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First Annual Conference of the American Society of Nanomedicine

Bolger Center, Potomac, Maryland

Thursday - October 22, 2009

10-6 pm **Registration**

1:00 pm **Welcome and Introduction**

1:10 pm **Session I**
Novel Nanomaterials and Their Biomedical Applications
Chairs: Marianna Foldvari, *U. of Waterloo*
Kuan Wang, *NIH*
Speakers: Carl Dieffenbach, *NIAID*: "NIAID/DAIDS Priorities in Nanomedicine"
Marianna Foldvari, *U. of Waterloo*: "Novel Biomaterials for Building Non-viral Gene Delivery Systems"
Eder L. Romero, *U. Nacional de Quilmes*: "Ultradeformable Tebenquisomes (UT): New Topical Adjuvants"
Xiaojun Zhao, *Sichuan U.*: "Fabrication of Nanobiomaterials through Molecular Self-assembling Peptides and Their Applications in Nanomedicine"

2:50 pm **Break**

3:10 pm **Keynote Lecture 1**
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Keynote Speaker: Kazunori Kataoka, *U. of Tokyo*: "Supramolecular Nanocarriers for Gene and Drug Delivery"

4:00 pm **Session II**
Vision for Nanomedicine Advancement
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Speakers: Richard Fisher, *NIH*: "The NIH Nanomedicine Initiative: The Next Five Years"
James Alexander Liddle, *NIST*: "Measurements at the Nanoscale"
Karen McCann, *Northern Virginia Technology Council*: "Nanomedicine in Northern Virginia"
Representative, *Technology Council of Maryland* (TBC)

5:30 pm **Poster Viewing and Dinner**

Friday - October 23, 2009

8:40 am **Session III**
Basic Science Advances Driving Innovation in Nanomedicine
Chairs: Wah Chiu, *Baylor College of Medicine*
Kostas Kostarelos, *U. of London*
Speakers: Wah Chiu, *Baylor College of Medicine*: "Conformational Changes of a Group II Chaperonin in Different States Revealed by Single-particle Cryo-EM"
Kostas Kostarelos, *U. of London*: "Promises, Facts and Challenges of Carbon Nanotubes in Medicine"
Dan Luo, *Cornell* U.: "DNA as Both a Genetic and a Generic Nanoscale Material"
Michael Sheetz, *Columbia U.*: "Shaping Cells by Force and Rigidity through Protein Stretching"
Michael Teitell, *UCLA*: "A Feedback-Control Approach to Identify, Quantify, and Control Essential Signaling Complexes in Lymphoid Malignancies"

10:20 am **Break**

10:40 am **Session IV**
Drug and Gene Delivery in Nanomedicine
Chairs: Alexander V. Kabanov, *U. of Nebraska Medical Center*
Dean Ho, *Northwestern U.*
Speakers: Mansoor Amiji, *Northeastern U.*: "Multifunctional Nanosystems for Cancer Diagnosis and Therapy"
Raj Bawa, *Bawa Biotech Consulting and Rensselaer Polytechnic Institute*: "Nanotherapeutics – Novel Delivery Technologies and FDA Regulatory Challenges"
Esther H. Chang, *Georgetown U.*: "A Tumor- Targeting Nanodelivery Platform on Trial"
Dean Ho, *Northwestern U.*: "Nanodiamond-Based Therapeutic Delivery Vehicles for the Treatment of Cancer"
Alexander V. Kabanov, *U. of Nebraska Medical Center*: "Polymeric Micelles: From Bench to Bedside"

12:20 pm **Lunch and Poster Viewing**

1:40 pm **Session V**
Diagnostics: Imaging and Biosensors
Chairs: James Tatum, *NCI/NIH*
Greg Lanza, *Washington U.*

Speakers: Matthew Freedman, *Georgetown U.*: "Tumor Specific Nanodelivery of Contrast Agents Enhances Early Detection of Lung and Pancreatic Tumors"
Cathy Galbraith, *NIH*: "Visualizing Cell Movement One Molecule at a Time"
Greg Lanza, *Washington U.*: "Molecular Photoacoustic Imaging with Gold Nanobeacons"
James Tatum, *NCI/NIH*: "Evolving Role of Imaging in Oncology Drug Development"
Donald Tomalia, *Central Michigan U.*: "Dendrimer Based Nano-Containers/Scaffolding for Targeted Imaging and Therapies"

3:20 pm **Break**

3:35 pm **Session VI**
Update on the International Society for Nanomedicine (ISNM)
Esther Chang, *American Society for Nanomedicine*
Kazunori Kataoka, *The Asian Society for Nanomedicine*
Beat Löffler, *The European Society for Nanomedicine*

4:20 pm **Group photo**

4:40 pm **Break**

5:00 pm **Keynote Lecture 2:**
Introduction: Lajos P. Balogh, *U. of Buffalo*
Keynote Speaker: Vladimir Torchilin, *Northeastern U.*: "Power of Medical Nanotechnology: Delivery of Undeliverable Drugs"

5:45 pm **Dinner and Poster Viewing**

Saturday - October 24, 2009

8:20 am **Session VII**
Nanomedicine for Neurological Disorders/Translation in Nanomedicine
Chairs: Rutledge Ellis-Behnke, *U. of Hong Kong and MIT*
Thomas Webster, *Brown U.*
Speakers: Rutledge Ellis-Behnke, *U. of Hong Kong and MIT*: "Controlling the Growth and Differentiation of Cells with Physical Interaction"
Lance Kam, *Columbia U.*: "Coordinating Neural Stem Cell Function through Nanoengineering"

Barbara Rouzi, *U. of Modena and Reggio Emilia*:
"Nanotechonology for Drug Delivery and Drug Targeting"
Thomas Webster, *Brown U.*: "How and Why is Nanotechnology Increasing Neural Tissue Growth?"

10:00 am **Break**

10:20 am **Session VIII (Panel Discussion)**
Nanomedicine Inventions – Patents, Business and Commercialization
Chairs: Brian Del Buono, *Sterne, Kessler, Goldstein & Fox*
Raj Bawa, *Bawa Biotech Consulting and Rensselaer Polytechnic Institute*
Speakers: Raj Bawa, *Bawa Biotech Consulting and Rensselaer Polytechnic Institute*: "Nanomedicine Inventions and Patents – A Primer"
Ricardo Carvajal, *Hyman, Phelps & McNamara*: "FDA's Regulation of Nanotechnology: Current Controversies and Potential Impacts on Nanomedicine"
Chris J. Katopis, *Computing Technology Industry Association*: "The Future of the Patent Office in the Obama Administration"
Jeffery P. Langer, *Finnegan, Henderson, Farabow, Garrett & Dunner*: "Intellectual Property Mapping – A Cornerstone of a Long Term IP Strategy"
Jeff Mills and Timothy J. Shea, *Sterne, Kessler, Goldstein & Fox*: "Getting to Market: Freedom to Operate in the Nanomedicine Space"
Steve Rutt, *Foley & Lardner*: "Connecting Nanotechnology, the Economy and IP Law"
Misti Ushio, *Harris & Harris Group*: "Nanotech for HealthcareTM: A Venture Capital Perspective"

12:00 noon **Lunch**

1:20 pm **Keynote Lecture 3**
Introduction: Esther H. Chang, *Georgetown U.*
Keynote Speaker: Douglas Lowy, *NCI/NIH*: "Current and Future Preventive HPV Vaccines"

2:30 pm **Session IX**
Top 4 Poster Submissions from Young Investigators, Oral Presentations and Award Ceremony
Chair: Raj Bawa, *Bawa Biotech Consulting and Rensselaer Polytechnic Institute*

3:15 pm **Break (North building)**

3:40 pm **Session X (North building)**
Nanomaterial Safety and Toxicology
Chairs: Lajos P. Balogh, *U. of Buffalo*
Speakers: Vicki Colvin, *Rice U.*: TBA
Fernando Martin-Sanchez, *NIH Spain*: "Scientific and Engineering Challenges for Informatics in the Context of Regenerative and Nano-medicine"
Nancy Monteiro-Riviere, *North Carolina State U.*: "Evaluating the Skin Hazards Associated with Nanomaterials"
Mark R. Wiesner, *Duke U.*: "Physical-Chemical Factors Controlling Nanoparticle Exposure, Transformation and Reactivity"

5:20 pm **Dinner**

Sunday - October 25, 2009

8:40 am **Session XI**
Nanomedicine as Prophylactic/Therapy
Chairs: Stephen Feinstone, *FDA*
Speakers: John Fulkerson, *Aeras Global TB Vaccine Foundation*: "Aeras RNA Nucleocapsid Vaccine Vector System"
Julianna Lisziewicz, *Genetic Immunity LLC*: "Plasmid DNA-based Nanomedicines in the Active Immunotherapeutic Field"
Marian Major, *FDA*: "The Use of Ligand-modified Immunoliposomes to Efficiently Deliver Plasmid DNA in Prime/Boost Vaccine Strategies against Hepatitis C Virus"
Krutika Sawant, *MS U. of Baroda* (TBC)

10:20 am **Break**

10:45 am **Session XII**

Clinical Applications of Nanomedicine

Chairs: Donald Tomalia, *Central Michigan U.*
Patrick Hunziker, *U. Basel*

Speakers: Patrick Hunziker, *U. Basel*: "Artificial Organelles"
Varvara Karagkiozaki, *Aristotle U. of Thessaloniki*: "Applications of Nanomedicine in Cardiology: Advances on Biomaterials for Coronary Stents"
H. Kobayashi, *NIH*: "Lymphatic Imaging with Nano-sized Gadolinium-dendrimer-based Contrast Agents: A Promising Application to the Clinical Diagnostic Imaging"
Patrick Lu, *Sirnamoics*: "Nanoparticle-Enhanced and Multi-Targeted siRNA Therapeutics for Critical Human Diseases"

12:15 pm **Conference Adjourns**

Session I: Thursday, October 22, 1:10 p.m.

Novel Nanomaterials and Their Biomedical Applications

Session I Chairs

Marianna Foldvari
Canada Research Chair, Professor of Bionanotechnology and Nanomedicine
School of Pharmacy, University of Waterloo

Biography: Dr. Marianna Foldvari is the Canada Research Chair in Bionanotechnology and Nanomedicine. She is also a Professor of Pharmaceutical Sciences and the Associate Director, Research and Graduate Studies, at the University of Waterloo's School of Pharmacy. Dr. Foldvari received a Pharmacy degree and a Doctorate in Pharmaceutical Sciences, both from Semmelweis Medical University in Budapest, Hungary. She then obtained her PhD in Pharmaceutical Sciences (Drug Delivery) from Dalhousie University in Canada. Dr. Foldvari's research program focuses on the development of intelligent delivery systems for macromolecular drugs and design of biomolecular devices for individually-responsive therapeutic systems. Dr. Foldvari has authored over 100 papers and 70 conference presentations and is the inventor on 14 patents. She founded two spin-off companies that focus on nanomedicine product development to commercialize the technologies that she and her research team have developed. She is Associate Editor of *Nanomedicine: Nanotechnology, Biology and Medicine.*

Kuan Wang
Lab Chief, Laboratory of Muscle Biology, NIAMS
National Institutes of Health

Bio: Dr. Kuan Wang is the Lab Chief of the Laboratory of Muscle Biology and at NIAMS. Dr. Wang received his BS degree from National Taiwan University and Ph.D. degree in Molecular Biochemistry and Biophysics from Yale University. Dr. Wang was a professor of Chemistry and Biochemistry at the University of Texas at Austin from 1977 to 1997 and is presently Lab Chief of Muscle Biology at National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health. Dr. Wang's research focuses on mechanotransduction in muscle cells and muscle proteins. We are identifying the key features of the molecular events of mechanotransduction of muscle proteins, especially their intrinsically disordered protein domains. These intrinsically unstructured regions link folded domains and are hot spots for protein/RNA/DNA interactions and posttranslational modifications. They play major roles in signaling transduction, cell control, and transcriptional and translational regulation by the characteristic high specificity and low affinity interactions. Nanomechanical and protein interaction studies from Dr. Wang's lab on two giant elastic proteins, titin and nebulin, led to the proposal

that the direct coupling of elasticity and ligand binding of intrinsically disordered protein segments are biologically important attributes for these key players in signaling and stress pathways. This is a novel mechanism for titin and nebulin to sense force and transduce force to biochemical signals in contractile machinery. Dr. Wang is an Academician of Academia Sinica and a founding member of the American Society of Nanomedicine.

"NIAID/DAIDS Priorities in Nanomedicine"

Carl Dieffenbach
Division Director, National Institutes of Allergy and Infectious Diseases' (NIAID), Division of AIDS (DAIDS)

Abstract: The National Institute of Allergy and Infectious Diseases (NIAID) Division of Acquired Immunodeficiency Syndrome (DAIDS) at the National Institutes of Health was formed in 1986 to develop and implement the national research agenda to address the HIV/AIDS epidemic. DAIDS supports a comprehensive research agenda to help ensure an end to the HIV/AIDS epidemic by increasing basic knowledge of the pathogenesis and transmission of the human immunodeficiency virus (HIV), supporting the development of therapies for HIV infection and its complications and co-infections, and supporting the development of vaccines and other prevention strategies. NIAID/DAIDS is interested in supporting projects implementing nanoscience and nanotechnology to address the following priorities:

- Development of nanotechnology-based delivery systems for:
  - Delivery of prevention strategies (topical microbicides, biomedical prevention agents e.g. PrEP, vaccines) and chemo-immuno-therapeutics
- Targeting of specific tissues, cells, organelles, proteins, and/or nucleic acids
- Development of tools and approaches to understand viral pathogenesis and HIV interactions at the tissue and cellular level in the presence or absence of prevention interventions
- Development of bioimaging applications to evaluate viral transmission and reservoirs, immune induction and modulation, and drug and prevention strategy transport and metabolism
- Development of cheap and rapid platforms for detection, diagnosis, biomarker evaluation, and genetic testing for both in vitro and in vivo evaluations
- Interrogation of the safety of current and proposed nanotechnology platforms and strategies

Biography: Dr. Carl W. Dieffenbach received his bachelor's degree in biochemistry from the University of Maryland in 1976 and his Ph.D. in biophysics from the John Hopkins University in 1983. He then completed his Postdoctoral Fellowship with the Uniformed Services University of the Health

Sciences (USUHS), Department of Pathology, in 1984, and was then promoted to the rank of Assistant Professor. While at USUHS he ran a highly productive research program, pioneering uses of Polymerase Chain Reaction in understanding mechanisms of cytokine gene expression and cloned the cellular receptor for the murine Coronavirus, Mouse Hepatitis Virus. In 1992, he joined the National Institutes of Allergy and Infectious Diseases' (NIAID), Division of AIDS (DAIDS) as the Chief of the preclinical therapeutics group. Upon his initial NIAID appointment, Dr. Dieffenbach spearheaded important research initiatives that accelerated the progress of basic research on HIV pathogenesis and directly resulted in new clinical studies of novel AIDS therapies. In 1996, he was promoted to director of the Basic Sciences Program within DAIDS, where he remained until being selected as the Division Director in 2008. Additionally, Dr. Dieffenbach has continued to serve as an Associate Professor of Pathology, F. Edward Hebert School of Medicine and as a faculty member and director for the HIV/AIDS course in the NIH graduate school, FAES. He is also a co-author of the Cold Spring Harbor Laboratory Manuals, PCR Primer 1st and 2nd Editions, which were published in 1995 and 2003 respectively. As the DAIDS director, Dr. Dieffenbach has oversight of a global HIV/AIDS research portfolio of over one billion dollars and a staff of over 140 federal employees.

"Novel Biomaterials for Building Non-viral Gene Delivery Systems"

Marianna Foldvari
Canada Research Chair in Bionanotechnology and Nanomedicine, School of Pharmacy, University of Waterloo

Abstract: The development of safe and effective non-viral delivery systems for non-invasive administration of nucleic acids is becoming increasingly important for both local and systemic treatments. This presentation will focus on some recent designs of non-viral delivery systems based on phospholipid-gemini surfactant compositions (gemini nanoparticles). Gemini surfactants with two cationic headgroups encapsulate plasmid DNA, creating an advanced type of nanoparticle-based delivery system designed to transfect DNA both *in vitro* and *in vivo* for subsequent expression of desired therapeutic proteins. Gemini surfactants provide a basis to develop novel non-viral delivery systems for gene therapy; however, gemini nanoparticles must possess several crucial properties to overcome difficult cellular and tissue barriers. Preclinical studies of topical formulations of gemini nanoparticles for dermatological conditions and topical vaccines will be presented. Delivery and expression of a therapeutic gene in Tsk mice, a disease model for localized scleroderma, and the efficiency of co-delivery of a model protein antigen (hen egg lysozyme [HEL]) and CpG ODN by gemini nanoparticles both intradermally and non-invasively as a topical vaccine in mice will be discussed.

"Ultradeformable Tebenquisomes (UT): New Topical Adjuvants"

Eder L. Romero
Laboratorio de Diseño de estrategias de Targeting de Drogas (LDTD),
University Nacional de Quilmes

Abstract: UT are 200 nm diameter vesicles composed by a matrix of soy PC, sodium cholate and total polar lipid (TPL) extracted from the non alkaliphilic halophilic archaea Halorubrum tebenquichense, found in the Argentinean Patagonia, at 3:3:1 w/w/w. Negative ion ESI-MS of TPL identified major signals for archaeal phosphatidylglycerol (PG), phosphatidylglycerophosphate methyl ester (PGP-Me) and sulfated diglycosyl diphytanylglycerol diether S-DGD as well as a small signal for archaeal cardiolipin (BPG). UT could be dehydrated by the savant method while their ultradeformability remained unchanged upon fully rehydration, even in the absence of sugars as lyoprotectans. Remarkably, in spite of being the UT completely lacking of lipopolysaccharides, when loaded with the model protein ovoalbumin g OVA/mg lipid and upon topical application in a regimenμ(OVA) at 15 g OVA/cm2 on the shaved skin of Balb/c mice, theμof three doses of 20 UT were found to induce systemic IgG responses three folds higher than OVA- loaded conventional ultradeformable liposomes after 6 weeks.

Biography: Eder Romero was educated at University of La Plata, Argentina where she obtained her M.A. Biochemistry and PhD in Exact Sciences (1996). Following a post-doctoral research in Groningen University, The Netherlands under the supervision of Prof. Gerrit Sherphof (1997-1998), she returned to Argentina where currently is and Adjunct Researcher at the National Council of Scientific and Technological Research (CONICET) (2006) an Associate Professor of chemistry (2008), at the Department of Science and Technology, National University of Quilmes, Buenos Aires, Argentina. From 2007 she is leading the Program of Nanomedicine Research (PNM), being under her supervision three finished PhD thesis in nanomedicine (2003, 2008 and 2009) and other five ongoing doctoral research subjects on different nanomedical therapeutic strategies. Her research interest deals with the development of targeted delivery of nanomedicines across the skin and the oral and olfactory mucosa, specifically for the treatment of infectious parasitic diseases and also for the delivery of macromolecules by the oral route. Additionally the PNM is developing vaccination strategies employing specifically tailored nanovesicles to be applied by the topical and mucosal routes. Romero has been responsible for the first and second Pharmaceutical Nanotechnology Schools in Latinoamerica (2006 and 2008) and is currently acting as scientific adviser of regional pharmaceutical companies aimed to development of nanomedical therapeutic strategies.

"Fabrication of Nanobiomaterials through Molecular Self-assembling Peptides and Their Applications in Nanomedicine"

Xiaojun Zhao
Institute for NanoBiomedical Technology and Membrane Biology,
West China Hospital, Sichuan University

Abstract: Nature has selected and evolved numerous and diverse chemical and molecular structural motifs through billions of years of molecular selection and evolution, these motifs are the basic building blocks of a wide range of sophisticated nanomachines that work at astonishing speed and efficiency with the finest controls. Only now we begin to learn from Nature—in its finest molecular details and intricate interactions of numerous fine parts: we are learning the basic molecular engineering principles for nano- and micro-fabrication at the exquisitely fine scale through the understanding of molecular self-assembly phenomena.

Molecular self-assembly is ubiquitous in Nature and has recently emerged as a new approach in chemical synthesis, nanotechnology, polymer science, materials and engineering. Two complementary strategies can be employed in the fabrication of molecular biomaterials. In the 'top-down' approach, biomaterials are generated by stripping down a complex entity into its component parts. This contrasts with the 'bottom-up' approach, in which materials are assembled molecule by molecule and in some cases even atom by atom to produce novel supramolecular architectures. The latter approach is likely to become an integral part of nanomaterials manufacture and requires a deep understanding of individual molecular building blocks, their structures, assembling properties and dynamic behaviors. Two key elements are required for molecular fabrication, which are chemical complementarities and structural compatibility, both of which confer the weak and noncovalent interactions that bind building blocks together during self-assembly.

We have designed and fabricated a set of self assembling peptides-mediated biomaterials and significant advances have been achieved at the interface of biology and materials science, including the fabrication of nanofiber materials for 3-D cell cultures, tissue engineering and regenerative medicine, the peptide detergents for stabilizing, and crystallizing membrane proteins as well as nanocoating molecular for cell organizations. Molecular fabrications of nanobiomateirals have fostered diverse scientific discoveries and technological innovations.

Biography: Xiaojun Zhao received his B.S. from Sichuan University, his M.A. in Biochemistry from the University of California at Santa Barbara and his Ph.D. in Biological Chemistry from the University of California at Los Angeles. He conducted his postdoctoral research on mouse model of mitochondrial disease at California Institute of Technology. He then moved to Cambridge, where he continued his studies on molecular and cellular mechanism of neuronal synaptogenesis and fabrication and application of the

self assembled peptide nanomaterials in tissue engineering and regenerative medicine at Massachusetts Institute of Technology. He has been appointed as Professor, Chief Scientist and Founding Executive Director at a newly established Institute for NanoBiomedical Technology and Membrane Biology, Sichuan University since 2005. He holds adjunct professorship in Department of Biological and Environmental Engineering, Cornell University. He is currently working with various self-assembling peptide systems to develop new classes of biological materials including peptide matrix scaffolds for tissue engineering and regenerative medicine, biological surface engineering and peptide surfactant nanotubes for stabilizing membrane proteins and their complexes. His lab is also involved in several other studies such as developing scaffolds for controlling stem cells differentiation and proliferation, tumor cells in vitro proliferation and drug therapy, virus proliferation and growth inhibition in modified peptide gel scaffolds and so on. He has written, co-written and contributed to over 100 technical papers including original research, review articles and book chapters as well as 8 patents. He has received several awards including the Asia Excellence Award from the Society of Polymer Science of Japan in 2008.

Thursday, October 22, 3:10 p.m.

Keynote Lecture 1

Introduction: Kuan Wang, *NIH*

"Supramolecular Nanocarriers for Gene and Drug Delivery"

Kazunori Kataoka
Professor, Department of Material Engineering and Center for NanoBio Integration, the University of Tokyo

Abstract: Polymeric micelle, the self-assembly of block copolymers with core-shell architecture, is a promising nanocarrier for drug and gene delivery. There are several relevant properties in polymeric micelle as nanocarrier systems, such as longevity in blood circulation, tissue-penetrating ability, spatial and temporal controlled drug release, and reduced inherent toxicity of cytotoxic reagents. Also, engineering of the block copolymer structure allows the preparation of polymeric micelles with integrated smart functions, such as targetability as well as stimuli-sensitivity. This presentation overviews the recent achievements as well as the future perspectives of polymeric micelles as smart nanocarriers for drug and nucleic acid delivery. Notable anti-tumor efficacy against hypovascular cancer, including pancreatic cancer and diffused-type stomach cancer, of the doxorubicin-incorporated polymeric micelles with pH-responding property was demonstrated to emphasize a promising utility of the nanocarrier-modulated chemotherapy for the treatment of intractable cancers. Gene-loaded polymeric micelles were applied as non-viral vectors in the fields of regenerative medicine, particularly bone regeneration. Generation of new bone in experimental animals was successfully achieved by transducting genes encoding differentiation factors using polymeric micellar carriers. Gene therapy by polymeric micelles was also demonstrated for intractable cardiovascular disease, pulmonary hypertension, by intratracheal transfer of therapeutic gene. Further, the supramolecular assebmlies, including polymeric micelles, polymer vesicles, and photosensitive dendrimer assemblies, were utilized as nanodevices directing to the new medical paradigm of smart nanotheranostic systems controlled by external physical stimuli, particularly, photo illumination (nano-photomedicine).

Biography: Kazunori Kataoka, Ph.D., is a Professor of Biomaterials at Graduate School of Engineering, the University of Tokyo. He has been appointed joint position since 2004 from Graduate School of Medicine, the University of Tokyo as a Professor and a Chair of Division of Clinical Biotechnology at the Center for Disease Biology and Integrative Medicine. He also serves as Director of the Center for NanoBio Integration at the University of Tokyo, an interdisciplinary initiative sponsored by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. He

received B.Eng. (1974) degree in Organic Chemistry, and M.Eng. (1976) and Ph.D. (1979) degrees in Polymer Chemistry at the University of Tokyo. He held positions at the Institute of Biomedical Engineering, Tokyo Women's Medical College (1979-1989) and Department of Materials Engineering at Tokyo University of Science (1989-1998) before joining the faculty of the University of Tokyo in 1998. He was a Visiting Professor at University of Paris XIII, France (1992, 1996), Tohoku University, Sendai, Japan (2007), and Ludwig-Maximillians University (LMU), Munich, Germany (2008). He served as the Adjunct Director of the Biomaterials Center at the National Institute for Materials Science (NIMS), Japan between 2001-2004. He is a past president of the Japanese Society for Biomaterials (2004-2006), a president of Japanese Society of Gene Design and Delivery (2004-), a Vice President of the Society of Polymer Science, Japan (2008-), a Fellow of the American Institute of Medical and Biological Engineering (AIMBE) (1999-) and a Fellow of Biomaterials Science and Engineering (FBSE) (2004-). He was the recipient of several awards, including the Award of the Japanese Society for Biomaterials (1993), the Outstanding Paper Award of the Controlled Release Society (1995), the Award of the Society of Polymer Science, Japan (2000), Clemson Award in Basic Research, Society for Biomaterials, USA (2005), Barré Award, University of Montreal (2006), and Founder's Award of Controlled Release Society (2008). He has almost 400 publications and is on the editorial board of twelve international journals. He is the Editor of Journal of Biomaterials Science, Polymer Edition and the Associate Editor of Biomacromolecules (American Chemical Society). His current major research interests include supramolecular materials for nanobiotechnology, focusing on gene and drug delivery.

Session II: Thursday, October 22, 4:00 p.m.

Vision for Nanomedicine Advancement

Session II Chair

Lajos Balogh
Professor, Co-Director of the NanoBiotechnology Center
Roswell Park Cancer Institute, University of Buffalo

Biography: Lajos (Lou) Balogh is the Editor-in-Chief of the journal *Nanomedicine: Nanotechnology, Biology and Medicine (Elsevier).* He is a former Professor of the Roswell Park Cancer Institute, of the University at Buffalo, SUNY, and of the University of Michigan, Ann Arbor, MI. Lou has recently started his own business: AA NANOMED Consultants. Dr. Balogh received his Ph.D. from the Kossuth L. University (KLTE) in Hungary in Chemical Technology and was invited to the University of Massachusetts Lowell in 1991. He has authored/coauthored over 150 scientific publications and has been awarded 12 patents in various disciplines. He is member of numerous USA and International expert committees, including the NIH NANO and the EPA Nanotechnology study sections. He is also a member of the Steering Committee of the American National Standard Institute Nanotechnology Panel and serves on the US Technical Advisory Committee to the International Standard Organization on Nanotechnology (TC-229). Lou is one of the five Founders of the American Society for Nanomedicine (ASNM). His present research interests involve the design, synthesis, and characterization of multifunctional hybrid nanodevices for targeted delivery of smart contrast agents and anticancer drugs, and interactions of these nanodevices with cells and tissues including toxicity and biodistribution of nanomedicines.

"The NIH Nanomedicine Initiative: The Next Five Years"

Richard Fisher
Associate Director for Science Policy and Legislation
Director, Office of Program Planning and Analysis
NIH

Abstract: The NIH Nanomedicine initiative consists of a consortium of eight Nanomedicine Development Centers that was established in September of 2005. Since the machinery in cells operate at the nanoscale, i.e., at dimensions of about 1-100 nanometers, the primary goal of this initiative is to characterize molecular nanoscale components inside cells at a level of precision that will lead to an understanding of the design principles required to build functional biocompatible molecular tools to repair or replace dysfunctional intracellular structures or systems caused by disease back to "normal" operating ranges. This is a monumental challenge especially within the 10-year time frame of

this initiative. This talk will provide a status report of the accomplishments and challenges of this initiative to date and will discuss the future of the program at the NIH.

Biography: Richard S. Fisher received a Ph.D in Physiology and Biophysics at the University of Illinois Urbana-Champaign in 1979 where he studied electrophysiological properties of transepithelial sodium transport. He continued studies on the mechanisms of sodium transport and cell volume regulation as a staff fellow at the National Institutes of Health, as a staff physiologist in the Department of Nephrology, Division of Medicine at the Walter Reed Army Institute of Research, and as a visiting scientist at the Catholic University of Leuven, Belgium. In 1996, Dr. Fisher returned to the NIH as a scientific review officer in the National Institute of Deafness and other Communication Disorders and three years later accepted a position in the National Eye Institute as the Corneal Diseases program director. He served on the Institutional Review Board of Frederick Memorial Hospital, Frederick, MD and numerous trans-NIH committees including the High Risk/High Reward Implementation Committee, the Bioengineering Consortium, the trans-NIH Nanotechnology task force. Currently, Dr. Fisher is the Director of the NEI Office of Program Planning and Analysis and also serves as the project team leader for an innovative NIH program in Nanomedicine.

"Measurements at the Nanoscale"

James Alexander Liddle
Project Leader, Center for Nanoscale Science and Technology,
National Institute of Science and Technology

Abstract: NIST's Center for Nanoscale Science and Technology is a new, interdisciplinary organization dedicated to solving nanoscale measurement problems. In this talk, I will describe the two components of the Center: the NanoFab and the research program. The NanoFab is a national user facility that provides its users with state-of-the-art equipment, expert training, and a high level of flexibility. It is able to satisfy the needs of users ranging from novice to the most advanced experts in the field. It provides access to a wide variety of measurement and characterization tools, technologies, and expertise to its users and acts as a point of contact to the many different areas of nanoscience and technology research occurring across NIST. I will give a brief introduction to the NanoFab and illustrate its capabilities through a description of user projects involving the engineering of SERS substrates and the use of micropillars to control dendrimer growth. I will also give an overview of the CNST's research program, which has three main research thrusts in the areas of energy, future electronics and nanomanufacturing and has research projects in areas as diverse as nanoplasmonics and MEMS. I will illustrate the variety of skills needed to address nanoscale measurement

problems with a discussion of two projects: tracking fluorescent nanoparticles to 10 nm precision and STORM microscopy of proton distributions in a photoresist polymer matrix.

Biography: J. Alexander Liddle received his B.A. and D. Phil. degrees in Materials Science from the University of Oxford in 1986 and 1989 respectively. He spent the next eleven years at Bell Laboratories, where his primary efforts involved the research, development and eventual commercialization of a novel electron-beam lithography technology. He subsequently became the leader of an optical telecommunications MEMS group when Agere Systems spun-off from Lucent Technologies. He spent the next three years as the head of the LBNL nanofabrication group in the Center for X-ray optics, before becoming lead scientist of the Molecular Foundry nanofabrication user facility, where he was involved in research ranging from quantum computation to guided self-assembly. In 2006 he moved to NIST as project leader of nanofabrication research in the Center for Nanoscale Science and Technology. His current focus is on nanofabrication and self-assembly for nanomanufacturing.

"Nanomedicine in Northern Virginia"

Karen McCann
Northern Virginia Technology Council

Abstract: Never before has the promise of nanomedicine been so real and the monetary support to bring this promise to fruition been so scarce. Our worldwide recession has caused a tightening of financial investment particularly in technologies like nanomedicine with no definite timeline for payoff. To continue research or to bring this technology to market, sound business principles must be utilized to obtain this type of support. In Northern Virginia, there are sources of support for strong business plans which may include financial support. This support can come from public sources and private sources, but these sources must be investigated and cultivated. My presentation will provide ideas obtaining for the necessary business support for your technology.

Biography: Ms. McCann has over 20 years of experience as a telecommunications professional in Northern Virginia. Recipient of numerous corporate awards, she studied at the University of Virginia, graduating with a degree in mathematics and computer science. She has also studied at the John's Hopkins Computer Science graduate program. Ms. McCann also holds a PMP certification and is a member of the international Project Management Institute. She holds a government security clearance and a technical certification in wide area networking.

Ms. McCann serves as the Nanotechnology coordinator for the Northern Virginia Technology Council's Business Technologies committee. In 2007, she organized and moderated a successful panel for the NVTC on the latest developments in the field of Nanomedicine, featuring Dr. Bawa, co-founder of the ASNM. This panel attracted a number of investment organizations looking to support this promising field. Ms. McCann will be speaking today on nanomedicine initiatives in Northern Virginia.

"TBA"

Representative
Technology Council of Maryland

Session III: Friday, October 23, 8:40 a.m.

Basic Science Advances Driving Innovation in Nanomedicine

Session III Chairs

Wah Chiu
Professor, Baylor College of Medicine

Biography: Dr. Wah Chiu obtained his B.A. in Physics and Ph.D. in Biophysics from the University of California, Berkeley. He is the Alvin Romansky Professor of Biochemistry at Baylor College of Medicine. He holds joint faculty appointment at the Computer Science Department at Rice University, Physics Department at the University of Houston and the School of Health Informatics at the University of Texas Health Science Center. His laboratory has pioneered various experimental and computational methods in biological cryo-electron microscopy (cryo-EM). He is the awardee of the Alexander von Humboldt Research Prize and an elected member of the Academia Sinica, Taiwan.

Dr. Chiu is the founding director of two NIH supported research Centers: National Center for Macromolecular Imaging (http://ncmi.bcm.edu/) and Center for Protein Folding Machinery (http://proteinfoldingcenter.org). Both Centers involve multiple investigators from diverse disciplines in biology, medicine, physics, chemistry, engineering and computing from different institutions and industries across the U.S. and oversee. Dr. Chiu is also the founding director of the Ph.D. Program in Structural and Computational Biology and Molecular Biophysics at Baylor College of Medicine (http://scbmb.bcm.edu) with over 70 faculty mentors from six academic institutions in Houston.

Dr. Chiu serves on the editorial board of *Structure, Journal of Structural Biology, Quarterly Reviews of Biophysics*, and *Journal of Structural and Functional Genomics*. He is presently serving on the scientific advisory boards for the Worldwide Protein Data Bank, the HIV Structural Biology Program of NIGMS, the Swiss National Science Foundation and the Ministry of Education in Singapore.

Kostas Kostarelos
Nanomedicine Lab, Centre for Drug Delivery Research, The School of Pharmacy, University of London

Biography: Professor Kostarelos is the Chair of Nanomedicine & Head of the Centre for Drug Delivery Research at The School of Pharmacy of the University of London, a Fellow of the Royal Society of Medicine (FRSM) and a Fellow of the Institute of Nanotechnology (FIoN). He obtained his Diploma in Chemical Engineering and PhD from the Department of Chemical Engineering, Imperial College London. Previous appointments include:

Assistant Professor of Genetic Medicine and Chemical Engineering in Medicine at Cornell University Weill Medical College, NY, USA; Deputy Director of Imperial College Genetic Therapies Centre, London, UK. Prof. Kostarelos is the Founding and Senior Editor of the journal *Nanomedicine* (ISI® 2008 Impact Factor: 6.1) and sits on the Editorial Board of *The Journal of Liposome Research*, *The International Journal of Nanomedicine* and *Nanomedicine: Nanotechnology, Biology and Medicine*. He is an advisor to the European Technology Platform in Nanomedicine (Brussels, Belgium) and the Max Plank Institute (Stuttgart, Germany).

"Conformational Changes of a Group II Chaperonin in Different States Revealed by Single-particle Cryo-EM"

Wah Chiu
Professor, Baylor College of Medicine

Abstract: Methanococcus maripaludis chaperonin (Mm-cpn) is a type II archael chaperonin that has a built-in lid. It is a 16-subunit homo-oligomer of ~1 MDa arranged in a two back-to-back rings that is structurally similar to the mammalian chaperonin such as TRiC. The substrate folding is accompanied by a conformational change triggered by nucleotide binding and hydrolysis. Using single particle cryo-EM and image reconstruction, we solve both the wild type and lidless mutant Mm-cpn in open and closed states respectively at resolutions between 10 and 4.3 Å. The open state is a nucleotide-free state while the closed state corresponds to the transition state of ATP hydrolysis. C-alpha backbone models of these four 3-D reconstructions have been hand traced or flexibly fitted depending on their resolutions. The models show clearly the subunits' equatorial domain rotation between the open and closed states, which is unique and dramatically different from the well-studied type I chaperonin (GroE) found in E.Coli.

"Promises, Facts and Challenges of Carbon Nanotubes in Medicine"

Kostas Kostarelos
Nanomedicine Lab, Centre for Drug Delivery Research, The School of Pharmacy, University of London

Abstract: The use of carbon nanotubes in medicine is currently at the crossroads between a proof-of-principle concept and an established preclinical candidate for a variety of therapeutic and diagnostic applications. Progress towards clinical trials will depend on outcomes of carbon nanotube toxicology studies that would provide the necessary risk-to-benefit assessments for these materials. In this presentation we focus on the types of carbon nanotubes that have been most extensively studied in preclinical

animal models today and draw attention to the promises, facts and challenges of these materials as they transition from the research to the clinical phase. We address common questions regarding the use of carbon nanotubes in imaging and therapy of diseases and highlight the opportunities and challenges ahead.

"DNA as Both a Genetic and a Generic Nanoscale Material"

Dan Luo
Associate Professor, Department of Biological and Environmental Engineering, Cornell University

Abstract: Our group has employed DNA as a true polymer utilizing its genetic as well as non-genetic properties. We have rationally designed and successfully created, in bulk, various DNA-based nanostructures and nanomaterials including DNA dendrimers and DNA hydrogels; we have also explored their real-world applications focusing on three main directions: DNA nano-barcodes, DNA gels, and DNA-nanoparticle hybrid systems. In this talk, I will highlight a few examples from these three directions with DNA as the central, common, nanoscale building blocks. Examples include 1) using anisotropic, branched, and crosslinkable (ABC) DNA monomers to achieve a novel polymerization scheme where DNA polymers are formed only in the presence of a pathogen. ABC monomers can also serve as a vector for multiplexed drug delivery; 2) using DNA hydrogels for 3D cell culture and more recently, we have created a DNA gel (termed P-gel) that can produce proteins without any living cells; 3) using DNA as a nano-organizer to fabricate nanoparticle-based 1D nanowires, 2D supralattices, and 3D dry crystals. Synthesis, characterization, engineering, and application of these DNA-based nanostructures and nanomaterials will be presented, and their underlying mechanisms will be discussed.

Biography: Dr. Dan Luo is currently an Associate Professor in the Department of Biological and Environmental Engineering at Cornell University. He is also a faculty member of the Nanobiotechnology Center, Cornell Center for Materials Research, Kavli Institute for Nanoscale Science, Biomedical Engineering and New Life Science Initiatives at Cornell. He obtained his B.S. degree from the University of Science and Technology of China in 1989 and his Ph.D. in Molecular, Cellular and Developmental Biology in 1997 from the Ohio State University. After his postdoctoral training at the School of Chemical Engineering at Cornell, he joined the Cornell faculty in 2001. He was awarded the National Science Foundation's CAREER award in 2006 and the Cornell Provost's Award for Distinguished Scholarship in 2007. He is also a recipient of the New York State Foundation for Science, Technology and Innovation (NYSTAR) Technology Transfer Incentive Program Award (2005), NYSTAR Faculty Development Program Award (2007), and the State University of New York (SUNY) Chancellor's Award for Excellence in Scholarship and Creative Activities (2008).

"Shaping Cells by Force and Rigidity through Protein Stretching"

Michael Sheetz
Professor of Biological Sciences, Columbia University and National University of Singapore

Abstract: Control of cell morphology involves the integration of mechanical sensing and cell motility to produce the desired shape of the organism 1. Nanometer level analyses of cell behavior have revealed only a limited number of types of motility involving complex mechanochemical steps 2. For example, cell spreading on matrix-coated surfaces have revealed three different types of motility, an initial blebbing, continuous spreading, and periodic contraction motility. Overall, cell traction forces are primarily dependent upon myosin II 3. Long term matrix forces appear to be sensed by protein unfolding and we have defined two different cytoplasmic mechanisms. One example is the activation of protein phosphorylation by stretching. The scaffolding protein, p130Cas has a central substrate domain with 15 tyrosines and active c-Src phosphorylates stretched p130Cas at least 7-fold faster than native, indicating that stretch is the major factor controlling the level of phosphorylation4. Secondly, the stretching of proteins can unveil binding sites such as the stretching of talin causing the increased binding of vinculin5. Thus, we suggest that the stretching of cytoskeletally attached proteins is the primary mechanism for sensing force and several mechanisms exist for transducing stretch into a biochemical signal.

1 Vogel, V. and Sheetz, M.,. Nat Rev Mol Cell Biol 7 (4), 265 (2006).
2 Döbereiner, H.G. et al., Phys Rev Letters 93 (10), 108105 (2004).
3 Cai, Y. et al., Biophys J 91 (10), 3907 (2006).
4 Sawada, Y. et al., Cell 127 (5), 1015 (2006).
5 del Rio, A. et al., Science 323 (5914), 638 (2009).

Biography: Dr. Michael Sheetz is currently Director of the RCE in Mechanobiology at NUS. He also is appointed as the William R. Kenan, Jr. Professor of Biological Sciences at Columbia University and co-Director of Nanotechnology Center for Mechanics in Regenerative Medicine. He holds a joint appointment in Biomedical Engineering at Columbia. Prior to joining Columbia, he was Chair of Cell Biology at Duke University Medical Center. His Ph.D. was in Chemistry at Caltech and he served as a postdoctoral fellow with Dr. S. Jon Singer (UCSD).

Past Accomplishments: The first quantitative assay of myosin motility in vitro was developed by him. He led the team that discovered kinesin by using a similar assay and was involved in the early characterization of microtubule-dependent membrane traffic. He made many contributions to our understanding of membrane structure (corral or fence model of the control of glycoprotein diffusion) and physical properties that influence cell shape (bilayer couple hypothesis). His lab used laser tweezers to show that

tension in membranes controls endocytosis, motility and membrane resealing rates.

Current Interests: Mechanosensing in the formation and regeneration of tissues; specifically, the role of mechanical stretching of proteins in force transduction. Examples include tyrosine kinase phosphorylation of p130Cas by stretch and signaling through mechanical exposure of binding sites in talin. Further definition of the mechanisms of cell motility at a mechanical and biochemical level. Understanding the membrane-cytoskeleton interface and its role in coordinating and controlling cell functions.

"A Feedback-Control Approach to Identify, Quantify, and Control Essential Signaling Complexes in Lymphoid Malignancies"

Michael Teitell
Departments of Pathology and Pediatrics
Chief, Division of Pediatric and Neonatal Pathology
Co-Director, Cancer Cell Biology Program Area, Jonsson Cancer Center
Co-Director, Center for Cell Control, a NIH Roadmap Nanomedicine Development Center
University of California, Los Angeles

Abstract: We are developing feedback-control algorithms to identify anti-cancer agent combinations that are efficacious against malignant lymphoid cells while sparing non-malignant cells. Optimized combinations will reveal key signaling complexes ('signalosomes') in the cancer cell signaling network that will be quantified for activity or repression by PhosphoFlow, a multi-modal flow cytometry technique. Clinically, anti-cancer drug cocktails have important advantages over single drug therapies that may include a) lowered concentrations of each drug than if used singularly; b) reduced chance to develop drug resistance; and c) increased drug efficacy through synergistic drug interactions. Our test system is comprised of the mouse B cell leukemia line WEHI-231 and non-malignant mouse embryonic fibroblast (MEF) cells. Six drugs were chosen for initial study, with 3 of these drugs targeting DNA, 2 drugs targeting the cytoskeleton, and 1 drug targeting the mTOR signaling pathway. We determined the effective concentration ranges of each of the six drugs individually in both cell types before combinatorial testing. Differential Evolution (DE) or Kipling algorithms were used with a total of 22 test cases for each generation. Cells were treated with drug cocktails and analyzed using flow cytometry after 48h. Non-optimized drug cocktails in early test iterations resulted in more than 90% cell death of both WEHI-231 and MEF cells. After ~15 search generations, optimized drug cocktails were attained that showed ~90% WEHI-231 cell death and only ~5% MEF cell death. Ongoing studies include the integration of Phosphoflow technology to elucidate the signalosome network that operates to support lymphoid

cancers, thereby revealing new therapeutic targets. This work is supported by the NIH Roadmap for Medical Research Nanomedicine Initiative (PN2EY018228).

Biography: Dr. Michael Teitell is Chief of the Division of Pediatric and Neonatal Pathology in the Departments of Pathology & Laboratory Medicine and Pediatrics at UCLA. He earned Bachelors and Masters degrees as a Departmental Scholar in Biochemistry from UCLA in 1985, and M.D. and Ph.D. degrees from the UCLA Medical Scientist Training Program in 1993. Dr. Teitell is co-Director of the Cancer Cell Biology Program Area at UCLA, co-Director of the Center for Cell Control, a NIH Roadmap Nanomedicine Development Center at UCLA, and Chair of the UCLA Intercollegiate Athletic Committee. He received the FOCIS/Millenium Pharmaceuticals Award for Genomics Research and a Leukemia and Lymphoma Society Scholar Award. In 2004 he was elected to the American Society of Clinical Investigators (ASCI) and in 2008 was a Stohlman Scholar of the Leukemia and Lymphoma Society. Dr. Teitell develops new imaging and nanomechanical approaches to study development and cancer of the immune system and utilizes feedback control algorithms to find optimal combinatorial therapies. His group generated the first genetic model that accurately resembles the majority of lymphocyte cancers afflicting humans.

Session IV: Friday, October 23, 10:40 a.m.

Drug and Gene Delivery in Nanomedicine

Session IV Chairs

Dean Ho
Assistant Professor, Departments of Biomedical and Mechanical Engineering, Northwestern University

Biography: Dr. Dean Ho is an Assistant Professor in the Departments of Biomedical Engineering and Mechanical Engineering in the Robert R. McCormick School of Engineering and Applied Science, and member of the Robert H. Lurie Comprehensive Cancer Center of Northwestern University where he directs the Laboratory for Nanoscale Biotic-Abiotic Systems Engineering (N-BASE).

Dr. Ho investigates the scalable fabrication of nanomaterial-based devices for applications in chemotherapy, anti-inflammation, and regenerative medicine. His research has garnered news coverage on the CNN homepage, Nature, Reuters, Yahoo, ABC News, CNBC, MSNBC, The Chicago Tribune, USA Today, United Press International. Additionally, Dr. Ho was featured in the National Geographic Channel program 'Known Universe'. He is the Editor-in-Chief of the Journal of the Association for Laboratory Automation and an associate editor of both the Journal of Biomedical Nanotechnology and Journal of Nanotechnology Law and Business.

Dr. Ho has published more than 100 peer-reviewed journal and proceedings papers in the areas of nanomedicine and drug delivery, and has delivered several plenary and keynote lectures as well as over 50 invited talks. Dr. Ho is a recipient of the National Science Foundation CAREER Award, Wallace H. Coulter Foundation Early Career Award in Translational Research, V Foundation for Cancer Research V Scholar Award, John G. Bollinger Young Manufacturing Engineer Award of the Society of Manufacturing Engineers, and Distinguished Young Alumnus Award of the UCLA School of Engineering and Applied Science.

Alexander V. Kabanov
University of Nebraska Medical Center

Biography: Alexander Kabanov is a Parke-Davis Chair in Pharmaceutics and the Director of the Center for Drug Delivery and Nanomedicine at the University of Nebraska Medical Center (UNMC), Omaha, Nebraska, United States. He obtained M.S. degree in chemistry in 1984 and Ph.D. degree in chemical kinetics and catalysis in 1987 in the department of Chemical Enzymology at M.V. Lomonosov Moscow State University (MSU), USSR. In 1990 at the age of 28 he was awarded Doctor of Chemical Sciences degree from MSU.

In 1988-1989 while working in Soviet Union he pioneered use of polymeric micelles for drug delivery to the brain and was among the first to develop DNA/polycation complexes for gene delivery ("polyplexes"). His work using amphiphilic block copolymers to overcome multidrug resistance in cancer led to human clinical trials of polymeric micelle doxorubicin. In 1993 Dr. Kabanov moved to Montreal, Canada, where he co-founded Supratek Pharma Inc. (www.supratek.com), which develops innovative therapeutics for treatment of cancer. Next year he joined the College of Pharmacy, UNMC in the United States, where he investigated interactions of block copolymers in blood-brain barrier to increase drug transport to the central nervous system (CNS) and developed unique chemical modifications of proteins that increase their transport to the brain. He also invented nanogels and nanosized block ionomer complexes and demonstrated their utility in pharmaceutics for delivery of biomacromolecules and small molecules to treat cancer and neurodegenerative diseases. He pioneered the field of "polymer genomics" that investigates effects of polymers and nanomaterials on cellular responses to biological agents to develop safe and efficient therapeutic modalities.

Dr. Kabanov published over 180 scientific papers, edited 5 books and journal issues and was named an inventor or co-inventor on 24 US patents and over 100 patents worldwide. His work was cited over 6,800 times. He chaired numerous scientific meetings, including a Gordon Research Conference on Drug Carriers in Medicine and Biology in 2006 and initiated the International Nanomedicine and Drug Delivery Symposium series (www.nanoodds.org) held annually since 2003-. He also served a program chair of Controlled Release Society Annual Meeting in 2007 and a chair of the Biomaterials and Biointerfaces Study Section at the National Institutes of Health (NIH) in 2006-2008. He is a co-founder and sits of the boards of three companies.

Dr. Kabanov is a recipient of the highest USSR award for young scientists, the Lenin's Komsomol Prize in 1988, the United States National Science Foundation (NSF) Career Award in 1995 and the NSF Special Creativity Award in 2002. He was named the UNMC Distinguished Scientist in 2006 and received the highest scientific award in the University of Nebraska, the Outstanding Research and Creativity Award in 2007. His research is supported by multiple grants from the NIH, NSF and US Department of Defense and he is a director of $ 10.6 M NIH Center of Biomedical Research Excellence in the field of Nanomedicine. Dr. Kabanov has given over 230 plenary, keynote and other invited lectures at conferences, academia and industry including 6 invited lectures at the Gordon Research Conferences.

"Multifunctional Nanosystems for Cancer Diagnosis and Therapy"

Mansoor Amiji
Professor and Acting Chair, Department of Pharmaceutical Sciences
Co-Director, Nanomedicine Education and Research Consortium (NERC)
Northeastern University

Abstract: There has been tremendous recent interest in nanotechnology application for cancer prevention, diagnosis, and treatment. In cancer therapy, overcoming biological barriers and target specific delivery are the key challenges. Furthermore, newer generation of molecular therapies, such as gene therapy oligonucleotides, and RNA interference, will require intracellular delivery strategies for effective outcomes.

In this presentation, I will provide an overview of our work in the area of multifunctional nanotechnology for cancer diagnosis and therapy. We have developed metal-, polymer-, lipid-based nanoplatforms for early disease diagnosis as well as targeted drug and gene delivery systems. Metal nanoparticles, primarily based on gold and iron oxide allow for cellular tracking, imaging, and delivery potential. Using biodegradable polymers, we have formulated nanocarriers for systemic delivery of hydrophobic anticancer drugs and therapeutic genes. Lastly, we have developed nanoemulsions, using oils rich in polyunsaturated fatty acids, which can facilitate drug delivery across different biological barriers, such as the blood-brain barrier.

Biography: Dr. Mansoor Amiji is Professor and Acting Chair of the Pharmaceutical Sciences Department, School of Pharmacy at Northeastern University in Boston. He is also the Co-Director of the Nanomedicine Education and Research Consortium (NERC). NERC oversees a doctoral training program in Nanomedicine Science and Technology that is co-funded by the NIH and NSF.

Dr. Amiji received his undergraduate degree in pharmacy from Northeastern University in 1988 and his Ph.D. in pharmaceutics from Purdue University in 1992. His areas of specialization include polymeric biomaterials, advanced drug delivery systems, and nanomedical technologies. He has three published books, *Applied Physical Pharmacy* (McGraw-Hill, 2003) and *Polymeric Gene Delivery: Principles and Applications* (Taylor & Francis, 2005) and *Nanotechnology for Cancer Therapy* (Taylor & Francis, 2007), along with over 150 published articles and conference proceedings. Dr. Amiji has received sustained funding from the National Institutes of Health, National Science Foundation, foundations, and private companies to support research activities in his laboratory. He is also an inventor of over 10 U.S. utility patent and patent applications. Dr. Amiji has received a number of awards including the 2007 American Association of Pharmaceutical Scientist's (AAPS) Meritorious Manuscript Award and AAPS Fellowship.

"Nanotherapeutics – Novel Delivery Technologies and FDA Regulatory Challenges"

Raj Bawa
Bawa Biotech Consulting
Rensselaer Polytechnic Institute

Abstract: In today's global economy, pharmaceutical companies are under enormous pressure to maintain profitability in light of numerous challenges ranging from revenue losses due to patent expirations on blockbusters to enhanced regulatory oversight to an ever-increasing challenge from generic manufacturers. These numerous market forces and drivers are dictating a change in pharma's quest for discovering, developing and delivering novel therapeutics. Clearly, new ground rules and competitive business strategies will be needed in the post-blockbuster world. As a result, pharmaceutical companies are turning to miniaturization and nanotechnology to enhance or supplement drug target discovery and drug development. In fact, nanomedicine is already influencing the pharmaceutical industry especially in the design, formulation and delivery of "nanotherapeutics." Nanotherapeutics are a relatively new class of therapeutic-containing nanomaterials that often have unique "nanoproperties" (physiochemical properties) due to their small size compared with their bulk-phase counterparts, high surface-to-volume ratio and the possibility of modulating their properties. They are, in essence, nanoparticles intended for a broad spectrum of clinical therapeutic applications. Nanotherapeutics present novel reformulation opportunities for active agents (e.g., small molecule drugs, proteins, nucleic acids, etc.) that were previously unsuitable for traditional oral or injectable drug formulations could now be "nanoformulated" for site-specific delivery due to superior pharmacokinetics/pharmacodynamics and/or active intracellular delivery. As a result, this approach has the ability to reduce toxicity and enhance bioavailability, thereby improving efficacy and patient compliance. Nanotherapeutics can also increase drug half-life by reducing immunogenicity and diminishing drug metabolism. With these advantages, nanotherapeutics have the ability to extend the economic life of proprietary drugs, thereby creating additional revenue streams. In fact, a large number of FDA-approved nanotherapeutics are on the market with many more poised to receive regulatory approval. Investors have been cautious as to what route, if any, the FDA will take in regulating nanotherapeutics in the future. Undoubtedly, regulating nanotherapeutics will require greater cooperation between drug companies, policymakers and drug regulators. Although the FDA has previously downplayed safety issues of nanoscale products, it is starting to recognize that there are knowledge gaps in this area. In light of these challenges, a multidisciplinary team of experienced drug regulators from the drug, biologic and device areas of the FDA (working with a scientific panel of experts), should: (a) identify unique safety issues associated with nanotherapeutics; (b) develop a new paradigm

for evaluating data pertaining to their safety and efficacy; and (c) assist in developing unique tools and techniques to characterize nanoscale materials (with an eye on quality, safety and effectiveness). Generally, nanotherapeutics will be viewed by the FDA as technologically overlapping from a review perspective. Therefore, they will be considered "combination products," for which established examination guidelines are already in place.

Biography: Dr. Raj Bawa is President of Bawa Biotechnology Consulting LLC, a biotechnology and patent law firm founded in 2002 and based in Ashburn, Virginia. He is a biochemist and microbiologist by training and is a registered patent agent licensed to practice before the US Patent and Trademark Office (PTO). Currently, Dr. Bawa is an Adjunct Associate Professor at Rensselaer Polytechnic Institute in Troy, New York, where he is an Advisor to the Office of Technology Commercialization. Previously he held various positions at the PTO, including Primary Examiner (6 years); Supervisory Patent Examiner (acting); and Instructor at the US Patent Academy. He has authored 65 scientific, legal and business publications. He is a Life Member of Sigma Xi, Founding Director and Secretary (acting) of the American Society for Nanomedicine, Advisory Board Member for the Albany Law School Center for Law & Innovation and serves on the Global Advisory Council of the World Future Society. Presently, Dr Bawa serves on the editorial boards of the following peer-reviewed journals: *International Journal of Nanomedicine*, *Cancer Nanotechnology: Basic, Translational and Clinical Research, Recent Patents on Biomedical Engineering, Nanotechnology Law and Business*. He is an Associate Editor of two peer-reviewed journals, *Journal of Bionanoscience* and *Nanomedicine: NBM.* He is a Co-Editor of *Clinical Nanomedicine - from Bench to Bedside* (Pan Stanford Publishing, 2010), *Nanotechnology - Law, Business and Commercialization* (Pan Stanford Publishing, 2010) and the Section Editor of the *Biomedical Engineering Handbook, 4th edition* (CRC Press/Taylor Francis, 2011). Some of Dr. Bawa's awards include - Innovations Prize from the Institution of Mechanical Engineers, London, UK (2009); Appreciation Award from the Undersecretary of Commerce, Washington, DC (2001); Talbot Travel Award of the US Biophysical Society (1988); Research Fellowship and Teaching Assistantship from Rensselaer (1985-90); Director's Award (2001) and Key Award (2005) from Rensselaer's Office of Alumni Relations.

"A Tumor- Targeting Nanodelivery Platform on Trial"

Esther H. Chang
Professor, Department of Oncology, Lombardi Comprehensive Cancer Center
Georgetown University Medical Center

Abstract: A platform nanodelivery system has been developed comprising a self assembled, biodegradable, cationic liposomal nanoparticle, which bears targeting molecules that home to receptors, such as the transferrin receptor, on the surface of tumor cells. When systemically administered, this

nanocomplex can efficiently and selectively deliver nucleic acid-based molecular therapeutics, diagnostic MRI contrast agents, and small molecules to not only primary tumors, but also metastases. The nanodelivery of imaging agents results in a marked improvement in the sensitivity and resolution in detection of minute metastatic lesions. Use of this nanocomplex for gene therapy has been shown to dramatically sensitize a number of human tumors, including prostate cancers, in mouse models to radiotherapy and chemotherapy. This synergy has resulted in long term tumor elimination and life span prolongation in the animals. Based upon our pre-clinical data, we hypothesize that this combinatorial approach could ultimately result in lower effective doses of both radiation and chemotherapy, thus reducing the current adverse side effects of these standard treatments.

This nanodelivery system, carrying the human tumor suppressor gene p53, has now entered a Phase I clinical trial as a single agent; the trial is nearing completion. Minimal side effects have been noted. The updated trial data will be reported.

Biography: Professor Esther H. Chang has served as a professor in the Departments of Oncology and Otolaryngology at the Lombardi Comprehensive Cancer Center of Georgetown University Medical Center since 1996. Before joining Georgetown University, Dr. Chang held positions in the National Cancer Institute, as a professor in the Department of Surgery at Stanford University, and as a professor in the Departments of Pathology and Surgery at the Uniformed Services University of the Health Sciences. Dr. Chang is also the interim President of the American Society for Nanomedicine.

Dr. Chang has been a pioneer and contributor to understanding genetic influences on both the development and suppression of cancerous tumors, as well as to understanding the tumor's resistance to radio/chemotherapy. More recently, her research has focused on the application of a nanodelivery platform in cancer therapy, diagnosis and prevention. When systematically administered, this nanocomplex can efficiently and selectively deliver nucleic acid-based molecular therapeutics, diagnostic MRI contrast agents, and small molecules to not only primary tumors, but also metastases in animal models of a number of human cancers. The tumor targeting delivery of various molecular therapeutics has also been shown to dramatically synergize with conventional radio- and chemotherapies. This approach is now in Phase I clinical trials.

Dr. Chang has over 130 publications and has served as a member of a number of scientific advisory boards for the National Cancer Institute, NASA, the US Military Cancer Institute, and the Department of Energy.

"Nanodiamond-Based Therapeutic Delivery Vehicles for the Treatment of Cancer"

Dean Ho
Assistant Professor, Departments of Biomedical and Mechanical Engineering, Northwestern University

Abstract: Nanodiamonds (NDs) possess multiple properties that enable their application as versatile drug delivery vehicles. For example, they can be functionalized with a broad array of therapeutics which includes small molecules, proteins, antibodies, and RNA/DNA for applications in cancer treatment, cardiovascular medicine, wound healing, and beyond. In addition, NDs possess uniform dimensions (~4nm in diameter per particle) and material stability that are coupled with observed biocompatibility in vitro and in vivo. Furthermore, NDs can be batch purified and functionalized for scalable and high yield processing. Among other functional groups, NDs also possess an abundance of surface-bound carboxyl groups which are conducive towards facile, application-dependent molecular linking/conjugation onto the diamond surface. Furthermore, NDs can be functionalized with additional chemical species to enable direct drug conjugation. Our previous studies have confirmed robust drug binding to NDs through transmission electron microscopy (TEM) and Fourier transform infrared spectroscopy (FTIR) coupled with in vitro tracking of cellular internalization and quantitative demonstration of bio-amenable cell response through quantitative real time polymerase chain reaction (RT-PCR) assays of inflammatory and apoptosis-regulating gene expression programs. Furthermore ND-mediated drug release against HT-29 and Raw 264.7 cell lines has also been observed. Towards the broadening of ND applicability in clinically-significant treatment scenarios, recent work pertaining to ND-based microfilm device formation for localized chemotherapy, pH-dependent therapeutic protein release, and pre-clinical efficacy and safety trials will be discussed.

"Polymeric Micelles: From Bench to Bedside"

Alexander V. Kabanov
University of Nebraska Medical Center

Abstract: Polymeric micelles have attracted major attention as nanocontainers for drug delivery. They were first introduced for this purpose in 80'-ies by the work of H. Ringsdorf, K. Kataoka and our group. Initial studies focused on polymeric micelles self-assembled from amphiphilic block copolymers containing hydrophilic and hydrophobic blocks. Such micelles represent small (10 to 100 nm) core-shell structures with the core formed by segregated hydrophobic blocks and the shell formed by hydrophilic blocks. Drug molecules are incorporated into the cores of the micelles either by covalent attachment through cleavable linkers or non-covalently through

solubilization. The latter approach is currently the most widespread with several polymeric micellar drug formulations undergoing clinical trials for treatment of cancer and other diseases. Many more polymeric micelle systems are undergoing preclinical development. Latest developments in this field include polymeric micelles with engineered cores that carry hydrophobic drugs, such as paclitaxel, with unprecedentedly high loading capacity of 45% wt. - 100 times greater than loading of commercial Taxol® formulation. Furthermore, ionic drug molecules as well as biomacromolecules are incorporated into micelle cores by electrostatic complexation with block ionomers of opposite charge. Such block ionomer complex micelles have been used for delivery of DNA, siRNA and proteins. The cross-linking of the micelle core or shell by biodegradable cross-links is used to stabilize polymeric micelles in circulation, yet to ensure micelles degradation and payload release in the target cells. Of particular interest are micelles with cross-linked polyion cores, which are swollen in water but collapse upon binding a drug. Such micelles display selective entry in cancer cells but not in normal epithelial cells due differential endocytic pathways in these cells. Following caveolae mediated endocytosis in the cancer cells they bypass the early endosomes and accumulate in lysosomes where they release drug in a pH-dependent fashion. Hence micelles loaded with a cytotoxic drug are toxic to cancer cells but not to normal epithelial cells, where they do not enter. Another remarkable example of phenotypic selectivity of polymeric micelle delivery system is "hypersensitization" of multidrug resistant (MDR) by Pluronic block copolymers. A Pluronic-based micellar formulation of doxorubicin, SP1049C, has completed Phase II clinical trial. *In vitro* and *in vivo* studies demonstrate that Pluronic block copolymers 1) selectively induce ATP depletion by inhibiting respiration in mitochondria of MDR1 cells, 2) inhibit P-glycoprotein (Pgp) drug efflux pump and 3) activate pro-apoptotic signaling in drug resistant cells in response to the drug. This results in a powerful modality for killing drug resistant tumors. Altogether, during last two decades polymeric micelles have greatly advanced from initial laboratory investigation towards clinical use for therapy of cancer and other devastating human diseases.

Session V: Friday, October 23, 1:40 p.m.

Diagnostics: Imaging and Biosensors

Session V Chairs

James L. Tatum
Associate Director, Division of Cancer Treatment and Diagnosis
National Cancer Institute, National Institutes of Health

Biography: Dr. Tatum began his career as a nuclear medicine physician specializing in nuclear cardiology. His early research focused on imaging of alterations in the pulmonary capillary membrane associated with ARDS and the application of imaging techniques to evaluate drug therapy. Later in his career, his focus shifted to studies of myocardial ischemia including acute coronary syndrome. This remains an active area of publication, especially as related to the use of imaging in medical decision making in the acute setting. In 1998 Dr. Tatum began collaboration with the Cancer Imaging Program at NCI applying his experience and expertise to oncology in two areas of interest that underpin his earlier work – drug development and the application of molecular and functional imaging to clinical decision making.

Dr. Tatum received his undergraduate degree in Biology from the College of William and Mary and his M.D. from the Medical College of Virginia. He completed his residency in Medicine and Radiology at MCV Hospitals, followed by a Nuclear Medicine fellowship at Duke University. He is board certified in Diagnostic Radiology, Nuclear Medicine, and Nuclear Cardiology. In 1978, he joined the faculty of Virginia Commonwealth University, where he was ultimately appointed Professor of both Radiology and Medicine (Cardiology). During his tenure at VCU, he served as the Chairman of the Division of Nuclear Medicine, Director of Nuclear Cardiology, Chairman of the Department of Radiology, Associate Vice President for Health Sciences, and Director of the Molecular Imaging Center. In 2006 he accepted the position of Chief of the Molecular Imaging Branch in the Cancer Imaging Program and in 2008 was appointed Associate Director in the Division of Cancer Treatment and Diagnosis at the National Cancer Institute.

Greg Lanza
Professor of Medicine and Bioengineering, Washington University

Biography: Dr. Lanza is Professor of Medicine and Bioengineering at Washington University in St. Louis with over 250 original publications, abstracts, and patents across multiple disciplines. He received his Ph.D. from the University of Georgia School of Agriculture and joined Monsanto Company in1981, where he established and directed the preclinical research

program supporting the development a 14-day parenteral, controlled release recombinant DNA product, which is marketed today as Posilac ®.

In 1988, Dr. Lanza matriculated at Northwestern University Medical School in Chicago, where he received an MD degree in 1992 and developed expertise in cardiac ultrasonic imaging and patented the first acoustic molecular imaging agent. He completed residency in Internal Medicine and fellowship in Cardiology at Barnes-Jewish Hospital at Washington University School of Medicine. In 1994, as a fellow he joined Dr. Samuel Wickline's new lab and they co-invented a new perfluorocarbon based, ligand-targeted contrast agent, which has been broadly patented for use as a multimodality molecular imaging agent as well as for targeted drug delivery platform. Dr. Lanza joined the WU faculty in 1999. Greg, Sam and coworkers have since developed and patented a myriad of novel nanomedicine agents and related technologies.

Dr. Lanza is the recipient of numerous awards for research excellence. He is an established principal investigator of the NIH. Dr. Lanza is co-Director of the Consortium for Translational Research in Advanced Imaging and Nanomedicine (C-TRAIN) where his research focuses on developing new nanomedicine tools and converting these tools into translatable solutions for medical problems in the fields of oncology, cardiology, rheumatology, and ophthalmology.

"Tumor Specific Nanodelivery of Contrast Agents Enhances Early Detection of Lung and Pancreatic Tumors"

Matthew Freedman
Department of Oncology, Georgetown University

Abstract: We have developed a nanosized (~100 nm) immunoliposome complex for delivery of molecular medicines to tumors. In this complex, an anti-transferrin receptor single-chain antibody fragment (TfRscFv) decorates the surface of a cationic liposome encapsulating the payload. In the research reported here, gadopentetate dimeglumine or superparamagnetic iron oxide were placed within the liposome to serve as magnetic resonance imaging contrast agents. These agents were formulated in an attempt to overcome specific clinical imaging challenges: 1. the detection of small pancreatic carcinomas; 2. the early detection of metastases to the lungs. Imaging studies employing our tumor-targeting nanocomplex in mice demonstrated that these novel nanocomplexes carrying contrast agents resulted in increased uptake and prolonged presence in the tumor cells, even in lung nodules as small as 100um, than conventional uncomplexed MR contrast agents.

Current commercial CT and MRI contrast agents provide dynamic enhancement based on tumor perfusion and diffusion of the contrast agents into the interstitial spaces of tumors; they are not tumor specific. When contrast is delivered via the transferrin targeting liposomes, malignant tumors are highly selectively enhanced.

The presentation will provide the background information on these nanocomplexes, images of tumor enhancement and graphs of the dynamic inflow and washout after iv injection of the nanocomplexed contrast agents compared to conventional uncomplexed contrast agents.

Biography: Matthew T. Freedman came to Georgetown in 1988 as Associate Professor of Radiology. He moved to the Department of Oncology in 2003. He does research on the use of medical imaging for the early detection of lung and breast cancer: (1) how to obtain the image that is best for showing the presence or absence of early cancer and (2) how to assure that the radiologist will detect what is on the image. Since 1967, he has received three medical school awards for teaching medical students, has been Program Director of one and Education Director of a second Radiology Residency, has mentored engineering graduate students, written two books, 12 chapters, 71 peer reviewed publications, 137 editor reviewed meeting papers and many abstracts. Prior to his move to Oncology, he led clinical divisions of Pulmonary Radiology and Musculoskeletal Radiology. From 1992 to 2004, he was Clinical Director of the Imaging Science and Information Systems (ISIS) Research Center.

"Visualizing Cell Movement One Molecule at a Time"

Cathy Galbraith
National Institutes of Health

Abstract: Cell migration choreographs morphogenesis, directs immunological responses, and underlies the spread of diseases such as the metastasis of cancer. Many of the processes guiding cell migration have been described. However, the mechanisms regulating the dynamic assembly and nanoscale organization of the sub-cellular molecular machinery responsible for directed movement are largely unknown. One of our approaches to identifying these mechanisms is the development of novel imaging and biophysical assays to visualize the dynamics of individual adhesion and cytoskeletal molecules in cells exploring their microenvironment while searching for preferred directions for migration. By advancing superresolution microscopy into multi-colors, living-cells, and 3D, we have developed the tools needed to determine the structure of the actin cytoskeleton as it probes the surroundings, the nanoassembly of proteins into adhesive scaffolds that bind to the surroundings, and the molecular organization of the signaling and structural proteins within the adhesive scaffolds. Analyzing the dynamic assembly and regulation of the individual molecules within these large protein ensembles can reveal the mechanisms governing why cells choose specific paths for migration and guide our development of therapeutic strategies for controlling migration.

Biography: Dr. Catherine Galbraith received her PhD in Bioengineering from the University of California, San Diego. She did her post-doctoral work in the laboratory of Dr. Michael Sheetz in the Cell Biology Department at Duke University before joining the National Institutes of Health in Bethesda, Maryland as a research fellow. Dr. Galbraith recently established her own lab at NIH to explore how interactions with the local microenvironment guide cell movement. One of the lab's approaches is to combine biophysical assays and live-cell imaging to analyze the spatial and dynamic interactions of the individual molecules as they organize into the signaling and structural scaffolds that become the nanomachines cells use for sensing and movement. This work relies heavily on the lab's recent advances in multi-color, live-cell, and three-dimensional superresolution microscopy. Her research into these mechanisms underlying why cells choose specific paths for migration will help guide the development of therapeutic interventions to control migration. Dr. Galbraith has been the recipient of the Bioengineering Society Young Investigator Award and a 2008 NIH Director's Challenge Award.

"Molecular Photoacoustic Imaging with Gold Nanobeacons"

Greg Lanza
Professor of Medicine and Bioengineering, Washington University

Abstract: Photoacoustic (PA) tomography (PAT) can enhance traditional ultrasound assessments of cancers, cardiovascular diseases, and skin diseases by affording noninvasive microvasculature visualization based on circulating hemoglobin in red blood cells. Although the signal derived inherently from hemoglobin is very high, we have developed novel lipid-encapsulated gold nanobeacons. These 140 nm emulsions incorporate numerous gold particles (2-4 nm) into the core of (GNB), providing 1080 μg gold/g of 20% colloid suspension. GNB provides 15-fold increase ($p<0.05$) in PA signal over blood in vitro. PAT signal from human fibrin-rich clot studied in vitro was increased significantly with the fibrin-targeted GNB versus control ($p<0.05$). In experiments with sentinel lymphnode (SLN) imaging, nontargeted GNB injected intradermally produced marked enhancement of SLN and the second LN. In rodent Matrigel plug angiogenesis models, high frequency PAT clearly delineated the established and nascent microvasculature. However, following the intravenous administration of targeted GNB, forming angiogenic sprouts were visualized distinctly arising from more established microvessels in a tree-branching architecture. Previous research has shown that even a single column of erythrocytes can be detected with PAT. These data strongly suggest that the integrin-targeted GNB recognized the primordial stages of neovessel formation, before endothelial polarization within the developing vessel wall and interconnected (arterial-venous) tube formation was complete. Nanomedicine markedly enhances the clinical potential and applications of hand-held PAT, particularly when used in combination with novel image-based targeted drug delivery.

"Evolving Role of Imaging in Oncology Drug Development"

James L. Tatum
Associate Director, Division of Cancer Treatment and Diagnosis
National Cancer Institute, National Institutes of Health

Abstract: While increasing information from the "omics" revolution has added to the wealth of data from the last two decades of advances in molecular biology, the promise of more effective and safer therapies for cancer in reality has been disappointing. Pharmaceutical companies who embraced the promise of the "one-gene, one-drug, one-disease paradigm are being forced to reconsider this strategy amidst increasing development costs, unacceptable late phase failures, and a paucity of drug approvals. While there are no simple answers it is clear that the 'magic bullet' concept fails to account for the complex systems biology that exists within human cancers. In this presentation we will review the current oncology drug pipeline with special attention to the role imaging currently plays in drug development and the opportunity that imaging could play in reversing the current trend. We will also address the issues related to imaging probe development which will need to parallel that of the aligned therapeutic in the future if this opportunity is to be realized. Lastly we will examine the potential for the future application of imaging to unraveling the complex systems biology of cancer which clearly has become the nemesis of rational drug development.

"Dendrimer Based Nano-Containers/Scaffolding for Targeted Imaging and Therapies"

Donald Tomalia
Central Michigan University,
The National Dendrimer & Nanotechnology Center

Biography: Dr. Tomalia received his B.A. in chemistry from the University of Michigan and while at The Dow Chemical Company completed his Ph.D. in physical-organic chemistry from Michigan State University under the mentorship of Professor Harold Hart. His discovery of the cationic polymerization of 2-oxazolines led to two international industrial research awards (R&D-100) for creative research in 1978 and 1986. His discovery of dendrimers (dendritic polymer architecture) in 1979 led to a third R&D-100 Award in 1991 and the Leonardo da Vinci Award (Paris, France) in 1996. He received the Society of Polymer Science Japan (SPSJ) Award for Outstanding Achievement in Polymer Science (2003) for discovery of the fourth major macromolecular architectural class, *dendritic polymers*.

In 1990, he joined the Michigan Molecular Institute (MMI) as Professor and Director of Nanoscale Chemistry & Architecture (1990-99). Dendritech, Inc., the first commercial producer of dendrimers, was co-founded by Dr. Tomalia in 1992 after which he was named founding President and Chief

Scientist (1992-2000). He became V.P. of Technology for MMI (1998-2000) while simultaneously serving as Scientific Director for the Biologic Nanotechnology Center, University Michigan Medical School (1998-2000). Dr. Tomalia founded Dendritic Nanotechnologies, Inc. (DNT), Mt. Pleasant, Michigan, in a joint venture with Starpharma Pooled Development (Melbourne, Australia) (2002) and served as President/Chief Scientific Officer and Company Director (2002-2007).

Currently, he is *Director* of The National Dendrimer & Nanotechnology Center and *Distinguished Professor/Research Scientist* at Central Michigan Campus (2007-). Other positions currently held by Dr. Tomalia include *Distinguished Visiting Professor*, Columbia University; *External Faculty*, University of Wisconsin-Madison (School of Pharmacy); *Chairman* - Peer Review Panel for Environmental Protection Agency (EPA) "*Nanotechnology White Paper*" (2006), Washington, D.C.; *Board of Directors,* American Society of Nanomedicine; *Advisory Board,* European Foundation for Nanomedicine and *Faculty Member*, Faculty 1000 Biology.

Abstract: Dendrimers are tuneable, soft nanoparticles that may be exquisitely designed and routinely synthesized as a function of their size, shape, surface chemistry and interior void space. They are obtained with structural control approaching that of traditional biomacromolecules such as DNA/RNA or proteins. This lecture will review the use of these tuneable features for both targeted imaging and drug delivery applications. Recent efforts have focused on the synthesis and preclinical evaluation of multi-purpose, STARBURST® poly(amidoamine) (PAMAM) dendrimer prototypes that exhibit suitable properties for use as: (a) passive targetable, diagnostic MRI contrast agents and/or (b) for controlled delivery of cancer therapies. Special emphasis will be placed on lead dendrimer scaffolding candidates; namely: [*core*: 1,4-diaminobutane]; (G=5 -6); {*dendri*-poly(amidoamine)-$(NH_2)_{64/128}$}which have been selected for their demonstrated targeting/imaging features and desirable kidney excretion properties which are briefly summarized below.

Session VI: Friday, October 23, 3:35 p.m.

Update on the International Society for Nanomedicine

Esther Chang
American Society for Nanomedicine

Kazunori Kataoka
Asian Society for Nanomedicine

Biography: Kazunori Kataoka, Ph.D., is a Professor of Biomaterials at Graduate School of Engineering, the University of Tokyo. He has been appointed joint position since 2004 from Graduate School of Medicine, the University of Tokyo as a Professor and a Chair of Division of Clinical Biotechnology at the Center for Disease Biology and Integrative Medicine. He also serves as Director of the Center for NanoBio Integration at the University of Tokyo, an interdisciplinary initiative sponsored by the Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan. He received B.Eng. (1974) degree in Organic Chemistry, and M.Eng. (1976) and Ph.D. (1979) degrees in Polymer Chemistry at the University of Tokyo. He held positions at the Institute of Biomedical Engineering, Tokyo Women's Medical College (1979-1989) and Department of Materials Engineering at Tokyo University of Science (1989-1998) before joining the faculty of the University of Tokyo in 1998. He was a Visiting Professor at University of Paris XIII, France (1992, 1996), Tohoku University, Sendai, Japan (2007), and Ludwig-Maximillians University (LMU), Munich, Germany (2008). He served as the Adjunct Director of the Biomaterials Center at the National Institute for Materials Science (NIMS), Japan between 2001-2004. He is a past president of the Japanese Society for Biomaterials (2004-2006), a president of Japanese Society of Gene Design and Delivery (2004-), a Vice President of the Society of Polymer Science, Japan (2008-), a Fellow of the American Institute of Medical and Biological Engineering (AIMBE) (1999-) and a Fellow of Biomaterials Science and Engineering (FBSE) (2004-). He was the recipient of several awards, including the Award of the Japanese Society for Biomaterials (1993), the Outstanding Paper Award of the Controlled Release Society (1995), the Award of the Society of Polymer Science, Japan (2000), Clemson Award in Basic Research, Society for Biomaterials, USA (2005), Barré Award, University of Montreal (2006), and Founder's Award of Controlled Release Society (2008). He has almost 400 publications and is on the editorial board of twelve international journals. He is the Editor of Journal of Biomaterials Science, Polymer Edition and the Associate Editor of Biomacromolecules (American Chemical Society). His current major research interests include supramolecular materials for nanobiotechnology, focusing on gene and drug delivery.

Beat Löffler
European Society for Nanomedicine

Biography: Beat Löffler, MA studied Communication Science and Philosophy and received his MA at Freie Universität Berlin. After working for 12 years in the new technology sector as conference organiser and creating concepts for emerging technology events he created in 1994 his own Company "Concept Engineering" and specialised in the fields of the development of innovation concepts and the development of science and knowledge promotion initiatives as well as to leadership-training and interdisciplinary bridging events. Fields of work are • Computational Fluid Dynamics • Materials Science, • Energy Technology and • Life Sciences. Beat Löffler had numerous mandates for by his company developed projects. He was the conceptor of the BioValley Initiative and was for 6.5 years its Sectretary General and Coach. Löffler worked for 4.5 years as life sciences business developer Europe for the Japanese company NEC High Performance Computing. In October 2006 he started the development of a concept for a conference for Applied Nanomedicine. He is co-founder of the European Foundation of Clinical Nanomedicine and of the European Society for Nanomedicine. He is CEO of the CLINAM-Foundation and Secretary General of the Society of Nanomedicine. He is a member of the board of the International Society for Nanomedicine. He is responsible for the Annual European Conference for Clinical Nanomedicine in Basel, Switzerland Beat Löffler is married and has 3 children.

Friday, October 23, 5:00 p.m.

Keynote Lecture 2

Introduction: Lajos Balogh, *U. of Buffalo*

"Power of Medical Nanotechnology: Delivery of Undeliverable Drugs"

Vladimir P. Torchilin
Department of Pharmaceutical Sciences and Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University

Abstract: Poorly soluble substances often represent promising drug candidates, however serious problems with their delivery in the body and preparation of bioavailable dosage forms of such substances prevents them from becoming real drugs. Various formulation strategies based on the use of nanocarrier systems have been suggested to overcome poor solubility of many drugs. Among such systems, polymeric micelles have drawn much attention. Micelles prepared from PEG-diacyllipids conjugates, such as PEG-PE, are of particular interest. Alternatively, a so-called layer-by-layer (LbL) technology (alternate coating of nanoparticles of poorly soluble drugs with layers of oppositely charged biocompatible soluble polymers) can also be applied to prepare stable nanocolloids of many poorly soluble drugs. In some cases, the use of nanopreparations is the only way to meet an unmet medical need. Thus, to keep contrast agent in the blood during the time sufficient for an effective CT imaging, one has to prepare long-circulating nanoparticles loaded with the contrast, such as heavily iodinated micelles. In other cases, poor stability of a potential drug in the body can represent a serious problem, such as in case of siRNA, and the use of nanocarriers may represent a possible solution. Polymeric micelles containing a hydrophobized derivative of siRNA can serve as a good example. Comparative analysis of various approaches for making deliverable dosage forms of "undeliverable" substances using nanotechnology approaches will be presented.

Biography: Vladimir P. Torchilin, Ph.D., D.Sc. is a Distinguished Professor of Pharmaceutical Sciences and Director, Center for Pharmaceutical Biotechnology and Nanomedicine, Northeastern University, Boston, Mass. He graduated from the Moscow University with MS in Chemistry, and also obtained there his Ph.D. and D.Sc. in Polymer Chemistry, Chemical Kinetics and Catalysis, and Chemistry of Physiologically Active Compounds in 1971 and 1980, respectively. In 1991 Dr. Torchilin joined Massachusetts General Hospital and Harvard Medical School as the Head of Chemistry Program, Center for Imaging and Pharmaceutical Research, and Associate Professor of Radiology. Since 1998 Dr. Torchilin is with Northeastern University. He was

there the Chair of the Department of Pharmaceutical Sciences in 1998-2008. His research interests have focused on biomedical polymers, polymeric drugs, immobilized medicinal enzymes, drug delivery and targeting, pharmaceutical nanocarriers for diagnostic and therapeutic agents, and experimental cancer immunology. He has published more than 300 original papers, more than 100 reviews and book chapters, wrote and edited 10 books, including *Immobilized Enzymes in Medicine*, *The Handbook on Targeted Delivery of Imaging Agents*, *Liposomes: A Practical Approach*, *Nanoparticulates as Pharmaceutical Carriers*, *Multifunctional Pharmaceutical Nanocarriers*, *Biomedical Aspects of Drug Targeting*, *Delivery of Protein and Peptide Drugs in Cancer*, and holds more that 40 patents. He is Editor-in-Chief of *Current Drug Discovery Technologies*, Co-Editor-in-Chief of *Drug Delivery* and on the Editorial Boards of many leading journals in the field including *Journal of Controlled Release* (Review Editor), *Bioconjugate Chemistry*, *Advanced Drug Delivery Reviews, European Journal of Pharmaceutics and Biopharmaceutics, Journal of Drug Targeting*, *Molecular Pharmaceutics, Journal of Biomedical Nanotechnology,* and few others. Among his many awards, Professor Torchilin was the recipient of the 1982 Lenin Prize in Science and Technology (the highest scientific award in the former USSR). He was elected as a Member of European Academy of Sciences. He is also a Fellow of American Institute of Medical and Biological Engineering and of American Association of Pharmaceutical Scientists (AAPS), and received the 2005 Research Achievements in Pharmaceutics and Drug Delivery Award from the AAPS and 2007 Research Achievements Award from the Pharmaceutical Sciences World Congress. In 2005-2006 he served as a President of the Controlled Release Society.

Session VII: Saturday, October 24, 8:20 a.m.

Nanomedicine for Neurological Disorders/ Translation in Nanomedicine

Session VII Chairs

Rutledge Ellis-Behnke
Faculty of Medicine, University of Hong Kong
Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology

Biography: Rutledge Ellis-Behnke is Associate Director of the Technology Transfer Office at the University of Hong Kong, as well as Associate Professor at the University's Li Ka Shing Faculty of Medicine: Department of Anatomy; State Key Lab for Brain and Cognitive Sciences; and Research Centre of Heart, Brain, Hormone and Healthy Aging. He is also a Research Affiliate in the Brain and Cognitive Sciences department at MIT. His primary research interest is using nanotechnology to reconnect the disconnected parts of the brain in order to restore function.

He received his PhD from MIT in Neuroscience, BS from Rutgers University and graduated from Harvard Business School's International Senior Manager's Program (AMP/ISMP).

Prior to returning to school to pursue his PhD, Ellis-Behnke held various management positions including Senior Vice President of Huntingdon, a public company for testing and consulting services and Co-founder/CEO in 1995 of one of the first internet companies to do online commerce.

Ellis-Behnke is Associate Editor/Neurology for the journal *Nanomedicine: Nanotechnology, Biology and Medicine*; member of both the Board of Directors and the Scientific Advisory Board for the Glaucoma Foundation; board member of the Asia Foundation for Cancer Research; founding board member of the International Society of Nanomedicine; member of the China Spinal Cord Clinical Trial Network, Society for Neuroscience, American Chemical Society, Association for Research in Vision and Ophthalmology and Sigma Xi, the scientific research society.

Technology Review named his "Nanohealing" discoveries one of the "Top 10 Emerging Technologies of 2007." His "Nano Neuro Knitting" and "Immediate Hemostasis" technologies have each been licensed for translation to humans.

In addition to his work in neuroscience and nanomedicine Ellis-Behnke introduced the TabletPC to MIT and the University of Hong Kong as part of the migration to the paperless classroom to deliver all course material and texts to the students digitally.

Thomas Webster
Associate Professor, Division of Engineering and Department of Orthopedics, Brown University

Biography: Thomas J. Webster is an associate professor for the Division of Engineering and Department of Orthopedics at Brown University. His degrees are in chemical engineering from the University of Pittsburgh (B.S., 1995) and in biomedical engineering from Rensselaer (M.S., 1997; Ph.D., 2000). Prof. Webster's research designs, synthesizes, and studies the use of nanotechnology for improving various implant applications (such as orthopedic, cartilage, vascular, bladder, and the central and peripheral nervous systems). His lab group has generated 6 books, 36 book chapters, 135 invited presentations, 385 literature articles and/or conference proceedings, and 345 conference presentations. His technology has resulted in two start-up companies. He is the founding editor-in-chief of the *International Journal of Nanomedicine* and he is on the editorial board 10 other journals. His research has appeared in the Boston and London Science Museums and on NBC, ABC, and PBS (on Dragon Fly TV).

"Controlling the Growth and Differentiation of Cells with Physical Interaction"

Rutledge Ellis-Behnke
Faculty of Medicine, University of Hong Kong
Department of Brain and Cognitive Sciences, Massachusetts Institute of Technology

Abstract: Within the emerging field of stem cells there is a need for an environment that can regulate cell activity to slow down differentiation or proliferation, in vitro or in vivo, while remaining invisible to the immune system. By manipulating the cell density and self-assembling nanofiber scaffold (SAPNS) concentration we can control the nano environment surrounding PC12 cells, Schwann cells and neural precursor cells (NPCs) and were able to control the proliferation, elongation, differentiation and maturation in vitro. We extended the method, using SAPNS, to living animals with implants in the brain and spinal cord demonstrating that a combination of SAPNS and young cells can be transplanted into a mammal, eliminating the need for immuno-suppressants. When cells are placed in a defined system it is possible to delay their proliferation, differentiation and maturation depending on the density of the cell population, density of the matrix, and the local environment.

"Coordinating Neural Stem Cell Function through Nanoengineering"

Lance Kam
Assistant Professor, Biomedical Engineering, Columbia University

Abstract: Development and maintenance of functional tissues relies on spatial coordination of stem cell function. Cells use local cues to read their environment, leading to differentiation of a pool of stem and progenitor cells and concurrent control over cell renewal and senescence. We have been developing micro- and nano-scale systems for capturing these cues outside the body, with the goal of integrating these factors together into an artificial stem cell niche. This talk will focus on mechanical forces and patterned biomolecules as powerful cues that regulate neural stem cell function. Further integration of these cues, along with materials defined at the nanoscale, will lead to new approaches for understanding stem cell biology and engineering of functional, long-lasting tissues.

Biography: Lance Kam is an Assistant Professor of Biomedical Engineering at Columbia University, focusing on applications of micro- and nano-scale technologies to cellular engineering. He earned his PhD in Biomedical Engineering at Rensselaer Polytechnic Institute, developing tools for directing assembly of neural networks. Further development of systems for patterning biomolecules were developed during his postdoctoral research at Stanford University (Chemistry) and his current position at Columbia University. He is part of the Nanotechnology Center for Mechanics in Regenerative Medicine, part of the NIH Nanomedicine Program. This center focuses on understanding how nano-scale effects, including structure and assembly of molecular complexes and mechanical rigidity, direct cell function, with particular emphasis on the adaptive immune system.

"Nanotechonology for Drug Delivery and Drug Targeting"

Barbara Rouzi
Researcher, Faculty of Pharmacy, University of Modena and Reggio Emilia

Abstract: The delivery of active substances is currently one of the most stimulating challenges due to the inability of conventional medicine to apply effective therapeutic strategies for the treatment of brain pathologies, including neurodegenerative diseases, brain tumors and HIV-related dementia as well as the application to other cancer diseases or leukemia. The use of nanodevices (ND), such as liposome (Lp), nanoparticles (Np) and solid-lipid nanoparticles (SLNp), have a long-time application as drug delivery systems.

Regarding brain delivery, it is notable that these systems, if not engineered, are totally unable to cross the healthy state BBB; thus, the role of

ND surface engineering surely represents the milestone for a promising future application in difficult-to-treat brain pathologies. These ND can be modified with specific ligands or, more generally, substances, able to increase their ability to cross BBB by means of specific mechanisms, such as absorptive-mediated transcytosis or receptor-mediated endocytosis. It is the case of specific peptides which have been conjugated with polymeric or lipidic nanodevices to allow a more selective drug delivery across the BBB, giving pharmacological evidences of the increase activity.

Regarding other liposomes application, these lipidic non viral vectors have deserved considerable attention, as they have been shown to efficiently incorporate a large variety of drugs, as well as of different biologically active molecules, such as proteins, plasmids, and siRNA/ODN (see background section). Additionally, the modification of the liposome surface with hydrophilic polymers such as polyethylene-glycol (PEG) does not only improve chemical stability of circulating drug-liposome formulations, but it also provides a natural support to conjugate specific ligands (e.g. monoclonal antibodies) on the nanocarrier surface and selectively direct the so-called immunoliposomes towards target cells. Considering the active role of the chronic infection in the development of cancer, the nanotechnological approach can be usefully applied to oncologic medicine, in particular to set up innovative strategies for the treatment of pathogen-associated diseases.

Biography: Dr. Barbara Ruozi is actually an academic researcher, belonging to Pharmaceutical Technology group, at the Faculty of Pharmacy, University of Modena and Reggio Emilia, Italy. She graduated in 1997 in CTF, Faculty of Pharmacy, University of Modena and Reggio Emilia and then developed a project on the delivery of FANS (Nimesulide), supported by HELSINN HEALTHCARE S.A. (Switzerland). From 1998 to 2001, she performed the Ph.D. course on "Scienze del Farmaco" and in 2001 the "Project Young Researcher" (Title: AFM use to characterize cationic liposomes"). From 2003 to 2004, she taught as fellowship and assistant professor for the degree course in Biotechnology and Pharmacy in the field of "Drug delivery and Drug targeting". Since 2005, she is assistant professor for the Faculty of Pharmacy, University of Modena and Reggio Emilia, Italy. Her scientific and research interests are mainly focused on the planning and development of novel pharmaceutical technologies to solve bioavailabilty limits of the drug, by using modified liposomes. AFM, SEM, confocal microscopy. Dr. Ruozi is author or co-author of more than 30 research articles, book chapters and reviews, published in international journal or book series. Moreover, her scientific production is based on more than 50 abstract for oral or poster communications.

"How and Why is Nanotechnology Increasing Neural Tissue Growth?"

Thomas Webster
Associate Professor, Division of Engineering and Department of Orthopedics, Brown University

Abstract: Much work is needed to design more effective tissue engineering materials for all organs. Frequently, current implants (for example, for the nervous system, bone, vascular, bladder, etc.) fail due to insufficient integration into juxtaposed tissues. Nanotechnology offers exciting alternatives to traditional implants since our tissues are composed of constituent nanostructured components. For example, bone is composed of nanofibered hydroxyapatite well-dispersed in a mostly collagen matrix. Thus, it stands to reason that cells are accustomed to interacting with nanostructured (not conventionally-structured) surfaces. Moreover, nanostructured materials have unique surface properties (such as energy, wettability, topography, etc.) that make them intriguing for applications involving interactions with proteins and subsequently cells. For these reasons, the objective of the present study was to design, synthesize, and test (using in vitro and in vivo analysis) nanostructured materials for various neural applications. To date, we have synthesized novel nanophase (that is, materials with dimensions less than 100 nm in at least one direction) ceramics, metals, polymers, and composites thereof using a wide range of techniques including chemical vapor synthesis, chemical vapor deposition, severe plastic deformation, anodization, chemical etching, etc. Examples of some materials tested include nanospherical alumina, titania, carbon nanofiber/nanotubes, c.p. Ti, Ti6Al4V, CoCrMo, poly-lactic-co-glycolic acid, poly-ether-urethane, and polycaprolactone. Importantly, increased responses from neurons and decreased responses from glial scar tissue forming cells have been observed on nanophase compared to conventional materials no matter what chemistry was tested or what route was used to synthesize such materials. Recently, increased in vivo motor functions have been observed when using a combination therapy of carbon nanotubes and stems injected into stroke-induced rats. In this manner, the present studies demonstrating increased tissue regeneration on nanophase compared to conventional materials suggest that nanophase materials should be further studied for a wide range of implant applications.

Session VIII: Saturday, October 24, 10:20 a.m.

Nanomedicine Inventions – Patents, Business and Commercialization

Session VIII Chairs

Brian Del Buono
Sterne, Kessler, Goldstein & Fox

Biography: Dr. Del Buono is a director in the Biotechnology/Chemical Group at the Washington, DC law firm of Sterne, Kessler, Goldstein & Fox PLLC, where he represents a diverse group of U.S. and international clients drawn from a variety of sectors of the biotechnology, pharmaceuticals, nanotechnology, chemicals and fast-moving consumer goods industries. He provides counseling with regard to patent portfolio strategy and management with issues that range from licensing, collaborations and technology acquisitions, to patent validity, infringement and design-around strategies. His practice also involves U.S. and international patent procurement and enforcement IP due diligence investigations, and providing opinions relating to patent infringement, validity and freedom-to-operate. Dr. Del Buono's practice also works with industrial clients on the intellectual property aspects of corporate strategic planning and product lifecycle management.

Prior to joining Sterne Kessler, Dr. Del Buono obtained extensive experience in biotechnology, pharmaceuticals and biomedical research and development in the academic and corporate settings. He obtained his M.S. and Ph.D. degrees in Microbiology and Cell Biology from The Pennsylvania State University, and his J.D. degree (*cum laude*) from Georgetown University, and is admitted to practice before the U.S. Patent and Trademark Office and is a member of the bars of Virginia, the District of Columbia, the U.S. Supreme Court, the U.S. Court of Appeals for the Federal Circuit and the U.S. Court of Appeals for the Fourth Circuit.

Raj Bawa
Bawa Biotech Consulting
Rensselaer Polytechnic Institute

"Nanomedicine Inventions and Patents – A Primer"

Raj Bawa
Bawa Biotech Consulting
Rensselaer Polytechnic Institute

Abstract: Nanomedicine is part of the high risk, high payoff global nanotechnology phenomenon. As companies develop nanomedicine technologies, securing valid and defensible patent protection will be vital to

their long-term survival. Without the market exclusivity offered by a patent, development of these products and their commercial viability in the marketplace will be significantly hampered. However, the US Patent and Trademark Office (PTO) continues to be in a state of crisis. Take the classic example of the emerging thickets of nanopatent claims in various technologies, resulting primarily from patent proliferation as well as continued issuance of surprisingly broad patents by the PTO. This is creating a chaotic, tangled patent landscape where the competing players are unsure of the validity and enforceability of numerous issued patents. If this trend continues, it could further stifle competition and limit access to some inventions. Therefore, reforms are urgently needed at the PTO to address problems ranging from poor patent quality and questionable examination practices to inadequate search capabilities, rising attrition, poor employee morale and a skyrocketing patent application backlog. Only a robust patent system can stimulate the development of commercially viable products that can enhance the US economy.

My presentation will highlight:

(a) critical issues, strategies and challenges for business planners and patent practitioners relating to: patenting such products; converting basic research into commercially viable products; and gauging the "white space" opportunities (no overlapping patents) prior to R&D efforts, patent filing or commercialization activities

(b) issues resulting from the current "patent gold rush" in emerging "patent thickets"

(c) the responsibility and interplay of federal agencies (FDA, EPA, Patent Office) to the long-term prognosis of nanomedicine

"FDA's Regulation of Nanotechnology: Current Controversies and Potential Impacts on Nanomedicine"

Ricardo Carvajal
Of Counsel, Hyman, Phelps & McNamara, P.C.

Abstract: FDA's regulatory authority over drugs and medical devices derived through nanotechnology is generally considered to be adequate to ensure that potential safety issues raised by those products are addressed prior to marketing. However, the agency has acknowledged that its authority over foods and cosmetics (which are generally subject only to postmarket oversight) is less comprehensive. Perceived gaps in the agency's authority over foods and cosmetics derived through nanotechnology has prompted numerous expressions of concern about whether the safety of those products has been properly addressed. This presentation will provide an overview of FDA's regulation of products derived through nanotechnology, with examples of different products that are already on the market as well as those that are still on the drawing board. The presentation will also examine controversies involving FDA-regulated products that could have an impact

on the development of nanomedicine, and will address the potential impact of state initiatives that target nanotechnology.

Biography: Ricardo Carvajal is Of Counsel with Hyman, Phelps & McNamara, P.C. in Washington DC, the largest dedicated food and drug law firm in the U.S. Prior to that, he served as Associate Chief Counsel in FDA's Office of Chief Counsel, where he participated in the formulation of regulatory responses to advances in food biotechnology and nanotechnology. Mr. Carvajal provides FDA regulatory counseling to manufacturers and marketers of foods, drugs, devices, and cosmetics. He has substantial experience with regulatory issues pertaining to foods, including dietary supplements. He has worked on GMP and HACCP compliance issues, and on a wide array of labeling compliance issues, including those that arise from the use of health, nutrient content, structure/function, and disease claims. He also has experience with drug, medical device, and cosmetics issues. He has worked on due diligence review teams for major acquisitions and initial public offerings, helped manufacturers to determine the regulatory status of products, and provided advice on labeling, advertising, and promotion issues. Mr. Carvajal is an active member of the Food and Drug Law Institute, the American Bar Association, and the Institute of Food Technologists, for which he has authored numerous publications on various aspects of food law and regulation. He holds a J.D. from Northwestern University School of Law and an M.S. in Biology from the University of Michigan. He is admitted to practice in the District of Columbia.

"The Future of the Patent Office in the Obama Administration"

Chris J. Katopis
Director, Global Intellectual Property Policy
Computing Technology Industry Association

Abstract: The operations and policies of the U.S. Patent and Trademark Office (PTO) will directly impact the future of nanotechnology and the lives of Americans for decades to come. During the eight years of the Bush administration, the PTO experienced a number of landmark events, challenges, and a record marked with both success and failure. The issues include sky-rocketing application workload (e.g., backlog and pendency), examination quality, and other institutional crises. Over the past eight years, the role of the patent system is now elevated. It has entered into mainstream with stories about the PTO and its management on the front pages of the newspaper.

The patent system will impact the future of nanotechnology, as well as other disciplines. The Obama administration offers change and the potential for a new era for the patent system for inventors, venture capitalists, consumers, and the patent bar. As many critics believe that the PTO is at a cross-roads, as its new political leadership helps shape the agency for the

challenges of the next four years and beyond. This presentation will address the following issues:
(1) Some of the long standing operational issues facing the agency (e.g., the more than one-century of application backlog);
(2) The successful agency operational reforms of the past 8 years;
(3) Some of the new agency initiatives expected to be introduced;
(4) The expected outcomes of any such challenges on the innovation ecosystem and the discipline of nanotechnology.

This presentation discussed many of the themes contained in Chris Katopis' recent paper: Perfect Happiness: Game Theory as a Tool to Enhance Patent Quality, 10 YALE J. OF LAW AND TECH. 360 (2008). See: http://www.yjolt.org/10/spring/-360

Biography: Chris J. Katopis serves as the Director of Global Intellectual Property Policy, for the Computing Technology Industry Association (CompTIA). He is an experienced Intellectual Property attorney who has worked in all three branches of the federal government, including the judicial branch, U.S. Court of Appeals for the Federal Circuit; the U.S. Patent and Trademark Office as the Director of Congressional Relations; and on Capitol Hill in various legislative positions. Notably, on the Hill, he was a counsel to the U.S. House Judiciary IP Subcommittee. In addition, Chris was an attorney in private practice where he advised technology companies about law and policy.

He received his undergraduate degree in engineering from the University of Pennsylvania and his law degree from Temple University. He is a native of New York City, N.Y. He frequently writes and lectures on technology and intellectual property law and policy matters.

"Intellectual Property Mapping – A Cornerstone of a Long Term IP Strategy"

Jeffrey P. Langer
Patent Agent, Finnegan, Henderson, Farabow, Garrett & Dunner, LLP

Abstract: Intellectual Property Mapping, or IP mapping, is a cornerstone of a long-term intellectual property strategy. In essence, IP mapping provides a comprehensive representation of a patent "landscape" at a given point in time. Understanding a patent landscape can prove extremely useful in assisting an entity to meet short-term and long-term goals on the path to successfully developing and commercializing the entity's intellectual property. In emerging technologies, such as nanotechnology where patent protection is diverse and dense, IP mapping can provide an entity with insights that are critical to success. Academic researchers and governmental agencies can use IP mapping to identify areas of research that may yield valuable intellectual property. For inventors and investors, IP mapping may identify problem areas early in the commercialization process of a product or

product line. Publicly available IP maps may provide a general overview of a landscape in a particular field and can serve as a starting point in the IP mapping process. Further customization of an IP map may yield beneficial results, such as additional details that define and illuminate the contours of the patent landscape by invention type, jurisdictional considerations, and/or other parameters.

Biography: Jeffery Langer is involved in the patent preparation, prosecution, and reexamination practices at Finnegan, law firm based in Washington DC. He provides technical assistance for opinion work, litigation, and due diligence projects. He is also a member of the firm's alternative energy and nanotechnology groups. Dr. Langer is an expert on semiconductor processing and has developed novel processing methods for emerging semiconductor materials used in the fabrication of antimonide based superlattices detectors and silicon carbide based power electronics. Dr. Langer also contributed to the development of optical character recognition software at Bell Labs. He has taught in the United States and the People's Republic of China. He is a member of the Giles S. Rich American Inn of Court and was elected to law review during law school. Dr. Langer served as a panelist discussing "The Practicalities of Being an Ethical Patent Practitioner," at the Symposium on Ethical Issues in Patent Law at The Catholic University of America Columbus School of Law.

"Getting to Market: Freedom to Operate in the Nanomedicine Space"

Jeffrey K. Mills
Timothy J. Shea
Sterne, Kessler, Goldstein & Fox

Abstract: Obtaining a patent to an invention is only one piece of the puzzle necessary to commercialize your technology. As important as being able to keep others from making, using and selling your invention, is determining whether you have freedom to operate, or whether there are patents that may block you from bringing your technology to market. This presentation will provide an overview of freedom to operate analyses, including why they are important and how they are conducted. In addition, we will address some of the challenges and strategies that are unique to freedom to operate analyses in the nanomedicine space. We will also discuss options that may allow you to clear freedom to operate and continue to develop your technology, even if a blocking patent may be in your path.

Biographies:
Jeffrey K. Mills
Dr. Mills is an associate in the Biotechnology/Chemical Group. He prepares and prosecutes U.S. and foreign patent applications. He also prepares

validity, infringement, and patentability opinions, and is involved in the firm's litigations practice. Dr. Mills has technical experience in materials science, focusing on the characterization of nano-structured materials and biomaterials, and the design of drug delivery systems. He has prepared and prosecuted patents in the areas of molecular and cellular biology, nanotechnology, medical devices, chemistry and pharmaceuticals.

Timothy J. Shea

Mr. Shea is a director in the Biotechnology/Chemical Group of Sterne, Kessler, Goldstein & Fox in Washington, DC where he specializes in advising biotech and chemical companies and research institutions on complex legal issues relating to the protection, enforcement and transfer of their intellectual property. He practices primarily in the fields of immunology, molecular biology, genomics, proteomics, medical diagnostics, biotherapeutics, and drug delivery. He has extensive experience advising clients on the creation and management of strategic patent portfolios, freedom-to-operate and patentability issues, complex prosecution strategies, validity and infringement issues, and due diligence investigations in connection with acquisitions and investments. A significant portion of Mr. Shea's practice involves counseling emerging companies on strategies for creating, protecting and leveraging their IP assets to grow their businesses. He frequently advises clients on all aspects of technology transfer, including the drafting and negotiation of patent and technology license agreements, material transfer agreements, sponsored research agreements, confidentiality and nondisclosure agreements, joint developments agreements, etc. Mr. Shea is currently Vice-Chair of the Life Sciences Committee for Licensing Executives Society International, an international network of IP licensing professionals. Prior to attending law school, Mr. Shea worked for several years in the biotech industry in the areas of medical diagnostics and genetic profiling.

"Connecting Nanotechnology, the Economy and IP Law"

J. Steven Rutt
Partner, Foley & Lardner LLP

Abstract: Recent headline news has featured some nanotechnology companies filing for bankruptcy, apparently driven by IP litigation according to court records and press reports. How does a company manage its patent and trade secret issues to avoid negative outcomes like bankruptcy? Strategies for managing IP will be discussed in view of larger economic context, developments in the law including reexamination, negotiating agreements such as joint development agreements, and international angles. Recent case law will also be noted, as well as practical developments at the Patent Office, including its new director and its examination of nanotechnology patents.

Biographies: J. Steven Rutt is a partner with Foley & Lardner LLP in Washington DC. He is vice-chairman of the Nanotechnology Industry Team and a member of the Chemical & Pharmaceutical Practice. His practice includes patent counseling, IP licensing and agreements, including technology transfer carried out under the Bayh-Dole Act , patent landscaping and clearance opinions, patent prosecution, patent litigation support, trade secrets, and trademarks. His technology background is with materials and polymers including applications in nanotechnology, cleantech, nanobio and nanomedicine, printed electronics, pharmaceuticals, semiconductors, and biotechnology. An area of focus for Dr. Rutt is coordinating the delivery of all aspects of IP legal services to emerging companies and representing them in their agreement negotiations. Dr. Rutt is a frequent writer and conference presenter with respect to nanotechnology and the law, actively helping to lead and participating in Foley's Nanotechnology Industry Team. Dr. Rutt received his law degree from Georgetown University Law Center in 1999. His chemistry doctorate was conferred in 1990 by The Pennsylvania State University (where he was a Braddock Fellow), and he holds a bachelor's degree in chemistry from Goshen College. He is the author of a dozen scientific publications and inventor on four patents. His experience includes nine years of hands-on research in polymer synthesis and morphological studies, and his experience in private industry includes two years of corporate chemical research with NTT in Tokyo, Japan.

"Nanotech for HealthcareTM: A Venture Capital Perspective"

Misti Ushio
Vice President, Harris & Harris Group

Abstract: Nanotechnology is enabling solutions in healthcare on several fronts including drug delivery, molecular diagnostics, and new materials for medical devices. Examples of commercial successes include new molecular probes developed by Quantum Dot Corporation which was acquired by Invitrogen, high-throughput DNA sequencing developed by 454 Life Sciences which was acquired by Roche, and nano-inspired biomaterials for spine surgery developed by Orthovita. Each of these successes started as a small company that successfully navigated the complexities of product commercialization. However, translating new technology to commercial products is a challenging endeavor, and venture capital can play a significantly beneficial role in bringing these nanotechnology solutions to the market.

Harris & Harris Group is one of the most active nanotechnology investors in the world with over 30 companies in its portfolio. Since 2001, Harris & Harris Group has funded companies developing nanoscale-enabled solutions in several industries including healthcare, electronics, cleantech, and metrology. Within the healthcare industry, investments have been made in companies developing drug delivery technologies, molecular diagnostics,

drug discovery technology platforms, and wound care technology. Harris & Harris Group considers three concepts when investing in Nanotech for Healthcare which are, engineering of biological systems, convergences of multiple disciplines, and new tools.

In the current state of the initial public offering (IPO) markets, venture capital investors are re-thinking their strategy on how to build successful companies. The presentation will discuss 1) Harris & Harris Group's strategy of investing in Nanotech for Healthcare™ by highlighting specific companies in its portfolio, 2) recent trends in the IPO and merger and acquisitions (M&A) markets, and 3) exciting areas for nanotechnology investing for the future.

Biographies: Ms. Ushio has served as a Vice President and Associate at Harris & Harris Group, Inc., based in New York City since May 2007. From June 2006 to May 2007, she was a Technology Licensing Officer at Columbia University, where she managed the nanotechnology and materials science invention and patent portfolios. From May 1996 to May 2006, she was employed by Merck & Co., Inc., most recently as a Senior Biochemical Engineer with the Bioprocess R&D group. She is a graduate of University College London (Ph.D., Biochemical Engineering), Lehigh University (M.S., Chemical Engineering) and Johns Hopkins University (B.S., Chemical Engineering).

Saturday, October 24, 1:20 p.m.

Keynote Lecture 3

Introduction: Esther H. Chang, *Georgetown U.*

"Current and Future Preventive HPV Vaccines"

Douglas Lowy
Chief of Laboratory of Cellular Oncology, Center for Cancer Research,
National Cancer Institute, National Institutes of Health

Abstract: Cervical infection by a sub-set of human papillomaviruses (HPV), especially HPV16 and HPV18, is the primary cause of virtually all cases of cervical cancer, which worldwide is the second most common cause of cancer deaths in women. HPV is also responsible for a variable proportion of several other cancers, including vulvar, vaginal, penile, anal, and oropharyngeal. Identification of HPV as the causative agent of cervical cancer has led to development of prophylactic HPV vaccines based on the observation that the L1 main structural protein of the HPV virion can self-assemble into empty virus-like particles (VLPs) which contain the conformationally-dependent neutralization epitopes of L1 and can induce high levels of neutralizing antibodies. Two pharmaceutical companies have developed commercial versions of the VLP vaccine. Clinical efficacy trials conducted by the companies have shown that, for fully vaccinated women, both vaccines induce almost complete protection against incident persistent genital infection attributable to the HPV types targeted by the vaccine and the associated lesions. However, the type-restricted nature of protection implies that ~30% of potentially cancer-causing infections will not be prevented by the current vaccines. Therefore, it would be beneficial to develop second generation vaccines that, ideally, could protect against a broader spectrum of serious HPV infections, were less expensive to produce and deliver, and required fewer doses. Efforts are underway to develop vaccines that may meet at some of these goals.

Biography: Douglas Lowy is chief of the Laboratory of Cellular Oncology in the Center for Cancer Research at the National Cancer Institute, National Institutes of Health. He is also a deputy director of the Center for Cancer Research. He received his medical degree from New York University School of Medicine, and trained in internal medicine at Stanford University and dermatology at Yale University. His research includes papillomaviruses and the regulation of normal and neoplastic growth. The papillomavirus research is carried out in close collaboration with John Schiller, with whom he has co-authored more than 100 papers in the past 25 years. In the 1980s, he studied the genetic organization of papillomaviruses and identified the oncogenes encoded by the virus. More recently, he has worked on papillomavirus vaccines and the papillomavirus life cycle. Their laboratory has been

involved in the initial development, characterization, and clinical testing of the preventive virus-like particle-based HPV vaccines. It is for this body of work that Drs. Lowy and Schiller received the 2007 Dorothy P. Landon-American Association for Cancer Research Prize for Translational Cancer Research, as well as several other awards. Dr. Lowy also received the 2007 Medal of Honor for basic research from the American Cancer Society. He is listed by the Institute for Scientific Information as one of the most highly cited authors in microbiology, and is a member of the National Academy of Sciences and the Institute of Medicine of the NAS.

Session IX: Saturday, October 24, 2:30 p.m.

Top 4 Poster Submissions from Young Investigators, Oral Presentations and Award Ceremony

Session IX Chair: Raj Bawa, Bawa Biotech Consulting

Session X: Saturday, October 24, 3:40 p.m.

Nanomaterial Safety and Toxicology

Session X Chair: Lajos Balogh, U. of Buffalo

"TBA"

Vicki Colvin
Rice University

"Scientific and Engineering Challenges for Informatics in the Context of Regenerative and Nano-medicine"

Fernando Martin-Sanchez
NIH, Spain

Abstract: Since the "Workshop on Nanoinformatics Strategies", supported by the National Science Foundation, that was held in Arlington, Virginia in 2007, the US National Institutes of Health and the US National Cancer Institute have supported several initiatives related to Medical Nanoinformatics. In Europe, the ACTION Grid project started in June 2008 with support from the European Commission (EC). ACTION Grid is the first European initiative that deals with Nanoinformatics and aims to create a Roadmap for the EC to address these issues in future research calls. Its main outcome will be the identification of needs and the discussion of future scientific challenges and priorities for Biomedical Informatics in terms of information processing in nanomedicine and regenerative medicine. From an engineering perspective, several current projects in which the Unit is currently involved will be presented such as, -ONTOMINEBASE (Databases of nanoparticles and their models and biological interactions), -COMBIOMED (Interoperability via web technologies and ontologies), -BIKMAS (Knowledge management 2.0), and -NANOSOST (standardization and nanosafety).

Biography: Dr. Martin-Sanchez holds a Bachelor's degree in Biochemistry and Molecular Biology from the Autonomous University of Madrid and a MSc in Knowledge Engineering and a PhD in Computer Science from the Polytechnic University of Madrid (Spain). He was a postdoctoral fellow at the Emory University Hospital-Georgia Institute of Technology Joint Research Program in Biomedical Engineering (USA).

Dr. Martin-Sanchez serves currently as Director of the Medical NanoBioInformatics Department of the National Institute of Health "Carlos III" in Madrid, Spain and serves as Associate Professor of Bioinformatics at the School of Biomedical Sciences. University "Francisco de Vitoria", Madrid.

His areas of research interest include: Research and development of information models and systems to facilitate the new approaches of genomic-

based, regenerative and nano-medicine. (DNA microarrays, integration of clinical and genetic databases, genetic-based clinical decision making support tools, nanoinformatics).

"Evaluating the Skin Hazards Associated with Nanomaterials"

Nancy Monteiro-Riviere
Professor of Investigative Dermatology & Toxicology, North Carolina State University

Abstract: Exposure of skin to nanomaterials may occur in environmental and occupational settings as well as after topical dosing with cosmetic or pharmaceutical formulations. There are two phases to assessing hazard and risk after such exposure: penetration and toxicity to cellular elements of the skin. The focus of this presentation is to review studies on skin penetration of topically applied nanomaterials (fullerenes, quantum dots, titanium, silver and aluminum nanoparticles) and their subsequent effects on human keratinocytes. Penetration and absorption was assessed by confocal microscopy, transmission electron microscopy as well as chemical analysis. The common results of these studies are that dermal absorption with subsequent systemic exposure is minimal to nonexistent although material penetration into the stratum corneum occurs. Formulation, surface chemical alterations, mechanical stressing of skin and species used can modulate the results. However, should particles penetrate the viable epidermis, keratinocytes are capable of taking up all types of particles with resultant biological effects including cytotoxicity and pro-inflammatory cytokine release. Keratinocyte cellular uptake pathways have been defined for quantum dots. These studies begin to define the hazard from cutaneous nanomaterial exposure and underline common issues that must be considered for proper conduction and interpretation of such studies.

Biography: Nancy Ann Monteiro-Riviere, Ph.D. is a Professor of Investigative Dermatology and Toxicology at the Center for Chemical Toxicology Research and Pharmacokinetics, North Carolina State University (NCSU). Dr. Monteiro-Riviere is also a Professor in the Joint Department of Biomedical Engineering at UNC-Chapel Hill/NCSU and Research Adjunct Professor of Dermatology, School of Medicine at UNC Chapel Hill. She received her M.S. and Ph.D. in Anatomy and Cell Biology from Purdue University and a postdoctoral fellowship in toxicology at CIIT in Research Triangle Park, NC. She was past-President of both the Dermal Toxicology and In Vitro Toxicology Specialty Sections of the National Society of Toxicology. Dr. Monteiro-Riviere is a Fellow in The Academy of Toxicological Sciences, and in the American College of Toxicology. She serves as Associate Editor for Wiley Interdisciplinary Reviews in Nanomedicine and Nanobiotechnology and serves on six toxicology editorial boards. She also serves on several national panels, including many in nanotoxicology, such as the National Research

Council of the National Academies to Review the Federal Strategy to Address Environmental, Health, and Safety Research Needs for Engineered Nanoscale Materials. She has published over 200 manuscripts in the field of skin toxicology and is Editor of the book "Nanotoxicology: Characterization and Dosing and Health Effects".

"Physical-Chemical Factors Controlling Nanoparticle Exposure, Transformation and Reactivity"

Mark R. Wiesner
Professor, Duke University
Director, Center for the Environmental Implications of NanoTechnology (CEINT)

Abstract: The properties of nanomaterials are transformed significantly due to interactions with environmental and physiological matrices. This presentation explores the role of nanomaterial-macromolecule interactions as they affect aggregation, deposition and reactivity using fullerenes as an example. The chemistry of reactive oxygen species (ROS) generation is presented and the relationship between the morphology of nanoparticle aggregates and their reactivity is explored. Alternations to nanoparticle ROS production as the result of matrix effects, in particular those representing commonly used growth media, are discussed. Changes in the affinity of fullerenes for a references solid phase are presented as function of the nature of adsorbing macromolecules, and the significance of these results for nanoparticle transport are highlighted. Finally, the importance of accounting for nanoparticle transformations in bioavailability and toxicity studies is discussed.

Biography: Mark R. Wiesner serves as Director of the Center for the Environmental Implications of Nanotechnology (CEINT) headquartered at Duke, where he holds the James L. Meriam Chair in Civil and Environmental Engineering with appointments in the Pratt School of Engineering and the Nicholas School of Environment. Dr. Wiesner's research has focused on the applications of emerging nanomaterials to membrane science and water treatment and an examination of the fate, transport, and impacts of nanomaterials in the environment. He co-edited/authored the book "Environmental Nanotechnologies" and serves as Associate Editor of the journal *Nanotoxicology*.

Before joining the Duke University faculty in 2006, Professor Wiesner was a member of the Rice University faculty for 18 years where he held appointments in the Departments of Civil and Environmental Engineering and Chemical Engineering and served as Associate Dean of Engineering, and Director of the Environmental and Energy Systems Institute. Prior to working in academia, Dr. Wiesner was a Research Engineer with the French company the Lyonnaise des Eaux, in Le Pecq, France, , and a Principal Engineer with

the Environmental Engineering Consulting firm of Malcolm Pirnie, Inc., White Plains, NY. Wiesner received the 1995 Rudolf Hering medal from the American Society of Civil Engineers and the 2004 Frontiers in Research Award from the Association of Environmental Engineering and Science Professors. In 2004 Dr. Wiesner was also named a "de Fermat Laureate" and was awarded an International Chair of Excellence at the Chemical Engineering Lab of the French Polytechnic Institute and National Institute for Applied Sciences in Toulouse, France. Professor Wiesner is a Fellow of the American Society of Civil Engineers and serves on the Board of the Association of Environmental Engineering and Science Professors.

Session XI: Sunday, October 25, 8:40 a.m.

Nanomedicine as Prophylactic/Therapy

Session XI Chair

Stephen Feinstone
Chief, Laboratory of Hepatitis Viruses, Division of Viral Products,
Office of Vaccines Research and Review,
Center for Biologics Evaluation and Research (CBER), FDA

Biography: Stephen Feinstone is the Chief of the Laboratory of Hepatitis Viruses in the FDA's Center for Biologics Evaluation and Research, where he has worked for the last twenty years. Among Dr. Feinstone's research interests are infectious diseases and vaccines, virology, viral vaccines, and viral hepatitis. He received his B.S. in Biology from Johns Hopkins University in 1966 and his M.D. from the University of Tennessee College of Medicine in 1969. He then completed his postdoctoral research at the Medical College of Wisconsin in the Division of Infectious Diseases. Prior to his current position, Dr. Feinstone was a Senior Investigator at the Laboratory of Infectious Diseases at NIAID. Additionally, Dr. Feinstone has served as the Associate Editor of *Hepatology,* on the Editorial Board for the *Journal of Viral Hepatitis*, and as a Visiting Professor at Kanazawa University School of Medicine in the Department of Molecular Oncology.

"Aeras RNA Nucleocapsid Vaccine Vector System"

John Fulkerson
Senior Director of Vaccine Discovery, Aeras Global TB Vaccine Foundation

Abstract: Aeras scientists have developed an oral vaccine delivery system that is flexible, cheap, rapid and easy to construct and manufacture and capable of inducing cellular and humoral immunity especially in the gut. Aeras has been able to produce and engineer highly attenuated delivery vectors that when given orally will invade gut cells and deliver self replicating nano-particle nucleocapsids into the cell cytoplasm. These recombinant double stranded RNA nucleocapsids (rdsRN) have been engineered to secrete messenger RNA (mRNA) that directs intracellular eukaryotic synthesis of immunogens which subsequently induce either cellular immunity or humoral immunity depending on the secretion pattern of the antigen and the type of adjuvant with which it may be co-expressed. Utilizing this system Aeras has already constructed rdsRN vaccines which induce high levels of cellular immunity against M. tuberculosis antigens. Non-human primate studies demonstrated cellular immune responses to Mtb antigens and a prototype rdsRN TB vaccine is scheduled for human phase I trials are scheduled for 2010. Aeras has

further constructed rdsRN vaccines against HIV, HPV, malaria, anthrax, influenza, plague, and viral meningitis.

Biography: John Fulkerson joined the Vaccine Discovery division of Aeras in 2004. Since joining Aeras, he has directed and conducted studies leading to the development of Aeras' novel recombinant RNA nucleocapsid vaccine vector platform, as well as directing the development of first and second generation TB, HIV and Malaria vaccines in a variety of platform technologies. Dr. Fulkerson came to Aeras from the FDA Center for Biologics Evaluation and Research where he served under the Counter-Bioterrorism/Biowarfare initiative in the Office of Vaccine Research and Review. While there he conducted studies into the pathophysiology and molecular biology of anthrax in the Laboratory of Bacterial toxins. Dr. Fulkerson earned his BS and PhD in biochemistry from the University of Maryland where he studied the molecular pathogenesis of *Helicobacter* and *Proteus ssp*, as well as the structure and mechanism of high-affinity ion transport systems.

"Plasmid DNA-based Nanomedicines in the Active Immunotherapeutic Field"

Julianna Lisziewicz
President and Chief Executive Officer, Genetic Community LLC

Abstract: Plasmid DNA based vaccines have been proved safe but poorly immunogenic in human subjects. To improve the immunogenicity of DNA-encoded antigens we have been developing nanoformulation and transdermal delivery technologies for nanomedicines. These technologies were first tested with DermaVir Patch, which is presently at Phase II clinical development stage for the treatment of HIV/AIDS. DermaVir is an HIV-specific immunotherapeutic nanomedicine containing a single plasmid DNA that is complexed with a mannobiosylated polyethylenimine (PEIm).

To effectively target and present the antigens into "professional antigen-presenting cells", we have invented a nanoformulation technology to structure pDNA-based antigens to pathogen-like nanoparticles. We have developed a stable liquid nanomedicine formulation suitable for transdermal administration and characterized the relationship between the structure and biological properties of nanomedicines.

To target the nanomedicines transdermally to the lymphoid organ, where the immune responses are initiated, we have developed a unique transdermal nanomedicine delivery device, called "DermaPrep". We have shown that topical administration of NanoComp with DermaPrep results in antigen expression in the lymph nodes by dendritic cells. DermaPrep device recently obtained the Certificate of Registration (CE-mark) from the European Competent Authority that permits marketing of the device throughout the EEA. DermaVir nanomedicine administered with DermaPrep is currently in phase II clinical trials in both US and EU.

Biography: Dr. Julianna Lisziewicz co-founded Genetic Immunity in 1998 and has served as the President and Chief Executive Officer of Genetic Immunity since its founding. In 1994, Dr. Lisziewicz co-founded the non-profit Research Institute for Genetic and Human Therapy (RIGHT) and directed its research and business affairs in the USA. RIGHT was focusing on the treatment of HIV/AIDS from multiple perspectives: virology, molecular biology, immunology and medicine. From 1990 to 1995, she was Head of the Antiviral Unit in the Laboratory of Tumor Cell Biology at the National Cancer Institute of the NIH in Bethesda, Maryland. While at NIH, she discovered and developed antisense oligonucleotide therapy and gene therapy for HIV/AIDS treatment. In 2005, she was appointed as the Marie Curie Chair at the Semmelweis University Budapest. She received her Ph.D in molecular biology from the Max-Planck Institute (Goettingen, Germany) and two Masters of Science in Chemistry and Biochemistry from the Technical University (Budapest, Hungary). She has co-authored over 100 peer reviewed scientific publications.

"The Use of Ligand-modified Immunoliposomes to Efficiently Deliver Plasmid DNA in Prime/Boost Vaccine Strategies against Hepatitis C Virus"

Marian Major
Senior Investigator in the Laboratory of Hepatitis Viruses (LHV), Division of Viral Products, CBER/FDA

Abstract: We have employed DNA priming in our hepatitis C virus (HCV) vaccine studies in order to induce HCV-specific T-cell responses in mice and chimpanzees. We developed an immuno-liposomal nanocomplex delivery system consisting of anti-transferrin receptor single chain antibody fragment and cationic liposome-DNA which binds to the transferrin receptor on antigen-presenting cells and enhances delivery and uptake of the encapsulated plasmid DNA. Using this delivery system we compared immune responses in mice following inoculation with DNA/immunoliposome complexes or naked DNA expressing HCV proteins NS3 and NS5A. The animals receiving the immunoliposome-complexed DNA had higher, broader and more consistent levels of IFN-γ producing cells to both NS3 and NS5A compared to the group receiving naked DNA. Furthermore, following challenge with vaccinia virus expressing NS3 immunization with the immunoliposome complex resulted in a significant (2-log10) reduction in viral titers compared to the PBS group ($p=0.02$) while immunization with naked DNA did not lead to reductions in viral titers ($p=0.38$). These same immunoliposome/DNA plasmid complexes were used to prime the immune system of chimpanzees in HCV vaccine studies. We found that after DNA priming the animals that received nanocomplexed DNA had a broader HCV-specific T-cell response that was amplified following an additional immunoliposome/DNA inoculation. Our data show

that DNA complexed with immunoliposomes is more efficiently delivered in vivo compared to naked DNA and more efficiently induces specific T-cell responses against HCV antigens.

Biography: Dr Marian Major is a Senior Investigator in the Laboratory of Hepatitis Viruses (LHV), Division of Viral Products at CBER/FDA. Dr. Major was trained in microbiology and virology, receiving her B.Sc. and Ph.D. degrees from the University of Warwick, one of the leading biotechnology universities in the U.K. After obtaining her doctoral degree she held post doctoral positions at the University of Cambridge, studying HTLV-I, and at INSERM, Lyon, France where she began working on HCV with Dr. Genevieve Inchauspé. In that laboratory, Dr. Major was one of the first to examine the DNA immunization strategy for eliciting HCV-specific immune responses. She joined CBER in 1996 and has continued to study the immunopathogenesis of HCV and strategies for vaccine development. Dr. Major has pursued vaccine studies examining both neutralizing antibody and T cell control of infection. She is particularly focused on immune escape following vaccination and exposure to virus. Her work has had a significant impact on the field of hepatitis C vaccine development, first demonstrating that natural infection with HCV can provide protection from reinfection, secondly showing that HCV replication is controlled significantly during the acute phase even when the infection results in persistence of the virus and, more recently, demonstrating that a mechanism for T-cell vaccine failure is the induction of immune escape mutants through the selection pressure exerted by the induced immune response.

"TBA"

Krutika Sawant
MS University of Baroda

Session XII: Sunday, October 25, 10:45 a.m.

Clinical Applications of Nanomedicine

Session XII Chairs:

Donald Tomalia, ***Central Michigan U.***

Patrick Hunziker
Deputy Head, Clinic for Intensive Medical Care Medicine, University of Basel

Biography: Patrick Hunziker has studied Medicine the University of Zurich, Switzerland. He received a doctoral decree based on thesis work in experimental immunology from the University of Zurich and did further research in experimental haematology at University Hospital in Zurich, Switzerland. He earned specialist degrees in Internal Medicine, Cardiology and Intensive Care Medicine. As a fellow the Massachusetts General Hospital, Harvard Medical School, worked on cardiac imaging in a joint project with the Massachusetts Institute of Technology, Cambridge. His professional activities in Europe, the U.S., Africa and China gave him a broad insight into the needs for the medicine of the future in a variety of settings. Hunziker became involved in medical applications of Nanoscience in the late nineties and has been the pioneer physician in Nanomedicine in Switzerland since then. With improved prevention, diagnosis and cure of cardiovascular disease as his main research topic, he worked in the nanoscience fields of atomic force microscopy, nanoptics, micro/nanofluidics, nanomechanical sensors and polymer nanocarriers for targeting. He is the founding president of the European Society of Nanomedicine, cofounder of the European Foundation for Clinical Nanomedicine and co-initiator of the European Conference for Clinical Nanomedicine and is clinically active as deputy head of the Clinic for Intensive Care Medicine at the University Hospital Basel, Switzerland. In November 2008 Patrick Hunziker became professor for Cardiology and Intensive Care Medicine at the University of Basel.

"Artificial Organelles"

Patrick Hunziker
Deputy Head, Clinic for Intensive Medical Care Medicine, University of Basel

Abstract: An astonishing characteristic of living organisms is the amount of control that exists across all size scales. Biologic activity of enzymes, organelles, cells and organs is highly controlled not only by internal control and feedback loops, but also by external stimuli and environmental variables. For example, defence against microbial pathogens typically starts with specific recognition that then triggers specification. Current artificial nanomaterials usually lack controllably or "intelligent", recognition-triggered activity. The question, how much complexity can be built into nanosize

system is an open question. The design of such synthetic "intelligent" systems at the nano scale may lead to novel therapeutic approaches including synthetic organelles for hereditary disease and disease-triggered therapeutic systems. We report the experimental proof of the concept of such synthetic organelles composed from polymer shells, integrated transmural channels, stimuli-triggered activity and the possibility to introduce such systems in a controlled fashion into target cells. Possible applications are discussed

"Applications of Nanomedicine in Cardiology: Advances on Biomaterials for Coronary Stents"

Varvara Karagkiozaki
Department of Physics, Lab for Thin Films -Nanosystems & Nanometrology, Aristotle University of Thessaloniki, Greece
AHEPA University Hospital, 1st Cardiology Department, Lab for "Cardiovascular Engineering & Atherosclerosis", AUTh, Greece

Abstract: Nanomedicine exploits the improved surface properties of implanted materials having a potential impact on the prevention, early diagnosis and reliable treatment of diseases. In cardiology field, coronary angioplasty with stenting offers therapeutic solutions for coronary artery disease and the underling arterial narrowing or obstruction. Especially, the currently used stents are the drug-eluting ones (DES) coated with a pharmacologic agent (drug) that is known to interfere with the process of arterial restenosis. There is some evidence, however, that drug-eluting stents despite their efficacy, may be susceptible to late stent thrombosis and in stent restenosis occurred at a rate of 0.2%/year, owing to their anti-proliferative drug elusion and polymers that impair the stent re- endothelization process[1].

In this presentation, the state of the art about stents and stent biomaterials are entailed, with focus on their pitfalls that nanomedicine has to address. Nanoapproaches in stent coating technology will be discussed and an example of non polymeric stent nanocoatings with tailored properties that inhibit platelets adhesion will be presented [2, 3]. Real time study of the mechanisms of platelets behavior towards biomaterials by means of Atomic Force Microscope, as well as the contribution of surface properties to the improvement of biomaterial haemocompatibility will be analyzed [4,5].

It is verified that access to nanotechnology has offered a completely new perspective to the production of vascular biomaterials with nanometre size, with finely controlled composition, architecture and effective manipulation of biological interactions, which will dramatically improve their functionality and address the drawbacks of stents.

References

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Biography: Varvara Karagkiozaki is a specialist **Cardiologist**, receiving her diploma from Aristotle University of Thessaloniki (AUTH). She holds a **BSc** in **Medicine** (Medical School, AUTH, 1998). **She received a MSc diploma with distinction of excellence,** (2007), after attendance of two years' interdisciplinary Postgraduate Program "**Nanosciences & Nanotechnologies**" of AUTH, focusing on Nanobiotechnology & Nanomedicine field. Formerly she had been working as an Honored Clinical Fellow in Congenital Cardiac Unit at University Hospital of Southampton in United Kingdom, to become a specialist in 3d heart echo in adult and congenital cardiac diseases. In one month she will present her nanomedical thesis. The **thesis** is on the advances of Nanotechnology that can bring to Stent coating technology aiming at manufacturing stent nanocoatings that avoid the late stent thrombosis which is considered to be the major pitfall of drug eluting stents. She is a specialist in the implementation of nanoscale imaging techniques such as Atomic Force Microscopy (AFM) and SNOM for in depth analysis of bio and non-bio interactions. She is a Member of Nanomedicine – Nanobiotechnology team of LTFN, member of Lab for Cardiovascular Engineering & Atherosclerosis, Ahepa Hospital, Medical School AUTH, member of European Society of Clinical Nanomedicine, a founding member of International Society of Nanomedicine, member of American Academy of Nanomedicine, member of Greek Pediatric Cardiology Association, of Greek Medical association for Obesity and of North Greek Society of Atherosclerosis. She had many oral and poster presentations in European, International and Greek at Nano-medical, Nanotechnology, Cardiology Conferences and numerous attendances at Greek, European and International congresses. Especially, these research presentations have been focused on many aspects of cardiology, such as atherosclerosis, hypertension, acute coronary syndromes, innovations in diagnosis and treatment of coronary artery disease, etc as well as on nanotechnology, nanomedicine, biocompatibility issues, biomaterials and stent technology.

She received a scholarship from the North Greek Society of Atherosclerosis and research awards from Greek Cardiology and Atherosclerosis Societies.

She published several academic research papers in peer reviewed journals and has been active in Nanomedicine field with papers on Nanotechnology's contribution on stent coating technology.

She has recently established her private cardiology clinic, she is a member of LTFN, working for EU research projects, promoting the research in Nanomedicine in Greece and Europe.

"Lymphatic Imaging with Nano-sized Gadolinium-dendrimer-based Contrast Agents: A Promising Application to the Clinical Diagnostic Imaging"

Hisataka Kobayashi
Chief Scientist, Affiliations Molecular Imaging Program, NCI/NIH

Abstract: Nano-particles are well suited for imaging the lymphatic system because such particles are physiologically drained from interstitial space into the lymphatic collector ducts, and are preferentially retained in the lymphatic vessels and nodes. When labeled with signaling moieties for the imaging, nanoparticles become useful for functional mapping of the lymphatic system. The pharmacokinetic characteristics of nano-sized contrast agents within the lymphatic system are dramatically altered by their physical size and chemical characteristics. We have used a variety of nano-sized contrast agents based on dendrimers to image the lymphatics. These agents can be used with nuclear medicine, MRI, and near infrared fluorescent labels to enable in vivo lymphatic visualization.

For instance a generation-6 polyamidoamine (PAMAM) dendrimer-based contrast agents of ~10 nm in diameter can clearly visualize the lymphatic system using MRI and/or optical imaging. Multi-color optical imaging enables the simultaneous depiction of multiple lymphatic drainage basins, which is not possible with radionuclide or MRI methods. The combination of multicolor optical imaging agents with MRI or scintigraphy based on nano-sized contrast agents is an attractive technique for lymphatic mapping, assessing lymphatic flow, and sentinel node imaging. This application requires only a minimal dose of the dendrimer-based contrast agent thus reducing the risk of toxicity. In this presentation, I will demonstrate these techniques in healthy mice and pigs, and mouse models of disease and discuss the possible roadmap for the clinical applications.

Biography: Dr. Hisataka Kobayashi is the Chief of the Basic/Preclinical Development Section in the Molecular Imaging Program at the National Cancer Institute/NIH in Bethesda, MD. Dr. Kobayashi is awarded MD in 1987 and PhD (Immunology/Medicine) in 1995 both from the Kyoto University, Graduate School of Medicine in Kyoto, Japan. He joined as a post-doctoral fellow in the Nuclear Medicine Department at the Clinical Center of the National Institutes of Health in 1995, and moved to the Molecular Imaging Program at NCI in 2004. His interest is in developing the novel molecular imaging agents and technologies employing various (nano-)materials especially for targeting cancers.

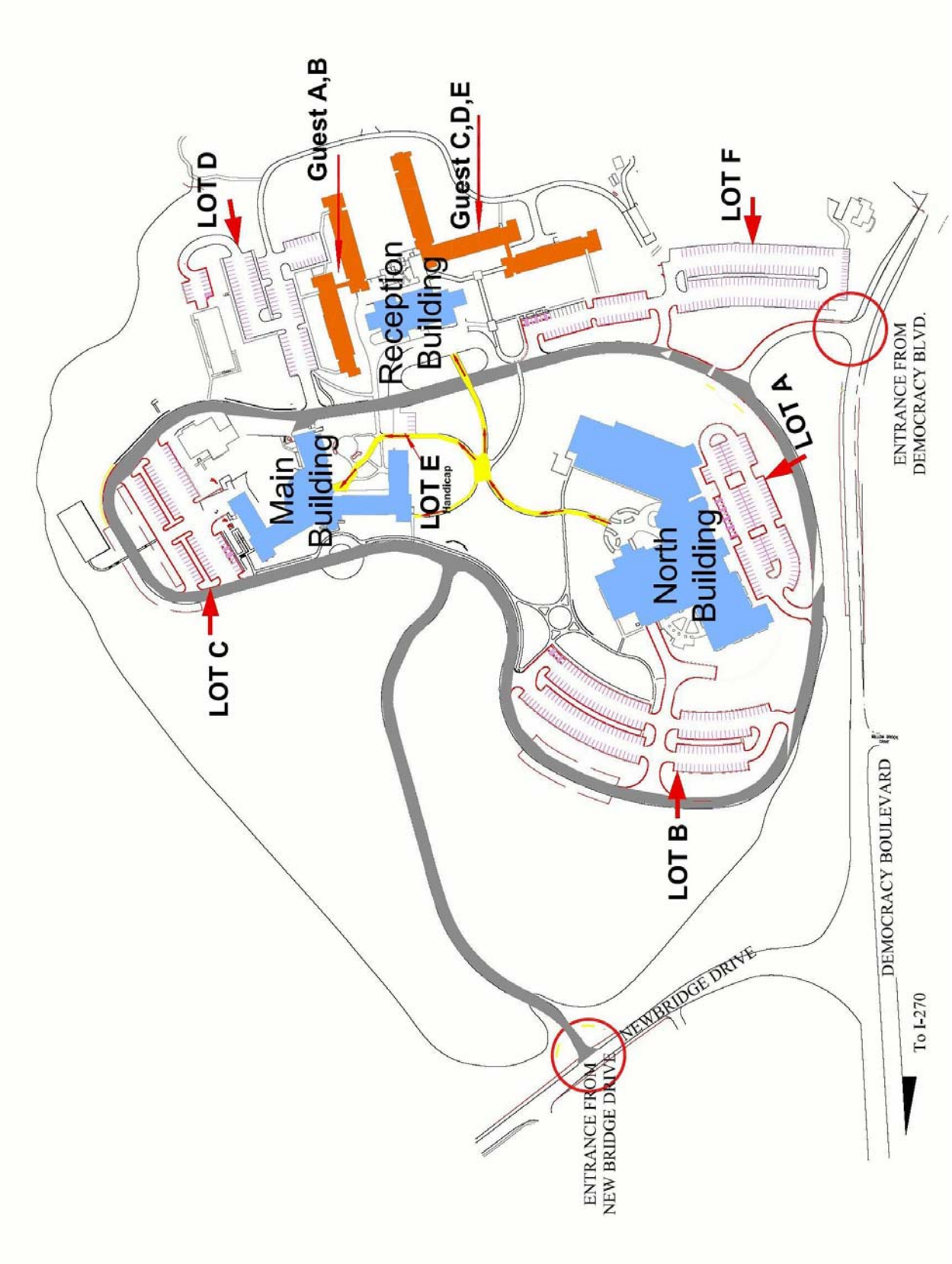
"Nanoparticle-Enhanced and Multi-Targeted siRNA Therapeutics for Critical Human Diseases"

Patrick Lu
Founder, President and CEO of Sirnamoics

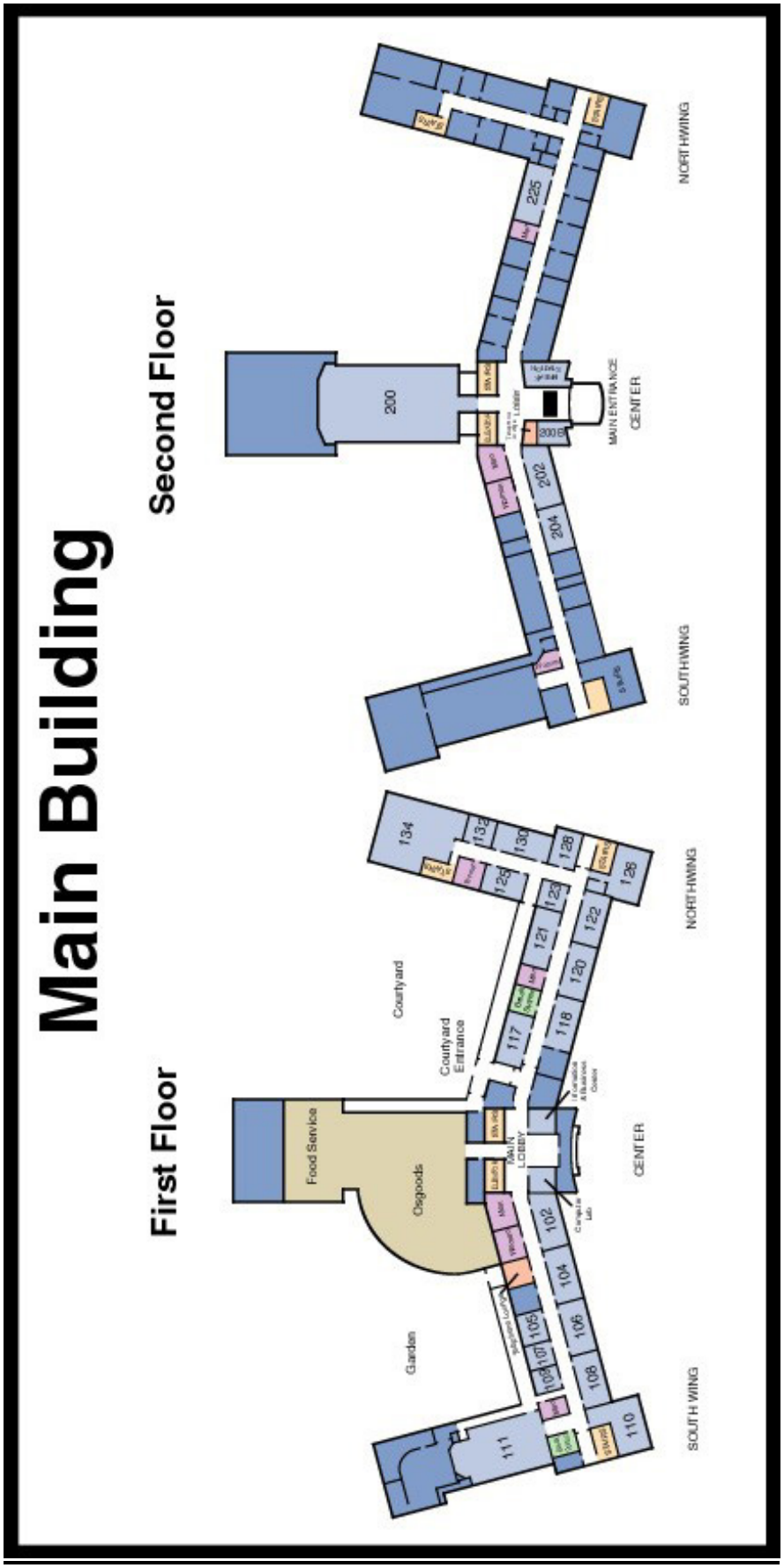
Abstract: Development of siRNA therapeutics has already demonstrated clinical benefits in several ongoing human trials. Using siRNA cocktail to silence multiple disease genes is truly realizing the advantage of small interfering RNA (siRNA)-based drugs. We have developed a set of siRNA cocktails using our proprietary algorithm and "Tri-Blocker™" platform, as the active pharmaceutical ingredient (API). Those siRNA cocktails were further tested and validated in the disease relevant animal models using Nanoparticle-base delivery systems. Local treatment with the siRNA therapeutics allowed us to treat influenza (H5N1/A(H1N1)) infections (STP702) and ocular neovascularization diseases (STP601), and to improve skin scarless wound healing (STP705). The systemic delivery of siRNA using a polymer Nanoparticle carrier revealed potent antitumor efficacy with mouse xenograft models of breast carcinoma and non-small-cell lung carcinoma (STP503). In addition, we are currently developing the systemic delivery vehicles, using Ligand-directed cell targeting, Infrared-activated Nanoparticle and Oral delivery Nano-microspheres. When the siRNA cocktail is applied with other drug modalities, such as monoclonal antibody, the therapeutic benefit was even further improved.

Biography: Patrick Y. Lu, Ph.D., is the founder, President and CEO of Sirnaomics, Inc., biopharmaceutical company found in 2007 and headquartered in Gaithersburg, Maryland, USA, focusing on RNAi technology for drug discovery and targeted therapeutics. Sirnaomics has its affiliate, Suzhou Sirnaomics Pharmaceutical, Ltd., in Biobay, Suzhou, China. Prior to Sirnaomics, Dr. Lu was the co-founder and Executive Vice President of Intradigm Corporation during year 2001 to 2006. Patrick has 25 years experience in biomedical research and pharmaceutical development, including 16-year biopharmaceutical industry career. Dr. Lu has been invited speakers in more than 40 international conferences throughout the world and has been authors of more than 50 peer-reviewed publications, and inventors of 26 issued and pending patents. One work led by him for the first RNAi therapeutics tested in non-human primate, published in *Nature Medicine,* was recognized as one of the Top 100 Science Stories of 2005 by *Discover* magazine. Recently, Dr. Lu received "Tech Pioneer" Award from Suzhou Industrial Park, China (2008) and his team also won "Yangzi Delta Innovation & Entrepreneurship Competition 2009" (top10). Before founding his own company, Dr. Lu held positions as a lab head and senior scientist in Novartis and Digene. Patrick received his Ph.D. in Life Sciences (1987) from Sun Yat-sen University, Guangzhou, China, and completed his postdoctoral training in University of Maryland at College Park (1990) and Georgetown University Medical School (1992).

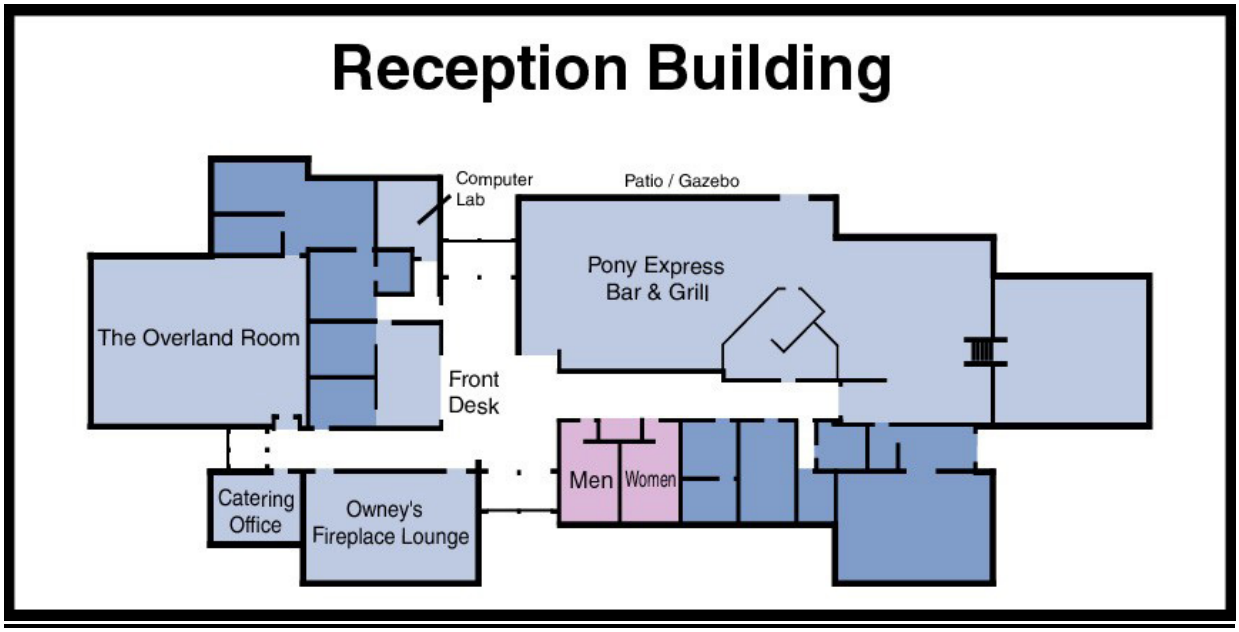
Map of the Bolger Center Complex

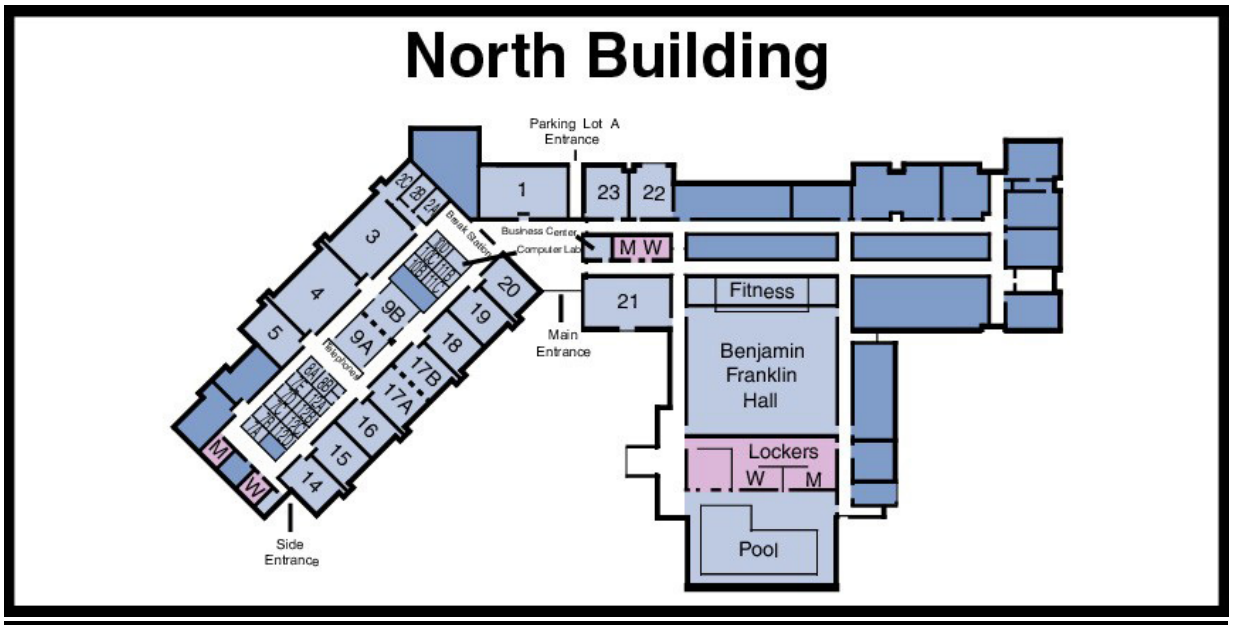


Maps of the Bolger Center Buildings



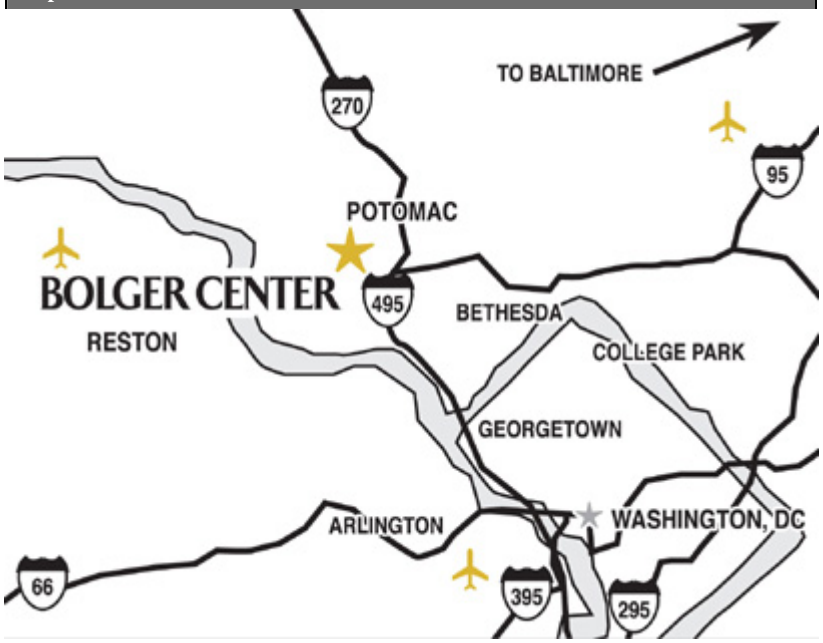
Maps of the Bolger Center Buildings





Map and Directions from Local Airports

Map



Driving Directions

Driving directions from:

REAGAN NATIONAL AIRPORT

1. As you exit the airport, you will be on the George Washington Parkway.
2. Bear right to take 495 North towards Frederick/Baltimore.
3. At the 495/270 split, take 270 North (left lanes).
4. Take the first exit, Democracy Boulevard and turn left at the end of the ramp.
5. The Bolger Center will be on your left hand side in approximately 2 miles. Follow signage to guest registration.

DULLES INTERNATIONAL AIRPORT

1. Take Dulles access road (toll road 267) towards Washington, D.C.
2. Take 495 North towards Frederick/Baltimore.
3. At the 495/270 split, take 270 North.
4. Take the first exit, Democracy Boulevard and turn left at the end of the ramp.
5. The Bolger Center will be on your left hand side in approximately 2 miles. Follow signage to guest registration.

BALTIMORE WASHINGTON INTERNATIONAL AIRPORT

1. Exit the airport on 195 towards 95.
2. Take 95 South towards Washington, D.C.
3. Take 495 West towards Northern Virginia and Silver Spring, MD.
4. Exit Old Georgetown Road and turn right at the end of ramp. Move into your far left hand lane.
5. Take left on Democracy Boulevard.
6. The Bolger Center will be on your left hand side in approximately 5 miles. Follow signage to guest registration.

Map and Directions to Westfield Montgomery Mall

7101 Democracy Boulevard
Bethesda MD 20817
(301) 469 6025

1. Start out going NORTHWEST on NEWBRIDGE DR toward DEMOCRACY BLVD. 0.1mi
2. Turn RIGHT onto DEMOCRACY BLVD. 2.5mi
3. Make a U-TURN onto DEMOCRACY BLVD. 0.5mi
4. End at 7101 Democracy Blvd Bethesda, MD 20817

Estimated Time: 5 minutes Estimated Distance: 3.04 miles

Bolger Center Services

Fifteen miles from the White House, the hotel and conference center is close to Reagan National and Dulles International Airports, the exciting nightlife of Bethesda and upscale shopping.

The Bolger Center's campus style setting creates an inviting retreat for both the business and leisure traveler. Our friendly staff will exceed your expectation for a peaceful and productive stay. The hotel features newly renovated guest rooms with beautiful garden views, complimentary parking and complimentary internet access. For your dining pleasure, the Bolger Center offers Osgood's, a buffet style restaurant and for nightly entertainment, the Pony Express Bar & Grill.

- Complimentary shuttle to Bethesda Metro station and shopping mall
- Fitness Center and indoor pool
- 83 beautifully landscaped acres
- Two ballrooms
- 70,000 square feet of IACC certified meeting space
- Team building ropes challenge course
- Property wide WiFi

Acknowledgements

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