Center for Continuing Education
University of Nebraska Medical Center
986800 Nebraska Medical Center
Omaha, NE 68198-6800
CIK 8704

University of Nebraska Medical Center

CODN Center for Drug Delivery and Nanomedicine

University of Nebraska Medical Center

Fourth International Nanomedicine and Drug Delivery Symposium

OCTOBER 8-10, 2006

Embassy Suites Hotel
Old Market
Omaha, Nebraska, USA

nanomedicine and drug delivery symposium - omaha

NanoDDS'06

SCIENTIFIC ADVISORY BOARD

Martyn Davies, Nottingham, UK
Ruth Duncan, Cardiff, UK
Adi Eisenberg, Montreal, Canada
Allan Hoffman, Seattle, WA, USA
Rudy Juliano, Chapel Hill, NC, USA
Kazunori Kataoka, Tokyo, Japan
Sung Wan Kim, Salt Lake City, UT, USA
Thomas Kissel, Marburg, FRG
Jindrich Kopecek, Salt Lake City, UT, USA
Robert Langer, Cambridge, MA, USA
Kalle Levon, New York, NY, USA
Kam Leong, Durham, NC, USA
Teruo Okano, Tokyo, Japan
Raphael Ottenbrite, Richmond, VA, USA
Kinam Park, West Lafayette, IN, USA
W. Mark Saltzman, New Haven, CT, USA
Edward A. Sausville, Baltimore, MD, USA
Francis Szoka, San Francisco, CA, USA

CALL FOR POSTERS

The poster session will be the highlight of the symposium. During the symposium, time will be dedicated for poster viewing with an opportunity to meet the authors and answer questions related to the abstracts. Additionally, a number of posters will be selected for short oral presentations. The selection will be based on the quality of research and abstract, which will be reviewed by a panel of experts.

If you are interested in presenting your work during the poster session at the symposium, please submit your abstract on our website www.nanodds.org. You can also e-mail the completed abstract form (available online) as an attachment to nanodds@unmc.edu. The abstract should be as informative as possible and include the most relevant data and illustrations. The deadline for submitting abstracts is **July 1, 2006**.

Authors will be notified of acceptance of their abstract by **August 7, 2006**. All accepted abstracts will be included in the symposium abstract book.

TRAVEL AWARDS

Several travel awards will be available to assist participation of graduate students and postdoctoral scientists in the symposium. If you are interested in being considered for a travel award, please indicate this in the abstract submission form.

nanomedicine and drug delivery symposium - omaha

NanoDDS'06

FOURTH INTERNATIONAL NANOMEDICINE AND DRUG DELIVERY SYMPOSIUM

October 8-10 2006, Omaha, NE, USA

The objective of the symposium is to provide a comprehensive overview of the latest advances in all aspects of nanomedicine and drug delivery. The use of nanomaterials and nanodevices to diagnose, treat and monitor diseases promises breakthrough advances and addresses clinical needs. The multidisciplinary field of "nanomedicine" joins engineering science with pharmaceutical and medical sciences to translate advances in nanotechnology research into clinical practice. The "next generation" therapies must be able to deliver drugs, radionuclides, therapeutic proteins and recombinant DNA to focal areas of disease or tumors to maximize clinical benefit while limiting untoward side effects. Several nanomaterial-based therapies have already been approved for clinical use and many more nanomaterials are being evaluated in clinics. Nanomedicine is not only a "futuristic" but also a "realistic" field with a near-term prospective to improve human health.

This 2.5-day symposium will include keynote and plenary lectures by more than 20 experts in the field, a poster session with oral presentations of selected posters and a roundtable discussion of the clinical prospects of nanomedicines. This symposium has proven to be particularly attractive to academic and industrial scientists and students, as well as clinicians and business specialists interested in this new and fascinating field.

SCIENTIFIC PROGRAM

Sunday, October 8, 2006

Keynote Lecture

Kazunori Kataoka, University of Tokyo, Japan - *Smart supra-macromolecular assemblies as nanocarriers for gene and drug delivery*

Nanomaterial Chemistry and Engineering

Kathryn Uhrich, Rutgers University, USA - *Functionalized amphiphilic macromolecules for targeted cell interactions*

Robert Prud'homme, Princeton University, USA - *Polymer-drug nanoparticles formation*

Judy Riffle, Virginia Tech, USA - *Toward the design of magnetic nanospheres and their interactions with lipid membranes*

Vladimir Tsukruk, Iowa State University, USA - *Nanocomposite membranes for sensor arrays*

Fate and Function of Nanoparticles in Cells

Arwyn Jones, Cardiff University, UK - *Endocytic pathways: therapeutic thoroughfares and biological barriers for macromolecular delivery*

Justin Hanes, Johns Hopkins University, USA - *Quantitative confocal nanoparticle tracking in live cells: Application to gene delivery*

Nanomedicine Research Reports

Alexander Cameron, University of Nottingham, UK - *Varying polymer architectures to deliver*

Stefaan DeSmedt, University of Ghent, Belgium - *Can we better understand the intracellular behaviour of nucleic acid containing nanoparticles by fluorescence correlation spectroscopy?*

Stavroula Sofou, Polytechnic University, USA - *Surface-active targeted liposomes for cancer therapy*

Maria Vicent, Prince Felipe Research Centre, Spain - *Polymer combination therapy: a novel approach to treat breast cancer*

Tarek Fahmy, Yale University, USA - *Nanoparticulate systems for targeted detection and modulation of T cells and antigen-presenting cells*

Chun Wang, University of Minnesota, USA - *Targeted multifunctional nanoparticles for DNA vaccine delivery*

Monday, October 9, 2006

Nanomedicines for Cancer Therapy

Vladimir Torchilin, Northeastern University, USA - *Targeted nanocarriers for cancer therapy*

Valery Alakhov, Supratek Pharma Inc., Canada - *Clinical evaluation of block copolymer-doxorubicin, SP1049C*

Ijeoma Uchegbu, University of Strathclyde, UK - *Targeted DNA delivery to tumors*

Nanotechnology Approaches for Bioimaging

King Li, National Institute of Biomedical Imaging and Bioengineering, USA - *Multidisciplinary approach to targeted drug delivery*

Otto Zhou, University of North Carolina, USA - *X-Ray imaging based on carbon nanotubes*

Karsten Mader, Martin-Luther University, FRG - *In vitro and in vivo characterisation of nanoscaled drug delivery systems by EPR spectroscopy and imaging*

Keynote Lecture

Henry Friedman, Duke University, USA - *New therapeutic strategies for malignant glioma*

Pathology and Therapy of Neurodegenerative Disorders

Charles Glabe, University of California, USA - *Nanomedicine approaches to target amyloid oligomers in degenerative disease*

Howard Gendelman, University of Nebraska Medical Center, USA - *Macrophage-mediated delivery of antiretroviral nanomedicines for treatment of HIV-1 infection in the central nervous system*

Tuesday, October 10, 2006

Nanotechnology Approaches for Pathogen Detection

Marc Porter, Iowa State University, USA - *Nanometric materials in optical and magnetic strategies for disease diagnosis*

Dan Luo, Cornell University, USA - *DNA based nanobarcodes for DNA detection*

Panel Discussion: Clinical Prospective of Nanomedicines

Moderator: Fred Ledley, Bentley College, USA

GENERAL INFORMATION

Information resources

Our website www.nanodds.org will be the major mode of communication where the registration and abstract submission forms and the latest information about the symposium will be posted. If you have any questions, please use fax: 1-402-559-9365 or e-mail nanodds@unmc.edu.

Symposium Location

The symposium will be held at the Embassy Suites Hotel Downtown/Old Market, Omaha, Nebraska. The hotel, which is a short five-minute drive from Omaha's Eppley Airfield, offers dining, shopping and entertainment options in the historic Old Market District. Several attractions are located within walking distance or a short drive, including the Holland Performing Arts Center, Joslyn Museum, Western Heritage Museum, Henry Doorly Zoo, Gallup University and the University of Nebraska Medical Center.

Accommodations

Accommodations are available at the Embassy Suites Hotel Downtown/Old Market and several nearby hotels. Additional information can be found on the symposium website.

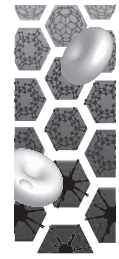
Symposium Registration

Registration fees on or before **July 1, 2006** are $200 for academia, $500 for industry and $35 for graduate students. After **July 1**, the fees are $275 for academia, $650 for industry and $50 for graduate students. The fee includes the abstract book, continental breakfasts, lunches and refreshment breaks. You can register online at www.nanodds.org or submit the registration form to the Center for Continuing Education, University of Nebraska Medical Center, 986800 Nebraska Medical Center, Omaha, NE 68198-6800, Phone: (402) 559-5929, Toll-Free: (877) 832-6924, Facsimile: (402)559-5915, e-mail: conted@unmc.edu.

Cancellations

If you need to cancel your symposium registration, a refund of your registration fee, less 10% will be issued until **September 8, 2006**. No refunds will be issued after this date. The date refers to the receipt of the written cancellation note to the University of Nebraska Medical Center, Center for Continuing Education.

For reprint orders, please contact:
reprints@futuremedicine.com



Delivery, detection and development in nanomedicine

The Fourth International Nanomedicine and Drug Delivery Symposium, October 8–10, 2006, Omaha, NE, USA

Joseph A Vetro[1]

[1]Center for Drug Delivery and Nanomedicine and the Eppley Cancer Center, Department of Pharmaceutical Sciences, University of Nebraska Medical Center, 985830 Nebraska Medical Center, DRC 1035, Omaha, NE 68198–5830, USA
Tel.: +1 402 559 9359; Fax: +1 402 559 9365; E-mail: jvetro@unmc.edu

The Fourth International Nanomedicine and Drug Delivery Symposium (NanoDDS'06; www.nanodds.org/) was held in Omaha, NE, USA, from October 8 to 10, 2006, to 'provide an overview of the latest advances in all aspects of nanomedicine and drug delivery' and attracted nearly 160 registered participants from 16 countries, 24 leading experts as guest speakers and over 80 poster presentations. The Symposium was chaired by Professor Alexander (Sasha) Kabanov from the University of Nebraska Medical Center (UNMC; NE, USA), bringing the conference full circle since it was first organized in Omaha by Dr Kabanov and Dr Kataoka as a mini-symposium on 'Nanomedicine and Drug Delivery' at UNMC in January 2003 (www.unmc.edu/pharmacy/nanomedicine/).

The conference

Professor K Kataoka (Department of Materials Science and Engineering, University of Tokyo, Japan) gave the keynote presentation in honor and memory of Sasha Kabanov's father, Professor Victor Kabanov (1934–2006). Among his many seminal contributions to macromolecular chemistry, Professor Kabanov discovered and quantitatively studied macromolecular exchange and substitution in interpolyelectrolyte complexes. These studies provided fundamental principles for developing bioimaging or drug-delivery nanoparticles through the complexation of charged polymers with oppositely charged imaging agents or drugs. Kataoka credited V Kabanov's work for inspiring him early in his career to explore the use of self-assembled polyelectrolyte complexes (PICs) for drug delivery. Kataoka then discussed one such PIC recently developed by his group. This latest PIC was formed from a diblock copolymer of poly(ethylene glycol)-poly(aspartate) with an ethylenediamine side chain (PEG-PAsp[DET]) and was used to successfully transfect a variety of primary cells with plasmid DNA. Kataoka also described studies where hypovascular and subsequently difficult-to-treat cancers, such as pancreatic cancer, were effectively treated by coinjecting a transforming growth factor (TGF)-β inhibitor with drug-loaded polymeric complexes. This increased intratumor perfusion and consequently enhanced nanoparticle penetration into the tumor for 24 h, but had no effect on free drug. Strong antitumor and antimetastatic effects were also observed.

Professor K Uhrich (Rutgers University, NJ, USA) discussed using micelles composed of amphiphilic scorpion-like macromolecules (AScMs) to prevent the uptake of oxidized low-density lipoproteins (LDLs) by macrophages and slow the progression of atherosclerosis. AScMs possess a hydrophobic region composed of highly branched alkyl chains and a hydrophilic region composed of linear PEG chains. Uhrich found that the presence of carboxylic acids on the PEG chain ends increased the aggregation of AScMs with LDLs and preferentially blocked macrophage uptake of highly oxidized LDLs. The possible concentration-dependent formation of pulmonary emboli after systemic administration was undetermined, however, and remains a major concern.

A Jones (Cardiff University, UK) discussed the intracellular trafficking of cell-penetrating peptides, such as HIV-transactivating transcriptional activator (TAT) and octaargine, in sensitive and drug-resistant immortalized cells. He observed that, unlike drug-sensitive cells, drug-resistant cells traffic peptides exclusively to the lysosomes. Furthermore, endocytosis of these peptides at low concentrations was inhibited at 4°C (energy-dependent endocytosis is inhibited), whereas a diffuse cytosolic pattern of peptide was observed at high concentrations. It remained undetermined, however, whether the surface activity of either peptide at high concentrations solubilizes the plasma membrane at 4°C to allow peptide entry.

J Hanes (Johns Hopkins University, MA, USA) compared the real time intracellular trafficking of synthetic drug-delivery nanoparticles with adenovirus using quantitative confocal nanoparticle tracking. Like others, he observed rapid perinuclear accumulation of a subset of both nanoparticles and adenovirus in the lysosomes within approximately 1 h and, unlike adenovirus, the majority of nanoparticles were unable to escape the lysosomes. He also observed that nanoparticle PEGylation increased the extent of endosomal trafficking and that nanoparticles appear to primarily escape the endosomes during endosomal sorting.

V Torchilin (Northeastern University, MA, USA) discussed a 'double targeted' PEGylated liposome he recently developed for cancer therapy to improve both extracellular and intracellular drug targeting. The nanocarrier was composed of PEGylated phospholipids having nucleosome-specific 2C5

antibodies attached to the ends of pH-sensitive PEG chains. The 2C5 antibody binds to nucleosomes found only on the surface of cancer cells to improve tumor targeting. The nanocarrier also contained surface-bound TAT peptides that are physically covered by the PEG chains. Upon endocytosis, the pH-sensitive PEG chains are released in the low pH environment of the endosomes, exposing the TAT peptides to facilitate endosomal release. Increased accumulation and antitumor activity *in vivo* were observed.

H Gendelman UNMC discussed using bone marrow macrophages (BMM), as cell-based drug carriers to improve the bioavailability and pharmacokinetics of nanoformulated antiretroviral drugs, such as indavir (IDV). The adoptive transfer (injection) of BMMs loaded with nanoformulated IDV increased IDV plasma levels above its effective dose (ED_{50}) and the tissue distribution of IDV delivered by IDV-loaded BMMs paralleled the distribution of BMMs. Survival of CD4+ T cells and antiretroviral activity in a humanized mouse model of HIV infection were also increased over untreated controls.

C Glabe (University of California, Irvine, CA, USA) discussed approaches to target amyloid oligomers for the treatment of neurodegenerative diseases. Antibodies were generated against three distinct sequences (prefibrillar oligomers, pore-like annular protofibrils and amyloid fibrils). These antibodies recognized the three β-structures in many different types of amyloids, indicating that a general structural motif responsible for toxicity may be common to all amyloid proteins. Glabe also observed that only the soluble, prefibrillar oligomers from all types of amyloidogenic proteins possessed membrane permeabilizing activity and that this may be the primary mechanism of amyloid pathogenesis. Thus, nanomedicine approaches that block amyloid pore formation by soluble prefibrillar oligomers may be effective in the treatment of a wide range of neurodegenerative diseases.

M Porter (Arizona State University, AZ, USA) discussed ultralow level detection and diagnosis of diseases using assays based on surface-enhanced Raman spectroscopy (SERS). Porter developed an assay similar to a sandwich enzyme-linked immunosorbent assay (ELISA), where alkylthiolated antibodies recognizing one region of an antigen were coupled to a gold film surface, and an extrinsic Raman label (homogeneously sized gold nanoparticles covered with alkylthiolated antibodies that recognize a different region of the antigen) was used to detect the captured antigen. This approach also allows for simultaneous detection of multiple antigens (multiplexing) by adding an appropriate pair of capture and detection antibodies and unique diameter of the gold nanoparticle for each additional antigen. Evidence of the high level of sensitivity and robustness provided by the SERS sandwich assay was demonstrated with prostate-specific antigen (PSA), where a limit of detection of 30 fM was observed in human serum.

R Prud'homme (Princeton University, NJ, USA) described a novel, scalable process called 'flash nanoprecipitation' for nanoparticle production. The process involves forming nanosized drug aggregates over very short time scales, then stabilizing the aggregates with biocompatible amphiphilic block copolymers containing PEG. Nanoparticle size is controlled by mixing intensity, degree of supersaturation and rate of drug nucleation. The process produces nanoparticles with high levels of drug loading that can be lyophilized and reconstituted without aggregation and are flexible enough to allow for the development of an almost unlimited number of applications.

F Ledley (Bentley College, MA, USA), cofounder of Genemedicine Inc., outlined a number of the lessons he learned in attempting to bring a therapy from the bench to the bedside. The need to choose a delivery technology capable of clinical success, perform achievable clinical trials before full-scale development and balance the role of academics, companies, investors and partners during the process were the major messages of his discussion.

A Polinsky (V.P. Global Technologies, Pfizer), a former graduate student of V Kabanov, discussed the current gap between academic and industrial development of nanomedicine technologies. Polinsky proposed that this gap is driven by the "wait and see" attitude of big Pharma, which produces a "Big business model gap". According to this model, start-up companies will fill in the gap to provide industrial nanomedicine applications that are either licensed or acquired through the purchase of start-ups by big Pharma. Polinsky predicted that the gap will narrow significantly in the next 5 years, but suggested that academia could help close the gap earlier by considering the same practical aspects of nanomedicine applications that must be considered by big Pharma.

B Rabinow (Baxter) discussed Baxter's NANOEDGE technology that increases the solubility of poorly water-soluble drugs. The process involves physically homogenizing larger crystals of pure drug into 200–400 nm nanoparticles. Increased oral bioavailability is observed with decreasing particle size, and extended intravenous release and lower toxicity are also observed compared with solubilized, free drug alone.

Acknowledgements

JAV is supported by the Nebraska Health and Human Services System (#2007–41) and a Department of Defense Breast Cancer Research Program 2005 Concept Award (#BC053471).

Major support for this conference was provided by the National Institute of Health, National Institute of Biomedical and Bioengineering and the National Cancer Institute (1R13EB006720–01), Abbot, Abraxis, American Association of Pharmaceutical Scientists, Controlled Release Society, Elsevier Publishers, Iowa State University, Nanopharmaceuticals, Inc., NANOVIP.COM, Novartis Oncology, Pfizer, Schering Plough, Supratek Pharma Inc., the University of Nebraska Medical Center (UNMC), the UNMC Center for Drug Delivery and Nanomedicine and the UNMC Center for Neurovirology and Neurodegenerative Disorders.

NanoDDS'07 is planned to be held in Boston, MA, USA, in 2007.

Highlights

- Coinjection of transforming growth factor-β inhibitors with drug-loaded polymeric complexes increases nanoparticle penetration into tumors and subsequent antitumor and antimetastatic activity.
- Conventional drug-delivery nanoparticles appear to primarily escape the endosomes during endosomal sorting.
- Nanomedicine approaches that block the formation of amyloid pores by soluble prefibrillar oligomers may be effective in the treatment of a wide range of neurodegenerative diseases.
- Cell-based delivery of nanoformulated antiretroviral drugs using bone marrow macrophages improves drug bioavailability, toxicity profile and pharmacokinetics.
- Ultralow level detection (e.g., 30 fM prostate-specific antigen in human serum) can be achieved using a surface-enhanced Raman spectroscopy based assay similar to sandwich enzyme-linked immunosorbent assay.
- 'Flash nanoprecipitation' is a novel, scalable method for producing stable nanoparticles with unusually high levels of drug loading that has great potential for developing unique drug and bioimaging nanoparticles.
- The gap in industrial nanomedicine applications between academia and industry is predicted to narrow significantly within the next 5 years, but academic consideration of the same practical aspects considered by big Pharma could increase the rate of gap closure.