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25th Nano Congress for Future Advancements

& 12th Edition of International Conference on Nanopharmaceutics and Advanced Drug Delivery

August 16-18, 2018 | Dublin, Ireland

Plenary Day 1

Nano Congress 2018 & Nano Drug Delivery 2018

12th Edition of International Conference on

Nanopharmaceutics and Advanced Drug Delivery

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Animesh Jha

University of Leeds, UK

Restoration of damaged dental enamels using nano-scale iron-calcium phosphate minerals and femtosecond pulsed near-IR lasers

ental enamel is a cellular and a vascular mineralized tissue with more than 95% mineral content. Although, the underlying softer dentine is connected with the microvasculature via the soft tissue therefore, possesses intrinsic regenerative capacity for mineralization which lacks in the enamel tissue. Consequently, the oral acid induced erosive damage on enamel is irreversible, and leads to lesion formation. Unattended lesion may lead to hypersensitivity and feeling of pain. Advanced stage of eroded enamel with symptoms of hypersensitivity might lead to tooth loss in adults. Traditional clinical strategies for the repair of acid-eroded enamel include the use of BIS-GMA polymeric materials which has incompatible mechanical properties with the adjoining hard minerals, and this type of bonding leads to failure of restored enamel area in a challenging oral environment. Modern toothpastes provide temporary relief from hypersensitivity; however, there is no long-term solution for treating early stages of acid erosion which may lead to sensitive teeth. Another condition, which affects especially the ageing population, is the tooth wear, which leads to tooth thinning and weakening in the lingual areas of mouth. Rebuilding the entire damaged tissue region remains a challenge. In the absence of any intrinsic regenerative means of restoring damaged tissue, our proposal focusses on developing a novel exogenous tissue re-engineering methodology, in which the mineralization of tooth surface involves: i) application of nano- and amorphous iron-calcium phosphate minerals (e.g. hydroxyapatite, fluorapatite and brushite) in the form of colloidal paste; which is then ii) bonded with the surrounding healthy enamel by irradiating with a femtosecond pulsed near-IR laser. The presence of a homogeneous dispersion of nano-scale of iron oxide in the calciumiron phosphate matrix acts as resonant antennae for absorbing near-IR pulsed laser radiation, and helps in the dispersion of thermal energy uniformly in the irradiated region without causing damaged to the healthy tissue. The two steps (i) and (ii) are illustrated in Figure 1. The mechanisms of phase transformation and dissipation have been analyzed for different irradiation conditions (e.g. at 1040 nm wavelength, 1 GHz repetition rate and 0.4 W average power), and the resulting phase transformation is compared for understanding the bonding and potential radiation induced damage mechanisms including ablation, thermal and toxicity effects. Potential opportunity for micro-surgical device engineering is discussed for ultimate clinical use. The mechanical properties including brushing trials on restored surfaces of bovine enamels are also reported.



Figure 1: Process of sintering and densification of iron rich calcium phosphates after laser irradiation

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Biography

Animesh Jha is Professor of Applied Materials Science with special research interest in glass based and nano-scale materials, photonic materials, laser gain medium engineering and laser-matter interaction. He obtained his Bachelor and Master of Engineering Degrees in Metallurgy from the University of Roorkee (UP, India) and the Indian Institute of Science Bangalore (India) in 1979 and 1981, respectively. In 1981, he joined the Imperial College of Science & amp; Technology, London for his PhD in thermodynamics of sulphide minerals for metal processing, and acquired significant interest in heterogeneous chemical reaction kinetics and multiphase equilibria. After finishing PhD in Oct 1984, he pursued his interest in the area of phase equilibrium and transformation kinetics in metallic and inorganic glasses as a post-doctoral research fellow at the University of Sheffield (UK) until April 1989, after which he was appointed as a lecturer at Brunel University in Uxbridge (UK). In March 1996 he joined the University of Leeds (Leeds, UK) as a Reader where he has been undertaking original research in nanoscience approaches for bio-materials, glass engineering and 2D-materials technology for device engineering. AJ became Professor in Aug 2000. He is author of more than 400 research papers and has also written a book on "Inorganic Glasses for Photonics" which was published in 2016. He is also inventor/co-inventor on more than 45 patents. AJ was awarded the Fellowships of Institute of Physics (London) and the Royal Society of Chemistry in 2010 and 2016, respectively. He has also won innovation awards (SMART, Yorkshire Concept) for technological demonstration of advanced glasses and fibres for lasers and amplifiers, and their applications. He is actively involved in PhD and PDRF training and promotes emerging scientists in achieving career goals via Marie-Curie and other prestigious Fellowship schemes.

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Han-Yong Jeon

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Effect of LCP/PET blend composition and spinning parameters on nanofiber formation condition

elt-blending method was performed to make nano fibers which have excellent properties of liquid crystal polymer(LCP). MIf nano fiber is manufactured depending on LCP, there is every possibility of utilizing in a higher value-added industry. Although there are some processes to produce nano fiber such as electrical spinning and sea-island fiber by conjugate spinning etc., it still has difficulties that electrical spinning has a low output and sea-island fiber by conjugate spinning using specified nozzle is restricted to reduce fiber diameter. It will be effective to solve the existing problems as mentioned above if to control of fibrillation shape is able to make a consecutive fiber morphology through spinning process. The research that deal with making continuity through the way to regulate size of fibril by sea-isaland fiber formation has not yet been achieved in existing dissertations of manufacturing of fibers related to spinning fibrillation method. This study is planned to verify control of sea-island fiber formation via study of its behaviors that are influenced by LCP and poly(ethylene terephthalate) (PET) blend composition and confirms size changes of fibril shape by spinning process. This fibrillation changes show fibril formation and morphology according to the spinning parameters including nozzle and spinning related condition. Distribution of nano fiber fibrillation were observed to LCP and PET blending process for conjugate spinning. Fibrillated fibers of sea-island morpholohy were distributed relatively evenly in the spinning parameters. Also, this phenomenon was assumed that the miscibility of LCP/ PET and the flow characteristics correlate with the phenomenon, so conducted the analysis. In this study, effect of LCP/PET blending and spinning parameters on sea-island fibrillation to make nano fibers was investigated through morphological and crystallographical analysis.

Biography

Han-Yong Jeon is an Geosynthetics/Technical Organic Materials Researcher and he was the 32nd President of Korean Fiber Society during 2014-2015. He has published more than 843 papers in domestic and international conferences. He wrote 20 texts including 'GEOSYNTHETICS' and also published 143 papers in domestic and international journals. He has awards of Marquis Who's Who-Science and Engineering in 2003-2017 and also he got the 33rd Academy Award of Korean Fiber Society in 2006 and Excellent Paper Award of 2012 by The Korean Federation of Science and Technology Societies.

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Naokazu Yoshikawa

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Synthesis, x-ray crystal structure, emission property, and DFT calculation of monoprotonated polypyridine

A series of metal-free compounds, i.e., bpyHPF6 (1), dmbpyHPF6 (2), phenHPF6 (3) dpphenPF6 (4), bqnHPF6 (5) and ppyHPF6 (7) were newly prepared and characterized by electrospray ionization mass spectrometry, and UV-vis spectroscopy. Abbreviations used are bpy =2,2'-bipyridine, dmbpy =4,4'-dimethyl-2, 2'-bipyridine, phen = 1,10-phenanthroline, bqn = 2,2'-biquinoline and ppy = phenylpyrizine. The x-ray crystal structures of the four compounds 1, 2, 3, 4 5 and 7 were determined. Monoprotonated pyridine rings are hydrogen bonded intramolecularly to the adjacent pyridine ring in compounds 1, 2, 3, 4 and 5. The π - π * absorption bands in the UV region for 1, 2, 3, 4 and 5 in acetonitrile were red-shifted relative to those of the corresponding neutral unprotonated compounds. Density functional theory was applied to interpret the planarity in 1. The attachment of one proton to the one nitrogen in 5 leads to the remarkable emission (ϕ = 0.10). The attachment of one proton to one nitrogen in 4 also gives the large quantum yield.

Biography

Naokazu Yoshikawa is a researcher from 2000. He have completed PhD in 2008 from Nara Women's University and continued postdoctoral studies with Osaka University and Nara educational University. He have published more than 25 papers in reputed journals. He have an interest in iridium complexes and Ruthenium complexes. Recently he also interested in metal free emission product.

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Thomas Maurer

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Nanogauges for integration of strain sensors integrated into matter

For the past twenty years, nano-optics has emerged as a promising research field thanks to huge progress in nanofabrication and offers great technological potential for applications in fields such as biology, medicine or chemistry. Coupling between plasmonic nanoparticles (NPs), well-known as the plasmon ruler equation, was recently investigated by fabricating arrays of NP dimers with various inter-particle distances using e-beam lithography. In this talk, we aim to illustrate how it should be possible to break through frontiers between mechanics and plasmonics in the next future by showing our first results on the use of gold nanogauges for strain investigation as well as recent advances published in the literature. In particular, the opportunity to develop a new generation of color-changing strain sensors will be discussed.

Biography

Thomas Maurer is Associate Professor at the University of Technology of Troyes. He has been developing a research activity at the interface of nanotechnology, mechanics and optics, which can be designed as mechanoplasmonics. In parallel, he is a member of the action laboratory of excellence executive committee and responsible of the smart sensors scientific work group whose aim is to integrate sensing functionalities into matter.

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Jae-Jin Shim

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Graphene-based nano materials for energy storage and photocatalysis

Nanomaterials have been employed to improve the performance of the energy storage devices (supercapacitor), sensors, and photocatalysts. Especially, oxides and sulfides of transition metals have been getting attention as they have good electrochemical performances. However, their performances are not satisfactory. Various materials such as graphene and carbon nanotubes have studied to enhance the electrochemical properties owing to their large surface area and high electrical conductivity. Synergistic effects from excellent conductivities of graphene and high electrical properties of metal oxides or sulfides have improved the overall electrochemical performances tremendously. Doping of graphene with nitrogen or sulfur, using metal sulfides instead of metal oxides, and using highly porous materials as substrates also contribute towards performance improvement.

Biography

Jae-Jin Shim received his BS degree from Seoul National University in 1980, MS degree from KAIST in 1982, PhD degree from the University of Texas at Austin in 1990. He has been a Professor in Yeungnam University since 1994 and served as School Chairman and Vice-Dean of Engineering. He was the President of the Korean Society of *Clean Technology* and Vice President of the Korean Society of Engineering Education. He is the Director of Institute of *Clean Technology* and Clean Energy Priority Research Center and served as the Chief Editor of *Clean Technology*. He has published 150 papers in reputed journals.

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Kent Peterson

Fluid Imaging Technologies Inc., USA

The use of flow imaging microscopy for nanoparticle analysis in biopharmaceuticals

Flow imaging microscopy has proven to be an important tool for the analysis of subvisible particulates in parenteral drugs. Now, due to the combined resolving power of blue LED light and patented oil immersion technology, flow imaging microscopes can image and analyze particles as small as 300 nm. The ability to detect transparent particles and differentiate them based on morphology yields significantly more detailed and accurate information than can be acquired using common laser diffraction and light obscuration techniques. Along with sophisticated statistical pattern recognition algorithms, these systems can be used to distinguish between different particulate types such as silicon oil, protein aggregates, and air bubbles. This presentation will present the techniques used to accomplish this.

Biography

Kent Peterson is a graduate with an honors from Boston University's Graduate School of Management, and a Member of American Mensa Society. He has lead Fluid Imaging Technologies since joining as the founder of the firm 12 years ago. The Company has sold over 600 FlowCams in over 52 countries. Ship-based FlowCam systems have also been at work sampling from every ocean in the world. He has served on a number of boards and is active in community affairs. He has also been named Mainebiz Business Leader of the Year. His achievements include: Fluid Imaging Technologies' Awards and recognitions include, the Governor's Award for Business Excellence, the SBA New England Exporter of the Year Award, and the Portland Regional Chamber's Robert R Masterton Award.

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Scientific Tracks & Abstracts Day 1

Nano Congress 2018 & Nano Drug Delivery 2018

Sessions

Nano Biomaterials | Nano Materials Synthesis and Characterisation | Nano Sensors | Advanced Nanomaterials | Nanotechnology and Biomedical Applications | Drug Delivery Research | Nanomedicine | Pharmaceutical Nanotechnology

Session Chair Anthony N. Papathanassiou National and Kapodistrian University of Athens, Greece

Session Co-Chair Laura Oliveira-Nascimento State University of Campinas, Brazil

| Session Introduction | | | |
|---|--|--|--|
| Title: Encapsulation of nanoparticles in composite gel microparticles for lung imaging and drug delivery | | | |
| Robert K Prudhomme, Princeton University, USA | | | |
| Title: Nanotechnology approaches for intensifying localized combination therapy for precision treatment early stage breast cancer | | | |
| Patrick J.Sinko, Rutgers, The State University of New Jersey | | | |
| Title: Attenuated protein toxins as intracellular nucleic acid delivery fibromyalgia and chronic pain vector | | | |
| Simon C W Richardson, University of Greenwich, UK | | | |
| itle: Smart combination nanopreparations for cancer: Bringing drugs inside cells and to individual organelles | | | |
| Vladimir P Torchilin, CPBN - Northeastern University, USA | | | |
| Title: Antibody-proteases as a novel biomarker and a unique target to suit translational tools to be applied for biodesign, bioengineering and regenerative medicine therapeutic for a treatment of EGFR-dependent breast cancer tumors | | | |
| Sergey Suchkov, Sechenov University, Russia | | | |

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Encapsulation of nanoparticles in composite gel microparticles for lung imaging and drug delivery

Robert K Prud'homme, Nathalie M. Pinkerton, Stacey W. Zhang, Richard L. Youngblood, Dayuan Gao, Shike Li, Bryan R. Benson, John Anthony, Howard A. Stone and II Patrick J. Sinko

Princeton University, USA

The intravenous delivery of composite gel microparticles (cGMPs) offers a platform for localized treatment of lung cancer. We describe a method for fabrication of cGMPs with average diameters of 35 to 100 μ m using shear emulsification and microfluidic droplet generation. We characterized the particles and describe the performance of these particles *in vivo*. Biodistribution of the cGMPs was selective to the lung after intravenous injection and particle clearance from the lung occurred in 7 weeks. One-week biodistribution studies demonstrated that larger, uniform particles produced by microfluidics provided optimal targeting to lung tissue. We demonstrated that highly loaded cGMPs containing a long wavelength fluorophore allow *in vivo* analysis of particle biodistribution without the need for *ex-vivo* organ analysis. The release of camptothecin conjugates from the nanopartricles, and thus, gel microparticles, is tuned from minutes to days by altering the polarity of the nanoparticle core.

Biography

Robert k Prud'homme is a professor in the Department of Chemical and Biological Engineering at Princeton University. He is the founding director of the Program in Engineering Biology. His research program focusses on polymer self-assembly applied to drug delivery. The development of Flash NanoPrecipitation (FNP) in his laboratory enabled the encapsulation of poorly soluble drug compounds and oligonucleotides for therapy directed towards cancer, TB, and injections. FNP is a scalable and continuous process that is enables integrated processing and spray drying for low cost oral and aerosol formulations. Under sponsorship by the Bill and Melinda Gates Foundation, the process is being adopted to formulate new compounds coming from TBA, MMV, and DNDi.

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Nanotechnology approaches for intensifying localized combination therapy for precision treatment of early stage breast cancer

Patrick J Sinko, Firas Al Zubaydi, In Heon Lee, Zoltan Szekely, Jennifer Holloway, Dayuan Gao and Hatem Sabaawy ¹Rutgers The State University of New Jersey, USA ²Rutgers Cancer Institute of New Jersey, USA

Ductal carcinoma *in situ* (DCIS) is a noninvasive breast cancer (BC) with possible microinvasions into the breast stroma. DCIS accounts for more than 16% of new BC diagnoses in women. DCIS progresses to Invasive Ductal Carcinoma (IDC) over time in 39-53% of patients, if left untreated. The vast majority of BC cases originate in the mammary duct. In this presentation, a nanoscale delivery system will be described that utilizes transpapillary delivery to achieve molecularly targeted, pathway-specific therapy in cancerous areas of the mammary duct. Our preliminary results with a nanosuspension of ciclopirox (CPX) in an orthotopic model of BC established the concept that sustained ductal exposure could completely suppress BC occurrence *in vivo*. For these studies polymeric NPs (nanoparticles) as well as lipid-polymer hybrid (LPH) NPs were the primary delivery vehicles. In order to achieve sustained precision treatment, HER2, transferrin receptor and/or EGFR were targeted using peptide ligands covalently bound to the surface of NPs. Ligand surface densities of 5% and 10% were evaluated and it was found that surface functionalized NPs enhanced binding and uptake into target cells. Cytoxicity was significantly increased with EGFR or TfR targeted NPs as compared to CPX alone or non functionalized CPX-loaded NPs. A synergistic effect was observed when CPX was administered with gedatolisib, a PI3K/Akt/mTOR inhibitor resulting in a dose reduction index of ~6. In addition, the treatments were effective not only in BC cells but also cancer stem-like cells. Our efforts in addition to describing these studies and results, the engineering of the NPs to enhance ductal retention and specificity will also be described.

Recent Publications

- 1. Gu Z et al. (2018) The effect of size and polymer architecture of doxroubicin-poly(ethylene) glycol conjugate nanocarries on breast duct retention, potency and toxicity. European Journal of Pharmaceutical Sciences. 121:118-125. Doi 10.1016/j.ejps.2018.04.033.
- Lee I H et al. (2018) Design and evaluation of a CXCR4 targeting peptide 4DV3 as an HIV entry inhibitor and a ligand for targeted drug delivery. European Journal of Pharmaceutics and Biopharmaceutics. pii: S0939-6411(18)30013-30014. Doi: 10.1016/j.ejpb.2018.06.004.
- 3. Singh Y D et al. (2012) Influence of molecular size on the retention of polymeric nanocarrier diagnostic agents in breast ducts. Pharmaceutical Research. 29(9):2377-2388. Doi:10.1007/s11095-012-0763-z.
- 4. Singh Y D et al. (2011) Noninvasive detection of passively targeted poly(ethylene glycol) nanocarriers in tumors. Molecular Pharmaceutics. 9(1):144-155. Doi:10.1021/mp2003913.

Biography

Patrick J Sinko is a Pharmacist (BS, Rutgers 1982) and a Pharmaceutical Scientist (PhD, University of Michigan 1988). He joined Rutgers, The State University of New Jersey in 1991 and rose through the academic ranks where he is currently a Distinguished Professor (II) and the Parke-Davis Endowed Chair in Pharmaceutics and Drug Delivery in the Ernest Mario School of Pharmacy. He is the Principal Investigator of an active research laboratory that focuses on biopharmaceutics, pharmaceutical formulations and molecular-, nano- and micro-scale drug delivery with specific applications to the treatment or prevention of HIV/AIDS, breast, brain and lung cancer, chemical terrorism countermeasures. He has received prestigious National Institutes of Health FIRST and MERIT awards and his lab has been continuously funded by the NIH for over 25 years.

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Attenuated protein toxins as intracellular nucleic acid delivery fibromyalgia and chronic pain vectors

Simon C W Richardson and Benedita Kac University of Greenwich, UK

any protein toxins have evolved to access a variety of relatively inaccessible intracellular compartments in order to exert virulence. Counted among this number are proteins such as ricin toxin, shiga toxin, diphtheria toxin and anthrax toxin. These proteins display diverse architecture ranging from AB5 to AB configurations and depending upon the specific B chain in question, entertain a number of strategies from direct membrane penetration to utilizing retrograde trafficking pathways to access a plethora of intracellular compartments including the cytosol. Typically the A chain will exhibit catalytic activity proportional to both cellular intoxication and virulence. However given the facile nature of protein recombination, attenuation is relatively simple. Here we describe the ability of attenuated anthrax toxin (ATx) to manipulate endocytic cargo sorting for the purposes of drug delivery, traversing intracellular compartmental boundaries for nucleic acid delivery. We report not only the efficiency with which siRNA and antisense effectors are delivered but also the mechanisms they utilize to traverse the barriers responsible for intracellular compartmentalization. Attenuated Atx:ASO complexes had transfection efficiency approximately equivalent to Nucleofection[®]. In HeLa cells, at 200 pmol ASO expression of the target gene was 5.4±2.0% relative to an untreated control after 24 h. Using 200 pmol ASOs, Nucleofection* reduced Synt5 expression to 8.1±2.1% after 24 h. PA:LFn-GAL4:ASO transfection of non- or terminally-differentiated THP-1 cells and Vero cells resulted in 35.2±19.1%, 36.4±1.8% and 22.9±6.9% (respectively) target gene expression after treatment with 200 pmol of ASO and demonstrated versatility. Nucleofection* with Stealth RNAi[™] siRNA reduced HeLa Synt5 levels to 4.6±6.1% whereas treatment with the PA:LFn-PKR:siRNA resulted in 8.5±3.4% Synt5 expression after 24 h (HeLa cells). These data underscore the tractability of this approach to both antisense and siRNA delivery.

Recent Publications

- 1. P D Dyer et al. (2016) An *in vitro* evaluation of epigallocatechin gallate (eGCG) as a biocompatible inhibitor of ricin toxin, Biochim. Biophys. Acta. 1860(7):1541-1550. Doi:10.1016/j.bbagen.2016.03.024.
- 2. P D Dyer et al. (2015) Disarmed anthrax toxin delivers antisense oligonucleotides and siRNA with high efficiency and low toxicity. Journal of Controlled Release. 220(PtA):316-328. Doi:10.1016/j.jconrel.2015.10.054.
- 3. S A Shorter et al. (2017) The potential of toxin-based drug delivery systems for enhanced nucleic acid therapeutic delivery. Expert Opinion on Drug Delivery. 14(5):685-696. Doi:10.1080/17425247.2016.1227781.
- 4. S A Shorter et al. (2017) Green fluorescent protein (GFP): is seeing believing and is that enough? Journal of Drug Targeting. 25(9-10):809-817. Doi:10.1080/1061186X.2017.1358725.
- 5. M W Pettit et al. (2014) Construction and physiochemical characterization of a multi-composite, potential oral vaccine delivery system (VDS). International Journal of Pharmaceutics. 468(1-2):264-271. Doi:10.1016/j.ijpharm.2014.03.046.

Biography

Simon C W Richardson is a Founder, Director and CSO at Intracellular Delivery Solutions Ltd, and Reader (Associate Professor) in Membrane Trafficking and Drug Delivery, at the University of Greenwich, UK. The driving theme behind his research is the intracellular delivery of antisense and RNAi to the cytosol. He is currently leading the Cell Biology Research Cluster within the Faculty of Engineering and Science, located at the Medway campus. His lab is currently working with several technologies based upon attenuated virulence factors that have very low *in vitro* toxicity profiles (and are minimally disruptive to the cell), and very high efficiency intracellular delivery profiles. We are also examining several methodologies to modulate protein stability and intracellular trafficking to aid the oral delivery of vaccines.

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Smart combination nanopreparations for cancer: Bringing drugs inside cells and to individual organelles

Vladimir P Torchilin CPBN - Northeastern University, USA

umor therapy, especially in the case of multidrug resistant cancers, could be significantly enhanced by using siRNA down-L regulating the production of proteins, which are involved in cancer cell resistance, such as Pgp or survivin. Even better response could be achieved is such siRNA could be delivered to tumors together with chemotherapeutic agent. This task is complicated by low stability of siRNA in biological surrounding. Thus, the delivery system should simultaneously protect siRNA from degradation. We have developed several types of lipid-core polymeric micelles based on PEG-phospholipid or PEI-phospholipid conjugates, which are biologically inert, demonstrate prolonged circulation in the blood and can firmly bind non-modified or reversibly-modified siRNA. Additionally, these nanopreparations can be loaded into their lipidic core with poorly water soluble chemotherapeutic agents, such as paclitaxel or camptothecin. In experiments with cancer cell monolayers, cancer cell 3D spheroids, and in animals with implanted tumors, it was shown that such co-loaded preparations can significantly down-regulate target proteins in cancer cells, enhance drug activity, and reverse multidrug resistance. This is illustrated by the efficient treatment of MDR (multi-drug resistance) cancer cells with combi-nations of siRNA-Pgp or siRNAsurvivin stabilized in polymeric mixed mi-celles and doxorubicin, or tariquidar (Pgp inhibitor) and paclitaxel loaded into the same lipo-some or lipid-core polymeric micelle. In order to specifically unload such nanopreparations inside tumors, we made them sensitive to local tumor-specific stimuli, such as lowered pH, hypoxia, or overexpressed certain enzymes, such as matrix metalloproteases. Using pH-, redox-conditions, hypoxia-, or MMP2-sensitive bonds between different components of nanopreparations co-loaded with siRNA and drugs, we were able to make the systems specifically delivering biologically active agents in tumors, which resulted in significantly improved therapeutic response. We have also developed approaches to target individual intracellular organelles to initiate the apoptosis in resistant cancer cells.

Recent Publications

- Zhu L et al. (2013) Enhanced anticancer activity of nanopreparation containing an MMP2-sensitive PEG-drug conjugate and cell penetrating moiety. Proceedings of National Academy of Sciences of the USA. 110(42):17047-17052.
- 2. Jhaveri A, Deshpande P and Torchilin V (2014) Stimuli-sensitive nanopreparations for combination cancer therapy. Journal of Controlled Release. 190:352-370.
- 3. Zhu L et al. (2014) Matrix metalloproteinase 2 sensitive multifunctional polymeric micelles for tumor-specific codelivery of siRNA and hydrophobic drugs. Biomaterials. 35(13):4213-4222.
- 4. Torchilin V P (2014) Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nature Reviews Drug Discovery. 13(11):813-827.
- 5. Perche F et al. (2014) Hypoxia-targeted siRNA delivery. Angewandte Chemie International Edition. 53(13):3362-3366.

Biography

Vladimir P Torchilin, PhD, DSc is a University Distinguished Professor of Pharmaceutical Sciences and Director, Center for Pharmaceutical Biotechnology and Nanomedicine of Northeastern University, Boston, USA. His interests include drug delivery and targeting, nanomedicine, multifunctional and stimuli-sensitive pharmaceutical nanocarriers, biomedical polymers, experimental cancer therapy. He has published more than 400 original papers, more than 150 reviews and book chapters, has written and edited 12 books, and holds more than 40 patents. Google Scholar shows more than 52,000 citations of his papers with H-index of 102. He is Editor in Chief of *Current Drug Discovery Technologies, Drug Delivery*, and *OpenNano*; Co Editor of *Current Pharmaceutical Biotechnology* and on the Editorial Boards of many other journals. He received more than \$30 M from the governmental and industrial sources in research funding. He has multiple honors and awards and in 2011, Times Higher Education ranked him number 2 among Top World Scientists in Pharmaceougy for the period of 2000-2010.

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Antibody-proteases as a novel biomarker and a unique target to suit translational tools to be applied for biodesign, bioengineering and regenerative medicine therapeutic for a treatment of EGFR-dependent breast cancer tumors

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Catalytic Abs (catAbs) are multivalent im-munoglobulins (Igs) with a capacity to hy-drolyze the antigenic (Ag) substrate. In this sense, proteolytic Abs (Ab-proteases) repre-sent Abs to provide proteolytic effects. Abs against myelin basic protein/ MBP with pro-teolytic activity exhibiting sequence-specific cleavage of MBP are of great value to moni-tor demyelination whilst in MS. The activity of Ab-proteases was first registered at the subclinical stages 1-2 years prior to the clin-ical illness. And the activity of the Ab-proteases revealed significant correlation with scales of demyelination and the disabil-ity of the patients as well. So, the activity of Ab-proteases and its dynamics tested would confirm a high subclinical and predictive (translational) value of the tools as applicable for personalized monitoring protocols. Of tremendous value are Ab-proteases directly affecting remodeling of tissues with multilevel architectonics (for instance, mye-lin). By changing sequence specificity one may reach reduction of a density of the neg-ative proteolytic effects within the myelin sheath and thus minimizing scales of demye-lination. Ab-proteases can be programmed and re-programmed to suit the needs of the body metabolism or could be designed for the development of new catalysts with no natural counterparts. Further studies are needed to secure artificial or edited Ab-proteases as translational tools of the newest generation to diagnose, to monitor, to con-trol and to treat and rehabilitate MS patients at clinical stages and to prevent the disorder at subclinical stages in persons-at-risks to secure the efficacy of regenerative manipula-tions.

Recent Publications

- 1. Ponomarenko N A et al. (2002) Catalytic antibodies in clinical and experimental pa-thology: human and mouse models. Journal of Immunological Methods. 269(1-2):197-211.
- 2. Ponomarenko N A et al. (2005) Catalytic ac-tivity of autoantibodies toward myelin basic protein correlates with the scores on the mul-tiple sclerosis expanded disability status scale. Immunol. Lett. 103(1)45-50.
- 3. Gabibov A G et al. (2006) Catalytic autoanti-bodies in clinical autoimmunity and modern medicine. Autoimmunity Reviews. 5(5):324-330.
- 4. Gabibov A A, Paltsev M A and Suchkov S V (2011) Antibody-associated proteolysis in surveillance of autoimmune demyelination: clinical and preclinical issues. Future Neu-rology. 6(3):303-305.
- 5. D Kostyushev et al. (2011) Myelin-associated serological targets as applicable to diagnostic tools to be used at the preclinical and transient stages of multiple sclerosis pro-gression. Open J. Immunology. 1(3):80-86.

Biography

Sergey Suchkov graduated from Astrakhan State Medical University and was awarded with MD; in 1985 maintained his PhD at the I M Sechenov Moscow Medical Academy and in 2001, maintained his Doctor Degree at National Institute of Immunology, Russia. From 1987 through 1989 was a Senior Researcher at Koltzov Institute of Developmental Biology. From 1989 through 1995, he was the Head of the Lab of Clinical Immunology, Helmholtz Eye Re-search Institute in Moscow. From 1995 through 2004, a Chair of the Department for Clinical Immunology, Moscow Clinical Research Institute (MONIKI). He has been trained at: Na-tional Institute of Health; Wills Eye Hospital, Pennsylvania, USA; University of Florida in Gainesville; University of California San Francisco; Johns Hopkins University, Baltimore, MD, USA respectively. He was an Exe Secretary-in-Chief of the Editorial Board, *Biomedical Science*, an international journal published jointly by the USSR Academy of Sciences and the Royal Society of Chemistry, UK. At present, he is a Chair, Department for Chemical Society (ACS), USA; American Heart Association (AHA), USA; European Association for Predictive, Preventive and Personalized Medicine (EPMA), Belgium; American Association for Research in Vision and Ophthalmology (ARVO); ISER (International Society for Eye Research); Personalized Medicine Coalition (PMC), Washington, USA.

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Volume 4

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25th Nano Congress for Future Advancements

& 12th Edition of International Conference on Nanopharmaceutics and Advanced Drug Delivery

August 16-18, 2018 | Dublin, Ireland

Plenary Day 2

Nano Congress 2018 & Nano Drug Delivery 2018

12th Edition of International Conference on

Nanopharmaceutics and Advanced Drug Delivery

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Joong Tark Han

Korea Electrotechnology Research Institute, Republic of Korea

Nanocarbon based electrode technology for soft electronics

Flexible electrodes fabricated with conducting soft electromaterials such as carbon nanotubes (CNTs), graphene and metal nanowires are of great interest for various applications, ranging from alternative electrodes for flexible electronics. However, the difficulty in processing these soft electro materials represents one of the key challenges to researchers working in this area. In this talk, author will present his recent progress in synthesis of nanocarbon hybrid materials and their processing technologies for applications in flexible electrode technology towards soft electronics. The judicious use of supramolecular chemistry and interfacial engineering technology allows fabrication of printable, spinnable, and chemically compatible conducting pastes with high-quality nanocarbon(NC) materials, useful in flexible electronics and textile electronics.

Biography

Joong Tark Han has completed his PhD from Pohang University of Science and Technology. He is the Center Director of Nano Hybrid Technology Research Center at KERI in Korea, and a Professor of Department of Electro-Functionality Materials Engineering at UST. He has published more than 90 papers in reputed journals.

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12th Edition of International Conference on

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Silvia Panseri

National Research Council of Italy, Italy

Attractive advanced cell therapy by using bioresorbable magnetic nanoparticles

Cell therapy is one of the most exciting and promising areas for disease treatment and regenerative medicine. However the success rate of cell-based therapies, despite their great potential, is limited mainly due the ineffective delivery and retention of therapeutic cells in the specific organ. Magnetic targeting has emerged as a method to overcome these limitations. So far these attempts have used superparamagnetic iron oxide nanoparticles (SPIONs), only clinically approved metal oxide nanoparticles. Nevertheless the exposure to SPIONs has always been associated with significant toxic effects such as inflammation, apoptosis and generation of ROS. Our group, by doping hydroxyapatite (HA), the mineral component of bone, with Fe²⁺/Fe³⁺ ions, had obtained novel biocompatible and fully bioresorbable superparamagnetic nanoparticles (FeHA). This work demonstrates the opportunity of FeHA in mesenchymal stem cells (MSCs) labeling. MSCs easily internalized the FeHA, and they became magnetic enough to be guided and retained to specific site by a magnet. Magnetic MSCs maintained their morphology and cell viability was not negatively affected. Due the well-known osteoinductive feature of HA, magnetic MSCs overexpress osteogenic genes. We are also investigating the possibility to combine these above-mentioned results with the contrast ability of FeHA for a real time imaging of the magnetic MSCs *in vivo* by magnetic resonance imaging. In conclusion, due to the intrinsic magnetic properties of FeHA, its fast degradation and very low iron content compared to SPIONs, this approach could be simply transferred to different cell types obtaining an attractive advanced approach for several regenerative medicine applications.

Biography

Silvia Panseri is a Biologist and has completed her PhD in 2009 at the University of Milan, Italy. Her research activity is mainly focus on nano and regenerative medicine. She has great expertise in cell-biomaterial interactions at the nanoscale, in magnetic cell guiding and 3D cell culture in bioreactor with several scaffolds. She is an author of more than 50 papers published in international peer-reviewed journals, 12 book chapters, co-inventor of two patents and H-index=19. She has been serving as a Guest Editor in *International Journal of Molecular Sciences* and Frontiers in *Bioengineering and Biotechnology*.

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Ying Wan

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Thermally reduced gold nanoparticles confined by ordered mesoporous carbon as an efficient catalyst for selective hydrogenation

old nanocatalysts represent a new generation of catalysts for the selective oxidation and reduction using molecular O₂ Jand H,, showing great potentials for green chemistry. Activated carbons are one of the most frequently used supports in industry. However, activated carbon has been seldom used for gold deposition. Here a coordination-assisted self-assembly approach is adopted for the intercalation of thermally reduced gold nanoparticles inside ordered mesoporous carbon frameworks. An almost complete conversion of benzyl alcohol to benzoic acid is achieved within 60 min over the Au/C catalyst with gold nanoparticles approximately 9.0 nm under 90°C and 1 MPa, using potassium hydroxide as a base. A reduction of gold particle size from 9.0 to 3.4 nm in the catalyst leads to a high activity toward the selective oxidation of benzyl alcohol to benzyl acid and toward the reduction of p-nitrophenol to p-aminophenol at low temperatures such as 0°C. The electronic modification of the d-orbitals of small particles is extremely important for chemisorption of O₂ at atmosphere pressure and low temperatures. Interstingly, thermally reduced Au/C nanocatalyst with gold nanoparticles approximately 2.8 nm is highly active and selective to convert p-chloronitrobenzene and 4-nitrophenol to corresponding amines using H₂ as a reducing agent, reaching an initial reaction rate of 12.7 and 6.5 min⁻¹, respectively. By comparison, the commercial Au/C catalyst is inert under the same reaction conditions. Trapping by the SH-functionalized SBA-15 solids confirms the negligible gold leaching and the heterogeneous active centers for thermally reduced Au/C. Obvious changes are undetected for catalytic performance after five runs. These results indicate that the gold-containing mesoporous carbon catalyst is stable and can be reused. The simultaneous thermal reduction of gold nanoparticles and pyrolysis of the matrix may facilitate the involvement of gold inside the carbon matrix, the modification of carbon atoms on the gold surface, and the reconstruction of the surface induced by CO adsorption. The generation of low-coordinated gold atoms possibly reduces the H, dissociation barrier, and can therefore significantly improve the hydrogenation activity.

Biography

Ying Wan received her PhD degree in Industrial Catalysis from the East China University of Science and Technology in 2002. Then, she joined Shanghai Normal University where she was promoted to a full professor in 2006. In 2005-2007, she carried out her postdoctoral research at Fudan University working with Professor Dongyuan Zhao. Currently, Ying Wan is the leader of the Program for Innovative Research Team in University, China. Her research focuses on sintering-, and poisoning-resistance metal nanocatalysts supported on mesoporous carbons, and their applications in green organic synthesis and energy chemistry. She has contributed to about 70 peer-reviewed scientific publications with more than 7000-times citations and 3 books. She has been an associate editor of *Journal of Porous Materials* since 2013.

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Monica Montesi

National Research Council of Italy, Italy

Smart biomimetic nanoparticles: A new platform for nanomedicine

The ever increasing need of more effective and targeted therapies for the treatment of cancer and various degenerative pathologies is pushing material scientists to develop new solutions associating enhanced safety with smart functionality, also permitting the establishment of personalized therapeutic approaches. In this respect, the development and use of nanoparticles is today limited by several factors among which: i) low biodegradability and biocompatibility; ii) toxic by-products; iii) uncontrolled drug release into the bloodstream; iv) limited cell-target specificity and v) low efficiency in crossing biological barriers. In this respect a novel apatite based nanoparticle(NPs) have attracted the attention of scientific community for biological and medical purposes as promising materials in drug or gene delivery, DNA/biomolecules separation, hypothermal treatment of tumours, contrast agents for imaging, and recently in tissue engineering and theranostic applications. Recently, novel biomimetic, fully biodegradable and cytocompatible NPs fabricated by doping hydroxyapatite (HA) with Fe ions (FeHA), avoiding the presence of magnetic secondary phases and coating, were developed and biologically tested as new drug delivery systems. The wide possibility of surface functionalization of apatitic nanoparticles significantly extends the potential to develop smart drug carriers with active or passive ability to cross physiological barriers and to reach relevant organs such as the brain, the lung or the heart.

Biography

Monica Montesi has obtained her PhD in Cellular and Molecular Biology at the University of Bologna and she has 12 years of expertise in cellular and molecular biology associated to material science for nanotechnology, tissue engineering research and regenerative medicine. She is a scientific coordinator of NanoBioMagnetism Laboratory. She is an author of 40 papers published in international journals, several book chapters and more than 30 congress communications. She has been serving as an Editorial Board Member of international *Journal of Bone and Mineral Metabolism* and Guest Editor of *International Journal of Molecular Sciences*.

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Scientific Tracks & Abstracts Day 2

Nano Congress 2018 & Nano Drug Delivery 2018

Sessions

Nano Applications | Nano Science and Technology | Medical Applications in Nanotechnology | Biomarkers and Personalized Medicine | Cancer and Nanotechnology | Nanomaterials for Drug Delivery | Novel Drug Delivery Systems

| Animes | | o-Chair Richardson f Greenwich, UK | |
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| Session Introduction | | | |
| Title: | tle: Title: Nanotheranostics: TPGS micelles for early diagnosis and therapy of cancer | | |
| | Muthu Madaswamy Sona, University of Singapore, India | | |
| Title: | e: Title: Influence of molecular structure and temperature on the adsorption behavior of PEO-PPO-PEO surfactants: A QCM-D study Lorenz De Neve, Ghent University, Belgium | | |
| Title: | le: Title: Nano particle targeting assessed by novel photo acoustic and PET imaging: Internal normalization by multi spectral imaging | | |
| Titles | Robert K Prudhomme, Princeton University, USA | | |
| Time: | Title: Nano-amorphous Abiraterone acetate formulation with improved bioavailability and eliminated food effect Tamás Solymosi, NanGenex Inc., Hungary | | |
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| Title: | tle: Title: Immunoliposomes containing simvastatin, targeted towards EGFR, as potential therapeutic for a treatment of EGFR-dependent breast cancer tumors Lucyna Matusewicz, University of Wroclaw, Poland | | |

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Nanotheranostics: TPGS micelles for early diagnosis and therapy of cancer

Muthu Madaswamy Sona University of Singapore, India

Manotheranostics have shown the development of advanced platforms that can diagnose cancer at early stages, initiate first-line therapy, monitor it, and if needed, rapidly start subsequent treatments. In nanotheranostics, therapeutic and diagnostic agents are loaded with nanomedicine in a single theranostic platform, which can be further developed as clinical formulations for targeting different types of cancer. This speech is concerned about theranostic micelles developed using TPGS (tocopheryl polyethylene glycol succinate), docetaxel and gold nanoclusters for the early diagnosis and therapy of cancer with advanced features. Micelles are amphiphilic spherical nanostructures consisting of hydrophilic shell and hydrophobic core. Micelles have advantages such as thermodynamic stability, kinetic stability, higher payload and smaller dimension (less than 50 nm). In our group, various research studies were done on targeted micelles for cancer diagnosis and therapy. In future, nanotheranostics will be able to provide personalized treatment which can make cancer even curable or at least treatable at the earliest stage.

Recent Publications

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- 2. Sonali et al. (2018) Nanotheranostics: Emerging strategies for early diagnosis and therapy of brain cancer. Nanotheranostics. 2(1):70-86.
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- 4. Muthu M S et al. (2015) Theranostic Vitamin E TPGS micelles of transferrin conjugation for targeted co-delivery of docetaxel and ultra bright gold nanoclusters. Biomaterials. 39:234-248.
- 5. Muthu M S et al. (2014) Nanotheranostics: Application and further development of nanomedicine strategies for advanced theranostics. Theranostics. 4(6):660-677.

Biography

Muthu Madaswamy Sona earned his Bachelor's Degree in Pharmacy in 2002; Master's Degree in Pharmaceutical Technology from India in 2004 and PhD Degree in Pharmaceutics from IIT, Varanasi, India in 2009. He did his Postdoctoral trainings in the Department of Chemical Engineering at National University of Singapore as a Recipient of Boyscast Fellowship and CREST Award from India. He is also an Awardee of DST Young Scientist in 2012. His research interest is to develop advanced nanomedicine as novel platform for diagnosis and therapy. He has authored over 64 peer-reviewed publications with a cumulative impact factor of >240, citation of 2100 and h-index of 24.

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Influence of molecular structure and temperature on the adsorption behavior of PEO-PPO-PEO surfactants: A QCM-D study

Lorenz De Neve and Paul Van der Meeren Ghent University, Belgium

Poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) block copolymer surfactants (poloxamers or pluronics) are used as stabilizer in various nanosuspensions, e.g. of rilpivirine, danazol, diclofenac, asulacrine and itraconazole. In order to have a stabilizing effect on hydrophobic particles, these PEO-PPO-PEO surfactants should adsorb to the particle surface. In this research, the adsorption behavior of pluronics with two different ethylene oxide contents (50% and 80%) and three different molecular weights of the propylene oxide part (i.e. 950, 1750 and 3250 g/mol) was studied at 20°C and 37°C onto gold sensors coated with 1-undecanethiol using a quartz crystal microbalance with dissipation (QCM-D). Pluronic solutions with 5 different concentrations were used, ranging from 0.02 mg/ml to 50 mg/ml. Our results indicate a significant (linear) effect of the pluronic concentration on the average adsorption during the adsorption steps. No clear effect could, however, be detected after rinsing of the sensors with ultrapure water. The molecular weight of the PPO part seemed to have a proportional effect on the adsorbed amounts after rinsing, but no clear effect during the adsorption steps. The ethylene oxide content seemed to have an effect during both the adsorption and rinsing steps at 20°C and 37°C. The obtained results were useful to gain more insight in the stability differences between nanosuspensions with different pluronic concentrations (and molecular structure).

Recent Publications

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- 4. Ganta S et al. (2009) Formulation and pharmacokinetic evaluation of an asulacrine nanocrystalline suspension for intravenous delivery. International Journal of Pharmaceutics. 367(1-2):179-186.
- 5. Mouton J W et al. (2006) Pharmacokinetics of itraconazole and hydroxyitraconazole in healthy subjects after single and multiple doses of a novel formulation. Antimicrobial Agents and Chemotherapy. 50(12):4096-4102.

Biography

Lorenz De Neve started his carrier as a Researcher with his master thesis on the sorption behavior of cationic surfactants. During this period he obtained experience concerning the preparation and characterization of liposomal dispersions, including viscometry using rotational viscometers, submicron particle sizing by dynamic light scattering and adsorption analysis by both QCM-D and by the traditional depletion technique. Currently he is conducting research on pharmaceutical nanosuspension formulations. More specifically the purpose of his research is to enlarge the fundamental knowledge of the link between the formulation parameters and the macroscopic properties of nanosuspensions and to understand the interactions between the different formulation parameters.

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Nano particle targeting assessed by novel photo acoustic and pet imaging: Internal normalization by multi spectral imaging

Robert K Prud'homme^{1,2}, Leon Z Wang¹, Hoang D Lu¹, Tristan L Lim¹, Brian K Wilson¹ and Andrew Heinmiller^{1,2} ¹Princeton University, USA ²FUJIFILM VisualSonics Inc., Canada

There is an increased demand for fast and inexpensive methods to determine cancer phenotypes and morphologies. Current in vivo diagnostic imaging modalities utilizing X-ray CT, MRI, and PET scans are limited to black-white images that cannot be used to differentiate multiple disease marker contrast agents at a time. In addition, targeting studies in which each nanoparticle (NP) type must be individually administered to an animal result in large numbers of animals that must be used in a study to obtain reliable statistics. This requires both significant time and expense. Photoacoustic (PA) imaging, a hybrid light and sounds imaging technique, has shown to be a safe and inexpensive diagnostic technique with high spatial resolution in 3D. Traditional PA contrast agents, however, tend to have broad absorption peaks in the NIR range which renders it difficult to simultaneously image more than one signal at a time in deep tissue. Here we present the formulation of a series of PA active NPs with sharp and separable absorbance profiles in the NIR range for simultaneous multiplexed imaging. PA dyes are encapsulated inside NPs using the controlled self-assembly mechanism, Flash nanoprecipitation (FNP). Four new contrast agents, with sharp absorbance maxima between 600-900 nm, were created by encapsulating a variety of phthalocyanine derivatives. We were able to simultaneously detect the concentrations of contrast agents mixed together with >95% deconvolution efficacy. As a proof of concept, we co-injected RGD modified NPs and non-modified NPs with different labeling agents and tracked NP biodistributions for both particles simultaneously. Using this technology, we accessed the effect of NP ligand modification on both targeting efficacy onto the tumors and off targeting accumulation in the liver using a single animal model. Over modification of the NPs resulted in rapid liver clearance and poor accumulation in the tumor; at low modifications, the tumor to liver accumulation ratio is 9.9±4.2, while at high RGD modifications the tumor to liver accumulation ratio is 52±22. The ability to simultaneously inject control particles and targeted particles, and to follow their fate greatly enhances the ability to design targeted nanoparticles. The same phthalocyanine dyes effectively chelate PET active cations to enable whole animal PET imaging. The FNP technology enables the production of both NPs that enable PAI and PET imaging.

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- 2. Lu H D et al. (2015) Modulating vibrio cholerae quorum-sensing-controlled communication using autoinducerloaded nanoparticles. Nano Letters. 5(4):2235-2241.
- 3. Lu H D et al. (2017) Copper loading of pre-formed nanoparticles for PET-imaging applications. ACS Applied Materials & Interfaces. 10(4):3191-3199.
- 4. Lu H D et al. (2017) Real-time and multiplexed photoacoustic imaging of internally normalized mixed-targeted nanoparticles. ACS Biomaterials Science & Engineering. 3(3):443-451.
- 5. Lu H D et al. (2017) Nanoparticle targeting of grampositive and gram-negative bacteria for magnetic-based separations of bacterial pathogens. Applied Nanoscience. 7(3-4):83-93.

Biography

Robert K Prud'homme is a Professor in the Department of Chemical and Biological Engineering at Princeton University, USA. He is the Founding Director of the Program in Engineering Biology. His research program focusses on polymer self-assembly applied to drug delivery. The development of Flash Nanoprecipitation (FNP) in his laboratory enabled the encapsulation of poorly soluble drug compounds and oligonucleotides for therapy directed towards cancer, TB, and injections. FNP is a scalable and continuous process that is enables integrated processing and spray drying for low cost oral and aerosol formulations. Under sponsorship by the Bill and Melinda Gates Foundation, the process is being adopted to formulate new compounds coming from TBA, MMV, and DNDi.

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Nano-amorphous *Abiraterone acetate* formulation with improved bioavailability and eliminated food effect

Tamás Solymosi, Réka Angi, Orsolya Basa Dénes, Tamás Jordán and Hristos Glavinas NanGenex Inc., Hungary

A biraterone acetate (AA) is a poorly water soluble drug molecule indicated for metastatic castration resistant prostate cancer. The drug product Zytiga possesses the highest food effect of all marketed drugs. Despite of the extremely poor absorption of AA in fasted conditions, Zytiga is to be taken strictly without food. We have developed a nano-amorphous abiraterone acetate formulation prepared by controlled precipitation followed by lyophilization. The formulation exhibited higher apparent solubility and passive permeability when compared to either the crystalline AA or Zytiga. DLS (Dynamic Light Scattering) measurements and filtration experiments yielded particle size in the 100-200 nanometer range when the solid formula was reconstituted in water. The active ingredient in the formulation was amorphous by XRD (X-ray Powder Diffraction). Beagle dog studies showed 10-fold increase in exposure from the novel formulation when compared to the marketed drug. Also, the marked food effect seen with Zytiga was not observed for the nano-amorphous AA. A first-in-human clinical trial was conducted with a lyophilized powder-in bottle formulation in healthy male volunteers. The active ingredient was rapidly absorbed in both the fasted and the fed states. Based on the PK (Pharmacokinetics) analysis a 250 mg dose of the novel formulation is predicted to give the same exposure as 1000 mg Zytiga in the fasted state. As in preclinical studies, the significant positive food effect was eliminated. Moreover, variability of exposure was reduced when compared to Zytiga. In conclusion we have developed a novel nano-amorphous AA formulation that significantly outperformed the marketed .

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- 2. Solymosi T et al. (2017) Development of an abiraterone acetate formulation with improved oral bioavailability guided by absorption modeling based on *in vitro* dissolution and permeability measurements. International Journal of Pharmaceutics. 532(1):427-434.
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- 5. Chi K N et al. (2015) food effects on abiraterone pharmacokinetics in healthy subjects and patients with metastatic castration-resistant prostate cancer. The Journal of Clinical Pharmacology. 55(12):1406-1414.

Biography

Tamás Solymosi holds an MSc Degree in Chemical Engineering and currently working on his PhD thesis about the formulation of abiraterone acetate. He has been working at NanGenex, Budapest, Hungary for the past 9 years, gaining experience in the formulation of poorly water soluble active ingredients. He is interested in the physicochemical background of nanoformulation and bioavailability increasing technologies.

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Controlled release of bovine serum albumin from surfactant modified alginate beads

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A lginate is a biopolymer which is used in several biomedical applications by means of its favorable properties, such as biodegradability, biocompatibility and non-toxicity. In the present study, the availability of alginate gel to encapsulate and release a protein type drug was investigated. The use of alginate has been reported before for the controlled release of bovine serum albumin (BSA), however favorable controlled release behavior was only achieved by the help of clay incorporation to alginate beads. Recently, it was reported that incorporation of anionic surfactant, sodium dodecyl sulfate (SDS) into alginate increases the Young's modulus of the alginate beads. Moreover, SDS and bovine serum albumin interaction via complexation mechanism was reported. In the light of the last two works, SDS was incorporated into alginate beads to enhance protein-loading efficiency of hydrogel and to prevent the burst release of protein drug. Bovine serum albumin (BSA) was used as model protein drug. It was found that SDS modified calcium alginate beads encapsulated almost the initial amount of loaded drug. The protein release experiments were done in simulated gastric fluid (SGF) and simulated intestinal fluid (SIF). Results of release experiments showed that SDS modified alginate beads showed controlled and time efficient drug release. Characterization of the beads was performed by Scanning electron microscope (SEM), Fourier transform infrared spectroscopy (FTIR), and swelling experiments, respectively.

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- 3. Matei I et al. (2014) Cationic spin probe reporting on thermal denaturation and complexation–decomplexation of BSA with SDS: potential applications in protein purification processes. Journal of Physical Chemistry B 118(38):11238-11252.

Biography

Nilay Kahya completed her MSc Degree in Chemistry at ITU Graduate School of Science Engineering and Technology in 2016. She is currently a PhD candidate working under the guidance of Professor F Bedia Erim Berker. Her research field of interest are mainly related to the applications of biopolymers in drug delivery systems and adsorption fields. She has four publications in Science Citation Index Expanded journals by March 2018.

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Immunoliposomes containing simvastatin, targeted towards EGFR, as potential therapeutic for treatment of EGFR-dependent breast cancer tumors

Lucyna Matusewicz and Aleksander F Sikorski University of Wroclaw, Poland

Introduction: Epidermal Growth Factor Receptor (EGFR) was shown to be highly expressed in many types of human cancer, among others, in breast cancers. EGFR overexpression correlates with advanced stage of the disease and with poor response to chemotherapy. One of the promising strategy for the treatment of EGFR-dependent tumors is to inhibit signal transduction from EGFR via disruption of cholesterol rich membrane rafts. We assume that targeted delivery of simvastatin, a popular cholesterol-depleting drug widely prescribed in the treatment of cardiovascular diseases, will specifically disorganize membrane rafts and therefore disturb the EGFR dependent signalling pathways that usually promote cell proliferation and metastases. Statins were shown to exert antitumor effects in high doses, but those may lead to serious side effects. Therefore, the main purpose of this work is to obtain targeted, long circulating liposomes with simvastatin and to test their anticancer activity both *in vitro* and *in vivo*.

Methodology: Liposomes were prepared via lipid film hydration method and modified by attachment of antibodies specific to EGFR. Stability, selectivity and toxicity of targeted liposomes were analyzed both *in vitro* and *in vivo*. The level of activation of selected kinases involved in transduction of signals stimulated via EGF in cells treated by immunoliposomal statin was examined. Moreover, changes in plasma membrane order of cells exposed to liposomal simvastatin were examined using FLIM (Fluorescence-lifetime imaging) method.

Findings: Designed immunoliposomes were stable over 6 months, selective towards EGFR overexpressing cells and showed antitumor efficacy both *in vitro* and *in vivo*. Inhibition of signaling pathway involving Akt in cells treated with immunoliposomal simvastatin and disruption in plasma membrane order were observed.

Conclusions: Presented immunoliposomal formulation of simvastatin seems reasonable solution of a specific delivery of high doses of this drug into tumor cells and a candidate of further evaluation for efficacy either in monotherapy or in combination in anticancer therapies in the future.

Recent Publications

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- 3. Alupei M C et al. (2015) Liposomal simvastatin inhibits tumor growth via targeting tumor-associated macrophagesmediated oxidative stress. Cancer Lett. 356(2 Pt B):946-952.
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- 5. Kutty R V and Feng S S (2013) Cetuximab conjugated vitamin E TPGS micelles for targeted delivery of docetaxel for treatment of triple negative breast cancers. Biomaterials. 34(38):10160-10171.

Biography

Lucyna Matusewicz graduated with MSc in Biotechnology in 2012. She is currently a PhD student at the University of Wroclaw, Poland. She started her PhD project and for almost 6 years has been focusing mainly on drug delivery systems in anticancer therapy.

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Plenary Day 3

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Nanopharmaceutics and Advanced Drug Delivery

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Laura Oliveira Nascimento

State University of Campinas, Brazil

Pre-formulation of Nanostructured Lipid Carriers (NLC) for drug delivery: Excipient-excipient interaction

N LCs are composed by at least one solid lipid, one oil, surfactant and water. Previous works used regular purified oils and focused mostly on dosage form optimization; however these approaches present contaminants that can mask or mislead interactions, whereas optimization designs allows few excipients to be tested. Therefore, our goal was to assess physicochemical interactions due to super refined lipids and surfactants in NLCs loaded with lidocaine. Free drug analysis included: drug solubility and partition coefficient, thermal profile of solid excipients. NLC was formulated according to nonregular design of experiment (Hall 2, 2 levels of substance concentration, 8 excipient inputs and 1drug input). NLC outputs included z-average, polydispersity index, zeta potential and entrapment efficiency. Z-average (ZA) presented unimodal distribution, mean size (322±47) nm. The interaction between polysorbate-80 (PS), castor oil (CA) and cetyl palmitate (CP) affected ZA. Polydispersity index (PDI) variated between 0.14 to 0.35, mean (0.23±0.05). The main factors that influenced PDI were PS, CP and CA. Zeta potential (ZP) presented mean value (-46.2±4.4) mV. Surfactants influenced ZP values depending on the liquid lipids. Entrapment efficiency was between 58% and 79%, mean (72±5)% and interaction among liquid lipids was crucial to this output, such as cottonseed (CS) and capric/caprylic (CC) oils. Based on the responses, CA, CP, CC and PS were the most interactive excipients; our innovative approach provided an extensive information base, broad excipient analysis, unpublished interactions and relevant information for further formulation optimization.

Biography

Laura de Oliveira Nascimento has completed her PhD from University of São Paulo (USP), Brazil in 2011 with Doctoral internship at Boston University, USA, and Postdoctoral studies in USP. She is a Professor at State University of Campinas, Brazil. Her research group is focused on nanotechnology and freeze dried pharmaceutical dosage forms.

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Anthony N Papathanassiou

National and Kapodistrian University of Athens, Greece

Dispersed nano-graphene platelets within water-soluble bio-compatible polymers: Characterization of multi-scale electric charge flow in combined pressure and temperature conditions

The electronic properties of polymer composites with dispersed nano-graphene platelets (NGPs) depend on the transition rate is determined by the concentration of conducting islands, pressure and temperature. Different electric charge flow mechanisms are characterized by different transition rates which can be resolved by employing broadband dielectric spectroscopy (BDS). Polyvinylalcohol (PVA) and polyvinylalcohol/polyvinylpyrrolidone (PVA/PVP) 50 w/w, which are flexible, water-soluble, bio-compatible polymers with sufficient optical transparency, were loaded with NGP fractions in the vicinity of electrical percolation threshold. BDS at temperatures below 313 K and pressures up to 30 MPa results in balancing conductivity vs. capacitance effects. A number of interesting phenomena are reported and interpreted, in terms of the critical behavior of the composites around the insulator to conductor transition, as well as to the glass transition of PVA. Pressure-temperature BDS enables a detailed insight into microscopic charge transport processes, providing the knowledge for functionalization and optimization of the physical properties of the nano-composites. The switching behavior of the nano-composites suggests that they may probably be used as pressure sensors.

Biography

Anthony N Papathanassiou is leading the Dielectric Spectroscopy Laboratory at the Department of Physics, National and Kapodistrian University of Athens (NKUA), Greece. He got his PhD in Solid State Physics from NKUA. He worked as Research Associate in NKUA, Universität Bayreuth and Lyman Physics Laboratory, Harvard University as a Research Scholar or Research Fellow. His current research interest is on electric charge transport and relaxation in electron-conducting polymers and nano-composites, emphasizing on the role of pressure and temperature on electronic properties and phase transitions of condensed matter.

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Ewa Kazimierska

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How carbon nanotubes functional groups influence copper electrodeposition for electrical transmission?

Ultraconductive copper-carbon nanotubes composites are novel advanced materials for fabrication of lighter and more stable electrical wires to provide more efficient energy transport. To overcome the limitation of copper and CNTs incompatibility various types of pre-functionalised nanotubes were used. The dynamics of electrochemical deposition and dissolution of copper in the presence of amine- and carboxylic- functionalized multiwalled carbon nanotubes has been studied in detail using an electrochemical quartz crystal microbalance. It was found that carbon nanotube functionalization has critical influence on the values of mass and current densities of copper deposition. Presence of amine functionalization increases competitive hydrogen evolution without significantly affecting the total amount of deposited copper, whereas carboxylic groups clearly enhance deposition of larger amounts of smoother copper deposits. Molar mass analysis of deposited species reveals interactions of carbon nanotubes with the electrode surface dependent on the type of functionalization. In the light of present results, the effect of carbon nanotube functionalization should be closely considered in the development of electrochemical strategies for the integration of carbon nanotubes in metallic copper.

Biography

Ewa Kazimierska is Ser Cymru II Recapturing Talent Fellow working in Energy Safety Research Institute at Swansea University in Wales, UK. She came back to academia after prolonged career break and the key research goal of her current project is to develop the next generation materials for electrical power transmission. Her interest is in the integration of carbon materials in metals aiming to develop ultraconductive copper-carbon nanotube composites. She has completed her PhD from City University of New York and Postdoctoral studies from Dublin City University.

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Carlo Bradac

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Nanoscale optical trapping: Current challenges and future directions

Probing biological processes down to the single-molecule scale, *in vivo*, is one of the prime yet unreached goals of biomedicine. This matters because at the most fundamental level human physiology and all biological processes are the result of intricate actions of single proteins such as enzymes, motor proteins, DNA or RNA molecules. Common fluorescence microscopy techniques employ luminescent bio-labels to image biological systems. They are ensemble methods which average over the whole population of molecules and provide a coarse overview of the process under investigation. Specialized, molecule-targeted techniques do exist. They are based on optical tweezers/traps (OTs), which allow for the manipulation of small bio-labels to probe, for instance, pico-Newton forces of molecular motors such as kinesin, dynein and myosin. Whilst being a great tool, OTs are limited by the size-range of objects they can address and the forces they can exert. Classical optical trapping relies on large (~0.1-1 µm) refractive beads to work, which clashes with the push, in biomedicine, towards reaching the (sub) nanometre-scale regime of single-molecule exploration. Also, forces within living cells can be relatively large (~10 pN) and require a high-power laser in the OT; this is not ideal as it can result in cell damage. After reviewing the main limitations of current OTs, author present some of the pioneering work which they are doing to overcome these limits and develop OTs compatible with delicate biological environment and which will potentially allow for reaching size (~tens of nm) and force regimes (~hundreds of pN) unattainable with current techniques.

Biography

Carlo Bradac is a Research Fellow at the University of Technology, Sydney. He studied Physics and Engineering at the Polytechnic of Milan, Italy where he achieved his Bachelor's degree in 2004 and Master's degree in Engineering for Physics and Mathematics in 2006. He received his PhD in Physics at Macquarie University in 2012. His research focuses on colour centres in diamond and on their potential use in quantum information technologies, biomedical applications and high-resolution single-spin sensing.

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