AS THERAPEUTIC CANDIDATES

Chang-Guo Zhan and Fang Zheng

University of Kentucky, USA

In this talk, I will first briefly discuss the general strategies and integrated computational-experimental approaches used to understand the detailed molecular mechanisms of increasingly complex biological systems (such as those related to cancers, HIV virus, neurodegenerative diseases, inflammation, cardiovascular diseases, and drug addiction) and perform mechanism-based design, discovery, and development of novel drugs including nanoparticles. I will also discuss the general trend of rational drug design and discovery through specific examples of our integrated efforts from understanding molecular mechanism to clinical development. The presentation will show how powerful understanding the detailed molecular mechanism and mechanism-based computational design are in the current drug design, discovery, and development. The integrated computational-experimental approaches are of great value not only for small-molecule drug discovery, but also for discovery and development of novel, therapeutically promising nanoparticles. Integrated computational-experimental drug design and discovery efforts have led to exciting discovery of promising drug candidates, including our designed novel drugs in Phase II clinical trials; one has received the Breakthrough Therapy Designation by the FDA.

Biography

Chang-Guo Zhan is an Endowed Professor of Pharmaceutical Sciences and Director of Molecular Modeling and Biopharmaceutical Center in the College of Pharmacy, University of Kentucky. He also serves as Director of Chemoinformatics and Drug Design Core of the Center for Pharmaceutical Research and Innovation at the University of Kentucky. His lab has successfully designed and discovered several promising therapeutic candidates, including two in Phase II clinical trials; one has received the Breakthrough Therapy Designation by the FDA. He is a winner of 2005 Emerging Computational Technology Prize, American Chemical Society (ACS) Division of Computers in Chemistry and is the current recipient of the NIDA Translational Avant-Garde Award from the NIH. He was elected AAPS Fellow in 2010 and won 2016 AAPS Research Achievement Award in Drug Discovery and Development Interface. He is also a UK Chapter Inductee of the National Academy of Inventors (NAI).

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NANOCARRIERS FOR NOSE-TO-BRAIN, NON-INVASIVE DELIVERY OF GENE THERAPY

Juan Sanchez-Ramos[1], Shijie Song[1], Xiaoyuan Kong[1], Gary Martinez[2], Shyam Mohapatra[3], Subra Mohapatra[4], Reka A Haraszti[5], Anastasia Khvorova[5], Neil Aronin[5], Vasyl Sava[1]

[1]University of South Florida, USA
[2]Moffitt Cancer Center and Research Institute, USA
[3]Nanomedicine Research Center, USA
[4]Department of Molecular Medicine, USA
[5]RNA Therapeutics Institute-UMASS, USA

The intranasal route of drug delivery has traditionally been used to administer small, lipophilic drugs that are rapidly absorbed into capillaries of the nasal epithelium, resulting in rapid onset of CNS actions. Many neuro-therapeutic agents, especially polynucleotides and proteins, do not readily cross the blood-brain barrier and cannot survive intact in the gut or blood. Hence, gene therapy for brain disorders has required direct neurosurgical microinjection or infusion into brain or cerebrospinal fluid. However, recent research has demonstrated direct nose-to-brain delivery of relatively large molecules, including neurotrophins (NGF and insulin-like growth factor [IGF]-1), neuropeptides, cytokines (interferon β-1b and erythropoietin as well as polynucleotides (DNA plasmids and genes). The present report describes development of a novel manganese-chelate nanocarrier system for direct nose-to-brain delivery of small interfering RNA (siRNA) or DNA. The manganese (Mn) chelate Mangafodopir served 2 functions: 1) as a marker of the NPs for intracerebral tracking with magnetic resonance imaging (MRI) and 2) as a cross-linker of the chitosan matrix in the nanocarrier structure. Using high field small animal MRI, the Mn-tagged NPs were visualized on T1-weighted images and were found to penetrate from nasal epitheliaum into olfactory bulb and across brain regions following intranasal instillation of the nanocarriers. In addition, Mn content of the nanocarrier did not impede the functional activity of siRNA directed against green fluorescent protein eGFP in transgenic green mice. Expression of eGFP mRNA in transgenic green mice was decreased by at least 50% in four brain regions. Those brain regions also exhibited significantly increased Mn signal in T1-weighted MR images. In separate experiments, we showed that mNPs loaded with dsDNA encoding the red fluorescent protein (RFP) was expressed in corpus striatum and other regions following intranasal administration. Hence, this novel nanocarrier system permitted *in vivo* tracking of the therapeutic agent and was effective in delivering nucleic acid payloads that exhibited the expected activity in brain tissue.

Biography

Juan Sanchez-Ramos received a PhD in Pharmacology and Physiology from the University of Chicago and a Medical Degree (MD) from the University of Illinois. He trained in Neurology at the University of Chicago and as a Fellow in Movement Disorders at the University of Miami. Currently, he is a Professor of Neurology at the University of South Florida in Tampa where he holds the Helen Ellis Endowed Chair for Parkinson's disease Research and is Director of the HDSA Center of Excellence for Huntington's disease. He is also Medical Director of the non-profit Parkinson Research Foundation based in Sarasota FL. In addition to teaching and attending to patients with Movement Disorders, he has directed basic research projects in neurodegeneration, neurotoxicology, adult stem cell biology and presently is focused on novel approaches for non-invasive delivery of gene therapy to brain.

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DIRECT MEASUREMENT OF THE LOCAL TEMPERATURE INCREMENT FOR INDIVIDUAL LIVE CELLS

Shengyong Xu
Peking University, China

Optical nano-thermometers have been well developed to measure the temperature distribution in live cells. Nano-sized indicators such as proteins, organic dyes, quantum dots, polymer particles and nano-diamond, are injected into live cells, and the change in intensity, peak position or lifetime of luminescence spectra for the nano-indicators are used to reveal the change of local temperatures. However, the results are remarkably affected by local environment, e.g., pH value, cellular viscosity and ion concentration in the cytosol, thus causing controversial arguments. Here, we report direct measurement results for the temperatures of individual cultured cancer cells. By using double-stabilized measurement system and array of micro-scale thin-film thermocouples, we have reduced the system thermal noise down to ±5 mK and observed local increments in temperature for individual live cells in the range of 30-280 mK. With further improvements, e.g., by using arrays nano-scaled thermocouples, the current method is promising for real-time 2D mapping for the local temperatures of a single cell.

Biography

Shengyong Xu received his BSc in Physics from the Peking University in 1988 and PhD from Department of Physics, National University of Singapore in 1999. He is currently a professor with Department of Electronics, School of Electronics Engineering and Computer Sciences, Peking University. He has published more than 200 journal and conference papers. His group currently works on the physics of electrical communication among neuron cells and normal cells, temperature sensing at the cell and sub-cell levels, as well as electrostatic tweezers at micro-nano-scales.

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FUTURE OF NANOSCIENCE IN NATURAL PRODUCT DRUG DISCOVERY: APPLICATIONS IN THYMOQUINONE-BASED NANOFORMULATIONS

Hala Gali-Muhtasib, Zeina Habli and Farah Ballout

American University of Beirut, Lebanon

Despite current advances in cancer therapy, cancer continues to be the second leading cause of mortality worldwide. The increasing cancer death rate and the rapid emergence of chemotherapy resistance necessitate the need to adopt new approaches for the discovery of novel anticancer agents. Therefore, a growing interest is heading towards 'safe' and widely available molecules, prominently from natural plant sources that have anticancer activities against human cancer cells with minimal toxicity to normal ones. Nanotechnology has played a role in overcoming the challenges of anticancer drug delivery, namely poor solubility and stability, undesirable cytotoxicity, rapid drug metabolism and non-specific drug targeting. This paper focuses on the future potential of clinical translation of plant-derived compounds with focus on the black seed active ingredient Thymoquinone (TQ), a promising anticancer molecule shown to inhibit cancer growth and progression in numerous systems both *in vitro* and *in vivo*. What makes TQ interesting is its efficacy and selectivity against cancer cells and lack of toxicity to normal tissues. In spite of the promising anticancer activities of TQ, the main limitation for its clinical translation lies in its hydrophobicity, poor bioavailability, limited solubility and high capacity to bind to plasma proteins. This can prevent TQ from reaching its targeted tumor sites. Several TQ-nanoparticle (TQ-NP) formulations have been tested and found to have enhanced anticancer and anti-inflammatory effects in comparison to free TQ. Our recent work presented evidence on a novel TQ formulation having improved activity and enhanced delivery in breast cancer. We showed that the efficacy of the TQ-NP formulations depends on the time for drug uptake, drug concentrations, route of entry and trafficking and cellular interactions. I will provide an overview of the various TQ-NP formulations, their characteristics and applications summarize limitations for developing biologically successful TQ-NP models and discuss up-to-date solutions to improve TQ bioavailability and anticancer potential for cancer therapy.

Biography

Hala Muhtasib is Professor of Cell Biology at the American University of Beirut. She received her PhD from Kansas State University, USA in 1990. Her research interests are in Cancer Chemotherapy and Anticancer mechanisms of plant-derived compounds. She has over 90 publications in peer-reviewed journals and is the recipient of four research achievement awards.

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ADVANCES AND CHALLENGES IN PHARMACEUTICAL NANOTECHNOLOGY

Abraham J Domb

The Hebrew University of Jerusalem, Israel

Pharmaceutical formulations are a key for the effectiveness of therapeutic agents. Nanotechnology provides a new direction to improve the solubility, stability and bioavailability of various active agents. Incorporation of bioactive molecules into nano-constructs improves their ability to safely cross biological membranes such as the GI tract, BBB, and skin. Nanoparticles made of lipid components, natural or synthetic polymers, carbon, metals and inorganic materials, have been used as drug carriers. Recently, exosomes have been used as natural carriers to direct drug loads to certain body sites. Nucleotide and protein based biological drugs require suitable nano-delivery systems that protect them from deterioration and direct them into specific cells and organs. In addition to the delivery of drugs, nanoparticles have been used as diagnostic agents and as carriers of combined diagnostic and therapeutic agents. The various nano-delivery systems should be tailored to fit the route of administration. The various nano-constructs that have been used for the delivery of active agents and diagnostics by different routes of administration will be discussed.

Biography

Abraham J Domb, is a Professor for Medicinal Chemistry and Biopolymers at the Faculty of Medicine of the Hebrew University, Jerusalem. He earned Bachelor's degrees in Chemistry, Pharmaceutics and Law from Bar-Ilan and Hebrew University and PhD degree in Chemistry from Hebrew University. He did his Postdoctoral training at MIT/Harvard and was R&D Manager at Nova Pharm. Co. Baltimore US from 1988-1992. Since 1992, he is a Faculty member at the Hebrew University with interests on Biopolymer synthesis and applications, Biodegradable polymers, Drug delivery systems, Medicinal Chemistry and Forensic sciences. During 2007-2012, he served as Head of the Division of Identification and Forensic Sciences (DIFS), Israel Police. Since April 2014, he is also President of the Jerusalem College of Engineering.

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ANTIBACTERIAL ACTIVITY OF GOLD NANORODS AGAINST *STAPHYLOCOCCUS AUREUS* AND *PROPIONIBACTERIUM ACNES*: MISINTERPRETATIONS AND ARTIFACTS

Nouf N Mahmoud, Alaaldin M Alkilany, Enam A Khalil and Amal G Al-Bakri

The University of Jordan, Jordan

The antibacterial activity of gold nanorod (GNR) suspensions of different surface functionalities was investigated against standard strains of *Staphylococcus aureus* and *Propionibacterium acnes*, taking into consideration two commonly overlooked factors: the colloidal stability of GNR suspensions upon mixing with bacterial growth media and the possible contribution of impurities/molecules in GNR suspensions to the observed antibacterial activity. The results demonstrated that cationic polyallylamine hydrochloride (PAH)-GNR were severely aggregated when exposed to bacterial growth media compared to other GNR suspensions. In addition, the free cetyltrimethylammonium bromide (CTAB) present in GNR suspensions is most likely the origin of the observed antibacterial activity. However, the antibacterial activity of GNR themselves could not be excluded. Probing these two critical control studies prevents misinterpretations and artifacts of the antibacterial activity of nanoparticles. Unfortunately, these practices are usually ignored in the published studies and may explain the significant conflicting results. In addition, this study indicates that GNR could be a promising candidate for the treatment of skin follicular diseases such as acne vulgaris.

Biography

Nouf Nawaf Mahmoud completed her Bsc in Pharmacy (the University of Jordan), MSc in Clinical Pharmacy (the University of Jordan) and a PhD in Pharmaceutical Technology (the University of Jordan) before joining the academic staff at Al-Zaytoonah University of Jordan. She is an Assistant Professor of Pharmaceutics at the faculty of Pharmacy and a member of Quality Assurance committee at the faculty. Her research focuses on the Nanotechnology and its biomedical applications, understanding the nano-bio interface and in particular the gold nanoparticles-skin interactions and developing advanced trasdermal delivery nano systems.

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SYNTHESIS OF SUB-10 NM IBUPROFEN DRUG MOLECULAR CLUSTERS VIA RESS PROCESSING

Sudhir Kumar Sharma and Ramesh Jagannathan
New York University Abu Dhabi, UAE

One of the major unsolved problems in pharmaceutical drug development is the poor water solubility of many active pharmaceutical ingredients (APIs) and hence reduced bioavailability. One of the preferred strategies to address this problem was to leverage the increased solubility with decreasing drug particle size. However, an ideal solution would be to eliminate the problem of solubility entirely, by reducing the API size to clusters of a few molecules, bound by weak, Vander Waal's forces that would readily dissociate into molecules, during enteral or parenteral drug delivery process. In order to have commercial impact, such molecular clusters should also be produced in sufficiently high yield. In our research, we have successfully addressed both these challenges. We report the precipitation of molecular clusters of ibuprofen using a rapid expansion of super critical solution (RESS) system. Our custom designed liquid N_2 cooled collection process of the molecular clusters embedded in dry ice, resulted in yields of up to 80% (w/w). Ambient dissolution of the dry ice in deionized water resulted in a stable dispersion, for up to six months, as confirmed by DLS and AFM characterizations. DLS measurements showed that PEI surfactant (M_w ~400,000) produced the smallest particle size of 7 nm, with a narrow size distribution of ±3 nm. Drop casting of these dispersions on silicon and sapphire substrates resulted in high quality, liquid like viscous films as observed by optical microscopy and AFM. XRD and confocal Raman characterizations confirmed that the molecular clusters retained their chemical identity of ibuprofen. Besides its scientific importance, this invention is expected to open up new drug delivery platforms.

Biography

Sudhir Kumar Sharma obtained his Masters' degree (MSc Physics and M. Tech-Materials) from Department of Physics, Barkatullah University Bhopal, India. He received his PhD from the Indian Institute of Science Bangalore, India. He joined as Postdoc fellow at Centre for Nano Science and Engineering (CeNSE), IISc. Bangalore, India. Later he moved to New York University Abu Dhabi UAE (NYU Abu Dhabi) as a Research Associate in 2013. Currently, he is working as a Research Scientist at NYU Abu Dhabi. His publication record includes more than 30 journals and 60 conference presentations. His research interest includes implementation of supercritical technologies for nanoparticle synthesis, smart materials for micro-sensors and actuators, micro/nano- fabrications, vacuum science, and thin film technology.

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DAY 2

Scientific Tracks & Abstracts

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DAY 2

July 13, 2018

Sessions

NanoMaterials | NanoRobotics |NanoElectronics | Cellular and subcellular Nanotechnology | Major Challenges in Nanobiotechnology

Session Chair	Session Co-Chair
Chantal Pichon University of Orleans, France	Stephen D. Miller Northwestern University, USA

Session Introduction

Title: **After the niche, preparing your R&D and nanotech business for the future!**

Aaron Claeys, Nanex Company, Belgium

Title: **Synthesis of thiolated, PEGylated and POZylated silica nanoparticles and evaluation of their retention on rat intestinal mucosa *in vitro***

Twana M. Ways, University of Reading, UK

Title: **Biophysical studies on the interaction of polymeric nanoparticles with the lung surfactant**

Weiam Daear, University of Calgary, Canada

Title: **Design and manufacturing of nanobiosensors suitable for protein detection**

Seyed Mohammad Mahdi Dadfar, Karlsruhe Institute of Technology, Germany

DAY 2

Special Session

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AFTER THE NICHE, PREPARING YOUR R&D AND NANOTECH BUSINESS FOR THE FUTURE!

Aaron Claeys

Nanex Company, Belgium

My talk will not be about my technical knowledge in my field of research; it will be about my experience and insights as a researcher and entrepreneur about the nanotech industry. As of my opinion sharing most important insights when running a nanotech business / R&D unit, my presentation includes short introduction, safety measurements when working with Nano particles and suppliers, working true the value chain, what's your net value or impact? Your personal and company mission, how to overcome difficult times when innovating, things to be considered to form your long-term strategy and community-based value creation, connecting minds to face current challenges.

Biography

Aaron Claeys is a young Entrepreneur and Owner of Nanex Company. He is a CEO and Nanotech Researcher running his own R&D unit with expertise in multifunctional Nano coatings to make materials smart, durable and more sustainable. He is also specialising in water and air purification true nanotechnology to face current challenges worldwide.

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DAY 2

Young Research Forum

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SYNTHESIS OF THIOLATED, PEGYLATED AND POZYLATED SILICA NANOPARTICLES AND EVALUATION OF THEIR RETENTION ON RAT INTESTINAL MUCOSA *IN VITRO*

Twana Mohammed M Ways[1], Wing Man Lau[2] and Vitaliy V Khutoryanskiy[1]

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Mucosal drug delivery is a technique for administration of drugs through mucous membranes lining the gastrointestinal tract, respiratory tract, urogenital tract and ocular surface. It has several advantages including increased residence time at the site of absorption/action, decreased administration frequency and thus better patient compliance. However, with conventional mucosal drug delivery these could only be achieved to a certain degree. Thus, in this study, two strategies have been used to improve the efficiency of mucosal drug delivery through the preparation of mucoadhesive and mucus-penetrating nanoparticles. Thiolated silica nanoparticles have been synthesised using 3-mercaptopropyltrimethoxysilane and functionalised with either polyethylene glycol (PEG) or poly (2-ethyl-2-oxazoline) (POZ). The sizes of thiolated, PEGylated and POZylated silica nanoparticles were 53±1, 68±1 and 59±1 nm, respectively. The particle size of both thiolated and POZylated nanoparticles significantly increased at pH≤2, whereas no particle size change was observed at pH 2.5-9 for both these two types of nanoparticles. On the other hand, the size of PEGylated nanoparticles did not change over the studied pH range (1.5-9). Thiolated nanoparticles were more mucoadhesive in the rat small intestine than both PEGylated and POZylated nanoparticles. This may indirectly indicate the mucus-penetrative properties of both PEGylated and POZylated nanoparticles. Each of these nanoparticles has potential applications in mucosal drug delivery.

Biography

Twana Mohammed M Ways has completed his MSc from University of Sulaimani. He is a PhD student at University of Reading, UK. He has published 1 review paper.

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BIOPHYSICAL STUDIES ON THE INTERACTION OF POLYMERIC NANOPARTICLES WITH THE LUNG SURFACTANT

W Daear and E J Prenner
University of Calgary, Canada

The pulmonary route offers many advantages for drug delivery such as the high surface area and the close proximity to the blood circulation. The air-blood barrier of the alveoli in the lungs is around 500 nm thick. Above the epithelium cells of the alveoli lies a thin aqueous layer with a thickness of 50-80 nm. A monolayer of phospholipids, natural lipids and few proteins called the lung surfactant (LS) adsorbs onto this aqueous film. The major phospholipid classes include phosphatidylcholines and phosphatidylglycerols. One of the main roles of the LS is to reduce the surface tension experienced in the lungs during breathing cycles in order to prevent lung collapse. From the perspective of pulmonary drug delivery, the LS is the first point of interaction for the drug carriers. With the advancements of nanomedicine, nanoparticles (NPs) became highly relevant as novel drug delivery systems. In particular, there is a great scientific interest for the use of biodegradable NPs for the pulmonary delivery route. The objective of our work is to develop a biomimetic model of the LS and study the effects upon interaction with NPs. Therefore, we focus on understanding the mechanism of interaction between biodegradable polymeric NPs with the biomimetic model of the LS and test whether the stability and lateral architecture of LS is affected. These measurements are done by using Langmuir monolayers at the air-water interface and imaged using Brewster angle microscopy. Results show that the film stability upon compression is not affected, but there are significant changes in the lateral domain organization of the LS upon NP addition. This work is significant because it helps understand the mechanism of NP-LS interaction and will provide an *in-vitro* screening approach to assess nanotoxicology.

Biography

W Daear is a PhD Candidate at the University of Calgary. She has a Bachelor's degree in Biological Sciences with a minor in Nanoscience. She currently has 3 publications in peer reviewed articles (*J. Phys. Chem. B., Colloids Surf. B, and Biochim. Biophys. Acta, Biomember*).

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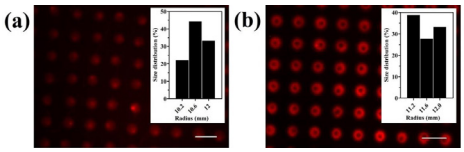
DESIGN AND MANUFACTURING OF NANOBIOSENSORS SUITABLE FOR PROTEIN DETECTION

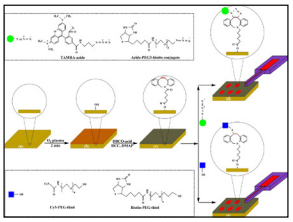
Seyed Mohammad Mahdi Dadfar, Sylwia Sekula-Neuner, Uwe Bog, Vanessa Trouillet and Michael Hirtz

Karlsruhe Institute of Technology (KIT), Germany

Different types of click chemistry reactions have been proposed and used for the functionalization of surfaces and materials, and covalent attachment of organic molecules. In the present work, we present and compare two different catalyst-free click approaches, namely azide-alkyne and thiol-alkyne click chemistry, for the generation of nanobiosensors suitable for protein detection. For this purpose, we first functionalized the surface of glass with dibenzocyclooctyne-acid (DBCO-acid), a cyclooctyne with a carboxyl group. Then, the DBCO-terminated surfaces were functionalized with different fluorescent and nonfluorescent azide and thiol inks via microchannel cantilevers spotting (µCP) (*Figure 1*). Click reactions were performed at different temperatures and times and the optimum conditions of 37 °C/20 min and 37°C/40 min was found for azide-alkyne and thiol-alkyne reactions, respectively. Although, due to no need for catalysts or additional additives, mild reaction conditions, and high reaction rate, both routes worked reliable for surface functionalization, the protein binding experiments revealed that using a thiol-alkyne route will obtain the highest surface density of molecular immobilization in such spotting approaches. The obtained achievements and results from the protein binding experiments with streptavidin proved the potential for application of these microarrays in manufacturing nanobiosensors for protein detection and other biomedical/biological applications (*Figure 2*).



Comparison between azide-alkyne and thiol-alkyne click reactions: (a) bare glass; (b) hydroxylterminated glass; (c) DBCO-terminated glass; (d) treatment of the DBCO terminated surface with TAMRAazide and azide-PEG3-biotin; (e) treatment of the DBCO-terminated surface with Cy5-PEG-thiol and biotinPEG-thiol



Fluorescence microscope images of microarrays of (a) azide-PEG3-biotin conjugate immobilized on the DBCO-terminated glass after incubating with streptavidin-Cy3, click reaction time = 20 min, click reaction temperature = 37 ˚C; (b) biotin-PEG-thiol immobilized on the DBCO-terminated glass after incubating with streptavidin-Cy3, click reaction time = 40 min, click reaction temperature = 37 ˚C. The insets show the size distribution of the spots. Scale bars equal 50 µm

Biography

Seyed Mohammad Mahdi Dadfar has completed his Bachelor and Master of Science at Tehran University and Shiraz University, respectively, both top-tier universities in Iran. He is pursuing his PhD at Karlsruhe Institute of Technology (KIT), Institute of Nanotechnology (INT) under supervision of PD Dr. Michael Hirtz and Prof. Dr. Annie Powell. His PhD project is about functionalized diamond optomechanical circuits for infrared spectroscopy and site-specific gas sensing applications. He is a Member of Iran's National Elites Foundation (The highest prestige and professional nation foundation for supporting elites). Mahdi Dadfar has published more than 10 papers in reputed journals, holds two national patents and recently has submitted another paper during his PhD.

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