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Scientific Tracks & Abstracts
November 06, 2017

Nanomedicine 2017




Global Meet on

Nanomedicine & Healthcare

November 06-07, 2017 | New Orleans, USA

Human mast cell response to nanosurfaces: Balancing innate and adaptive immunity

Marianna Kulka
National Institute for Nanotechnology, Canada

Located at mucosal surfaces and surrounding blood vessels and nerves, human mast cells are uniquely situated to regulate the function of the vasculature, to initiate the recruitment and activation of leukocytes into tissues and to trigger physiological responses that are mediated by the nervous system. Mast cells are primarily responsible for the acute allergic response to allergen exposure, including bronchoconstriction and edema. Mast cells and immunoglobulin E (IgE) are also felt to be important in the evolution of allergic late phase responses, which are largely responsible for the pathogenesis of chronic allergic diseases such as asthma, atopic dermatitis and rhinitis. Our recent research has shown that human mast cells respond to a vast array of proteins, each of which activates a unique signaling pathway through specific surface receptors. Our laboratory is interested in modulating human mast cell function using proteins, lipid nanoparticles and silver oxysalt nanofibers with the goal of producing hypoallergenic nanosurfaces. In one of our projects, we have focused on complement and specific complement protein receptors. The anaphylatoxin C5a regulates diverse innate and adaptive immune responses by chemoattracting and activating immune cells, such as mast cells (MC). It is postulated that C5a regulates human MC function by activating a G protein-coupled receptor (GPCR) However, C5a can bind to C5aR, a G protein-coupled receptor, or C5L2, not coupled to G proteins and thought to activate distinct signaling cascades. The presence and role of C5L2 in human MC remain unknown. Using a human mast cell model that expresses C5L2 but not C5aR, we have shown that C5L2 is a functional receptor, capable of modulating specific mast cell responses. C5a activates LAD2 cytokine and chemokine production and initiates adhesion and migration by human mast cells. Our research suggests that functionalizing surfaces with specific proteins may be an effective way of modulating human mast cell responses and regulating allergic inflammation.

Speaker Biography

Marianna Kulka is currently a Group Leader and Project Leader at the National Institute for Nanotechnology located at the University of Alberta, Edmonton, Canada. She is also an Adjunct Professor in the Department of Medical Microbiology and Immunology at the University of Alberta. Currently, she is investigating the role of G protein-coupled receptors in inflammatory disease and mast cell activation pathways. Her focus is on activation pathways of human mast cells and their regulation of human inflammatory diseases. Her work aims to use novel nano-packaging strategies to manipulate these pathways. She has published numerous articles in peer-reviewed journals and serves on several review panels, including national and international granting agencies.

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Polymeric micellar paclitaxel: Approval challenges and lessons learned

Kouros Motamed
NantBioscience, Inc., USA

Cynviloq™ (Genexol-PM®), a non-biologic micellar formulation of paclitaxel, utilizes biodegradable di-block copolymers composed of methoxy poly (ethylene glycol)-poly (lactide) to form micellar nanoparticles with paclitaxel containing a hydrophobic core and a hydrophilic shell and is being developed as the next generation nanoparticle paclitaxel. Its target indications are solid tumors such as metastatic breast cancer, lung, ovarian, bladder, pancreatic and melanoma. Herein, we discuss challenges faced and lessons learned from a PK bioequivalence trial of Cynviloq vs. the FDA approved nanoparticle albumin-bound (nab)-paclitaxel (Abraxane®).

Speaker Biography

Kouros Motamed has been the Director of Drug Development at NantBioScience, Inc. since April 2016. Prior to that, he has served as VP of Strategic Alliances and Clinical Communications and VP of Clinical Development and Nanomedicine at Sorrento Therapeutics from 2013 to 2016. He has also served as a Co-Founder and CSO/CTO of Igdrasol, Inc. and Biomiga Diagnostics start-up companies from 2011-2013. Prior to that, he has served as the MOA and Molecular Biology Group Head at Celgene Corp. and Abraxis BioScience Inc. from 2007-2011. He has held an Assistant Professorship position in the Department of Pathology and Vascular Biology Center at Georgia Health Sciences University from 2002-2007. He has over 30 original publications in peer-reviewed journals, over 50 conference presentations and has 5 issued patents. He has served on the Editorial Board of *Journal of Nanomaterials and Molecular Nanotechnology* since 2013. He has received his BS degree in Biology from University of San Francisco and a PhD degree from the University of California, Davis in Microbiology.

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Nanofluorophore assisted fluorescence image-guided cancer surgery

Jian Xu
Louisiana State University, USA

Surgical resection is still the major treatment for solid tumors. The complete surgical resection of the cancer tissues in the surgery is essential to the prognosis of cancer patients. However, 40% of the US patients have the local recurrence in 5 years from the initial surgery, due to the failure to detect all the cancer tissues intraoperatively. In the surgery, in case of uncertainty, the surgeon may take biopsies and send for the frozen section procedure. This pathological procedure is expensive and inefficient: it may take 20-30 min, while keeping the patient under anesthesia; due to the non-optimal preparation of the tissues, the diagnosis accuracy is lower than "formalin fixed paraffin embedded tissue procedure". The latter procedure takes even longer time (several hours to days after the surgery) to obtain the diagnosis result. Our lab developed an imaging system, together with ICG-protein complex as nano-imaging contrast agent, to help the intraoperative diagnosis of tissues. We have conducted dozens of clinical trials on human pancreatic cancer in major hospitals in USA. Over two hundred sample tissues from various pancreatic cancer surgeries, including distal pancreatectomy, whipple procedure, and total pancreatectomy, were inspected with our imaging system. Within one sec, our device can quantitatively differentiate cancerous tissues from non-cancerous tissues intraoperatively: Primary tumor and positive margins showed more than 200% stronger ICG fluorescence than normal tissues and negative margins did. The overall diagnosis accuracy of cancer by our system is 94.9%.

Speaker Biography

Jian Xu is currently an Assistant Professor in the Division of Electrical and Computer Engineering at Louisiana State University, USA. He has received his PhD degree in Engineering from the Yale University, USA. His work has been published on well-recognized journals (e.g. *Nature Nanotechnology* (IF: 38.986), *Advanced Materials* (IF: 19.791), and *Soft Matter*) and widely reported by international media (e.g. Süddeutsche Zeitung-the largest newspaper in Germany, the Economist, and Science Daily). He is a reviewer of IEEE transactions on biomedical engineering, IEEE international symposium on circuits and systems, Full Member of Sigma Xi, and so on. His research interests include biomedical instrumentation for image-guided surgery and biomimetic energy harvesting scheme with bio-nano electronics. His medical devices have been put into clinical trials in several major hospitals in US.

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Biomarkers evaluation in clinical trials: Important factors for success

Miriam Moscovitch-Lopatin
Massachusetts General Hospital, USA

Biomarkers translational research in clinical trials that lead to potential diagnostic and/or prognostic applications require the implementation of certain key factors that will be discussed and illustrated with concrete examples.

Speaker Biography

Miriam Moscovitch-Lopatin, PhD, PMP: NCRI Biorepository Lab Supervisor, Neurology at Massachusetts General Hospital Assistant; Instructor in Neuroscience at Harvard Medical School. Dr. Moscovitch-Lopatin was the Program Manager for the Huntington's Disease (HD) Biomarkers Program and directed proteomic biomarkers translational research, validation, and GLP deployment in clinical studies, as well as major aspects of the MGH' HD biorepository. Her major focus has been measuring different species of mutant and normal Htt proteins in tissues and biofluids from preclinical and multicenter clinical trials. She has demonstrated the feasibility of using huntingtin (including the novel detection of oligomeric mutant huntingtin -mtHtt) as a pharmacodynamic marker and showed that CSF and plasma levels of several mtHtt species are highly correlated with each other and with some clinical outcomes. She recently co-developed with scientists at Quanterix the first ultra-sensitive Simoa assay for quantifying low levels of BDNF in CSF samples from HD patients for use in BDNF stem cell repletion therapy. Prior to her current position, Dr. Lopatin directed the development of qualification and release of personalized vaccines against Follicular Non-Hodgkin's Lymphoma at Biovest/BioVax and conducted pre-clinical research in transplantation immunology as an Instructor in Medicine at Harvard Medical School/ BIDMC. Dr. Moscovitch-Lopatin holds a Ph.D. in Immunology from the Weizmann Institute, Rehovot, and a BSc and MSc in Life Sciences and Microbiology/Immunology from the Hebrew University, Jerusalem, Israel and she has a Project Management Profesional (PMP) certification..

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Scientific Tracks & Abstracts
November 07, 2017

Nanomedicine 2017




Global Meet on

Nanomedicine & Healthcare

November 06-07, 2017 | New Orleans, USA

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Global Meet on

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Highly efficient gene carriers based on carbon nanotubes: A new method for friedel-crafts acylation of single-walled carbon nanotube using trinuclear oxo-centered iron complex

Azadeh H Nia
Mashhad University of Medical Sciences, Iran

Carbon nanotubes (CNTs) have been extensively explored due to their unique physical, optical and chemical properties. Their biocompatibility and ability to penetrate cell membrane have extended their application to biomedical research. Chemical functionalization is the main method to overcome the low solubility of CNTs. Friedel-crafts acylation, non-destructive method preserving the superior properties of CNTs, is the least studied method compared to other chemical functionalization approaches. We previously reported a method for friedel-crafts acylation of multi-walled carbon nanotube (MWNT). In this study, we report a novel method using trinuclear oxo-centered iron complex for acylation of single-walled carbon nanotube (SWNT) using different alkyl carboxylic acids with different alkyl chain length (C_6, C_{10} and C_{16}). Functionalized SWNTs (F_6, F_{10} and F_{16}) were then conjugated with polyethylenimine (PEI) with different molecular weights (MW: 1800, 10000 and 25000 kDa). In this project, different nanocarriers were synthesized all capable of effective condensation of plasmid DNA. All nanocarriers were characterized by TGA, TEM, zetasizer, IR spectra. Cytotoxicity of all vectors were evaluated by MTT assay. All synthesized nanocarriers were tested for their transfection efficacy after condensing plasmid encoding enhanced green fluorescent protein (EGFP). The effect of length of alkyl chain and molecular weight of PEI on transfection efficiency of final conjugates were studied. Results of luciferase assay and fluorescence live cell imaging confirmed the high levels of EGFP gene expression.

Speaker Biography

Azadeh H Nia has completed her PhD in the field of Organic Chemistry at Ferdowsi University and Postdoctoral studies in nanomedicine at Mashhad University of Medical Sciences. Her area of research covers biomedical application of nanomaterials in health sciences. She has recently joined World Academy of Medical Sciences (WAMS) as a Faculty Member and Editor In-Chief of *WAMS journal.* She has served for more than 10 years in academic research positions, she has published more than 12 papers in reputed journals and has been serving as an Editorial Board Member of different journals in the nanotechnology field.

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Fabrication and evaluation of nanofibrous biomaterials for biomedical applications

Lina Fu
University of Nebraska Medical Center, USA

Bacterial nanocellulose (BC), a natural three-dimensional nano-biomaterial fabricated via microbial fermentation with a primary fiber diameter of ~14nm, distinguishes itself from cellulose derived from other sources mainly by its purity, crystallinity, mechanical strength, three dimensionalities, high water holding capacity, and good biocompatibility. BC has found many biomedical applications such as bioscaffolds in the repair and regeneration of skin, blood vessel, cornea, heart valve prosthesis, urethra, nerve, bone, cartilage and knee menisci, as well as for the delivery of drugs, hormones and proteins. A combined method to control the thickness of the BC film was a part of my research. BC was biosynthesized by gluconacetobacter xylinus (ATCC53582) and modified by chitosan. The nano-composites of BC and chitosan form a cohesive gel structure, and the cell toxicity of the composite is excellent. A novel strain could reduce the cost of BC production and accelerate the manufacturing process of wound dressings and antimicrobial wound healing products from this novel strain. With different oxygen availability and different biofabrication parameters, microbes can produce BC in forms of hydrogel and that can be processed to different forms as film, tube, sphere and nanocrystal. Incorporation of reactive functional groups and nanosilver particles into the polymer backbone via heterogeneous surface reactions can be used as delivery platforms from biosynthesized nanofibers using microbes to synthesize nanofibers using electrospinning. My focuses aim to heal damaged skin tissues and can also applied in other fields in tissue engineering and nanomedicine.

Speaker Biography

Lina Fu received her Ph.D. degree in Microbiology from Department of Biomedical Engineering, Huazhong University of Science and Technology, China. Upon the completion of MITACS Accelerate Internships and Postdoctoral Fellow in Western University and Axcelon Biopolymer Corporation, Canada, she started doing the postdoctoral research in Mary & Dick Holland Regenerative Medicine Program, University of Nebraska Medical Center, USA. Her work resulted in 5 peer-reviewed publications, 2 book chapters and 1 issued innovation patent and has been cited over 300 times since 2012. She was awarded the MITACS Accelerate Awards from 2014 to 2016. She serves as the reviewers for Advanced Functional Materials, Journal of Materials Chemistry A, Nanoscale, Chemical Communications, Acta Biomaterialia, Biofabrication, Oncotarget and Carbohydrate Polymers. She is also a member of professional scientific organizations including BMES, CBS, ACS and RSC. Fu has had more than ten years' experience in biomaterials and polymers, in terms of hydrogel, electrospun fibers, film, sponge, 3D printed materials, elastomer, microspheres and nanoparticles, etc. Her research is focused on engineering bacterial nanocellulose based materials and the use of a combination of cells/tissues, as well as suitable biochemical and physical cues to restore, maintain, or improve biological functions of damaged/diseased tissues or organs.

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NanoBindi: A clinical-outcome focused, patient-centric precision therapeutic development platform

Arkesh Mehta
OncoBindi Therapeutics, USA

A technology-driven clinical outcome focused, patient-centric precision therapeutic development platform is operationally efficient and enables rapid, parallel development of multiple products in the portfolio without additional cost burden. Functional fabric encapsulated drugs (single or combination), where clinical function interfaces are integrated in the functional fabric architecture. The preconfigured clinical function interfaces enable dynamic integration of active targeting, increased availability at the cancer cell, protection from host defense and on demand controlled release for the optimal efficacy of the drug regimen. The smart dynamically transformative, clinical-outcome focused platform for the development of precision therapeutics has a small foot-print, is globally scalable and regulatory agency compliant. In this way, the platform allows biopharmaceutical companies to develop a sustainable product portfolio in a collaborative ecosystem.

Speaker Biography

Arkesh Mehta is a lifelong Entrepreneur with experience up and down the biopharmaceutical spectrum, since his first startup more than 15 years ago. He has co-founded and/or served as CEO or Executive Chairman for a set of leading-edge biotechnology, molecular diagnostics and healthcare IT companies. These companies had successful exits including BPI technologies, AT-GC BioPharm, Avanti NanoSciences and CBTEK. He is an Advisor and Board Member of several bio and healthcare startups. He has organized, Chaired and participated in number of international panels, including organizing the First NASDAQ panel on Bio-IT. He is a Member of Trustees for Sushita Group, a non-profit that fosters entrepreneurship.

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Investigating the effects of electrical stimulation via gold nanoparticles on *in vitro* neurite outgrowth: Perspective to nerve regeneration

Moein Adel
Tehran University of Medical Sciences, Iran

Statement of the problem: Following the injury of nervous tissue spinal cord injuries, axons do not regenerate appreciably in their native environment and current clinical approach to treating damaged nerves is inefficient; thus, medical treatment approaches are needed. Neural tissue engineering research field has been progressed by using different approaches especially for repairing of damaged neural cells. In addition, it is known that electrical stimulation can be used for neurite growth and nerve regeneration.

Methodology & theoretical orientation: In this study, conductive properties of gold nanoparticles (GNPs, 39 nm) and their contribution to the enhancement of electrical stimulation to nerve cells have been conducted. In experimental section, polyethyleneimine (PEI) polymer coated cover glasses was used to create a positively charged glass surface and adsorption of GNPs was used in conjugation with this polymer coated substrate. Subsequently, PC12 cells were cultured on the modified glass surface and pulsed electric field of 1.5 V, 20 Hz was applied as electrical stimulation for 55 min duration.

Findings: Images from FESEM showed a uniform distribution of GNPs on glasses surface. In addition, enhanced neurite outgrowth (120 µm) using electrical stimulation was determined by inverted phase contrast microscopy images.

Conclusion & significance: Finally, our study showed that pulsed current stimulation induced neurite outgrowth of PC12 cells adhered to the GNPs coated surfaces. Altogether, synergist combination of GNPs together with pulsed electrical stimulation can be used for enhanced nerve regeneration. Our future works will direct towards optimizing properties of NPs and stimulation parameters for *in vivo* nerve regeneration and do a comparative study with other nanomaterial including silk, carbon materials etc.

Speaker Biography

Moein Adel has his expertise in nerve regeneration and nanotechnology. His open and contextual evaluation model creates new combination and optimization pathways for treatment of CNS damages. He has built this model after years of experience in research, evaluation and teaching both in research and education institutions. The foundation is based on fourth generation evaluation (Guba and Lincoln, 1989) which is a methodology that utilizes the previous generations of evaluation: measurement, description and judgment. It allows for value-pluralism. This approach is responsive to all stakeholders and has a different way of focusing.

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