

Multifunctional Large Pore Mesoporous Silica Nanoparticles as a novel gene carrier

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Small interfering RNA (siRNA) based therapeutics for cancer treatments have gained considerable attention due to the high potency of siRNA in suppressing pathogenic gene expression [1]. Yet, there are drawbacks that limit siRNA application *in vivo*: the vulnerability of siRNA against nucleases and the inability of the nucleic acids molecules to diffuse across the cellular membranes [1]. Nanovectors hold great promise for overcoming these limitations towards the development of efficient siRNA therapy. Various nanovectors such as lipids, polymers and inorganic nano-particles have been extensively studied [2]. Among these nanovectors, mesoporous silica nanoparticles (MSN) show promising potential as the next-generation gene delivery carriers [3,4,5].

The main prerequisite for gene therapy is the accumulation of the therapeutic agents on target cancer site [6], which can be achieved through the modification of MSN with targeting moieties such as biological ligand or magnetic particles. Numerous studies on the encapsulation of magnetic nanoparticles (iron oxide) within porous silica for drug delivery have been reported. However, study on MSN with large pores (> 3 nm, termed LPMSN) loaded with magnetic nanoparticles for siRNA delivery is still limited.

This work reports the synthesis of novel polyethyleneimine (PEI) functionalized, and iron oxide nanoparticles loaded LPMSN (PEI-Fe-LPMSN) as a multifunctional nano-carrier for gene delivery. LPMSNs with a particle size around 200 nm, a large pore size of 11 nm and a pore connection size of 5 nm are used as a host to impregnate iron oxide

nanoparticles inside the mesopores (Figure 1). The large pore in our study has two advantages. Firstly, it provides adequate space for the formation of large iron oxide particles to enhance the magnetic properties. Secondly, the large pore as well as the connection size opens the possibility to adsorb more siRNA molecules not only on the surface but also within the pores, which can enhance siRNA protection against biodegradation.

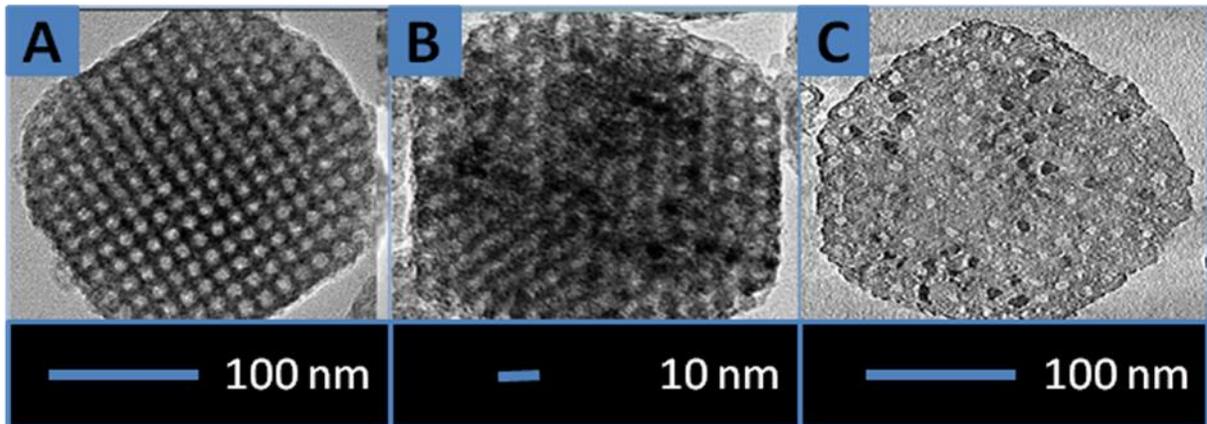


Figure 1. Electron microscopy images for LPMSNs (A), Fe-LPMSN (B) and an ET (Electron Tomography) slice of Fe-LPMSN

PEI is grafted on the silica pores (PEI-Fe-LPMSN) and surface to enhance the nano-carrier's affinity against genes and target the cell membrane. Furthermore, polyethylene glycol (PEG) is introduced into the hybrid nanoparticles to improve the biocompatibility and dispersibility. The products have been characterised with various instruments: X-ray photoelectron spectroscopy (XPS), solid-state ^{13}C magic-angle spinning nuclear magnetic resonance (MAS-NMR), Elemental Analysis (EA) and thermogravimetric analysis (TGA). PEI functionalization significantly improves the interaction between the silica particles and oligo DNA / cell membrane, which enhances the cell uptake. The internalization of PEI-Fe-LPMSN can be accelerated by a magnetic field, which causes a high transfection within a short period of time. In addition, the PEGylated nanoparticles show a high biocompatibility. The multifunctional materials enable siRNA delivery within KHOS cancer line and achieve knockdown of PLK-1 oncogenes.

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**International Conference on
Nanotechnology in Medicine**

7-9 November 2012

University College London, London, United Kingdom

TECHNICAL PROGRAMME

Dear Colleagues,

Welcome to the **International Conference on Nanotechnology in Medicine** (NanoMED) held at University College London in London, United Kingdom. NanoMED has emerged from the highly successful NANOSMAT conference (www.nanosmat-conference.com), which is held each year, since 2005, in Europe, USA and now in Asia (Asia launch in 2013). I would like to thank Dr Nasar Ali, the founder and chairman of NANOSMAT, for his hard work in organising this extraordinary meeting.



The conference will focus on five critically important areas of active and evolving research in the application of nanotechnology in medicine, with a full session devoted to each. The session themes are 1) Tissue Engineering & Biomedical Sciences, 2) Diagnosis and Imaging, 3) Drug Delivery, 4) Nanoscale Biomaterial Surface Modification and 5) Biosensors.

On the first day of the meeting we have invited speakers in the scientific program to cover these topics, whereas, days 2 and 3 are dedicated to selected abstracts for oral as well as poster presentations.

The oral presentations are in two parallel sessions, which you should attend based on your preferred topic of interests. A dedicated poster session on first and second day will be held at 4:30 PM and will include poster presentations based on accepted abstracts chosen by the Program Committee based on scientific merit. I strongly encourage all participants to view the posters and discuss them with the authors (who should try to stand by them at the dedicated poster sessions). An exciting exhibit of "Artificial Human Body Parts" from "UCL Centre for Nanotechnology & Regenerative Medicine" research team will also be presented. The exhibit will demonstrate how nanotechnology played a big role on development of organs from laboratory into humans, including world first synthetic trachea, bypass graft, lacrimal duct, and other organs. There will also be an opportunity for a limited number of attendees to visit "UCL Centre for Nanotechnology & Regenerative Medicine" at Royal Free Campus, based at Hampstead, one of the most beautiful parts of London.

The NanoMED conference is organized to bring together multidisciplinary experts in from wide backgrounds including academia, industry and government. We strive to promote dialogue and collaborations between scientists and clinicians, recognized scientific leaders and trainees, and among nanotechnologists, physicists, chemists, biologists, engineers, biomaterials researchers, surgeons and others whose work addresses fundamental aspects of nanomedicine. While the ambitious program is built around lectures from carefully selected speakers, the success of the meeting will rely on free flowing thought-provoking discussions and debates among all attendees and the generation of cross fertilizing new collaborations and new synergies that facilitate the successful application of nanotechnology in medicine.

London is a dynamic city and Bloomsbury is centrally situated making exploration of the city quite accessible. Bloomsbury has a remarkable literary heritage and the British Museum is a short walk away from the conference venue. The facilities of the recently concluded Olympic Games are a short tube ride away. I hope you will find time before or after the conference to explore this exciting city.

Thank you for participating in this exciting conference. The NanoMED has many new programs in development and I strongly encourage all participants to remain active in this extraordinary Society.

Best Wishes,

Alexander Marcus Seifalian (Chair), Professor of Nanotechnology & Regenerative Medicine, UCL, UK
Jawwad Darr (Co-chair), Professor of Chemistry, UCL, UK

9th November 2012

Time	Topic: Drug delivery (Nano-vehicle delivery systems) Chair: Prof. Stanislaw Mitura (Poland) Room: Old Refectory	Time	Topic: Diagnosis and Imaging Chair: Prof. Chia-Liang Cheng (Taiwan) Room: Chadwick Lecture Theatre
09:00 - 09:20	NANO-126: Sandy Budi Hartono , The University of Queensland, Australia <i>"Multifunctional Large Pore Mesoporous Silica Nanoparticles as a novel gene carrier"</i>	09:00 - 09:20	NANO-10: M. Clara Gonçalves , Technical University of Lisbon, Portugal <i>"Potentiality of ORMOSIL nanoparticles as negative Contrast Agents for MRI"</i>
09:20 - 09:40	NANO-188: Francesca Baldelli Bombelli , University of East Anglia, UK <i>"Development of Engineered Nanocarriers for the Treatment of Metastatic Melanoma"</i>	09:20 - 09:40	NANO-116: Elnaz Yaghini , University College London, UK <i>"Cadmium Free Quantum Dots as a Novel Fluorescence Probe for In Vivo Sentinel Lymph Node Imaging"</i>
09:40 - 10:00	NANO-92: Petr Toman , University of Portsmouth, UK <i>"Nanoparticles of Alkylglyceryl-Dextran-poly(lactic acid) for Drug Delivery to The Brain"</i>	09:40 - 10:00	NANO-118: Maria Luisa Bondi , Consiglio Nazionale delle Ricerche, Istituto per lo Studio dei Materiali Nanostrutturati, Italy <i>"Oligonucleotide-decorated carboxyl-modified PVP nanogels: a new platform for diagnosis and gene-therapy"</i>
10:00 - 10:20	NANO-35: Ana Maria Carmona-Ribeiro , Universidade de São Paulo, Brazil <i>"Supramolecular assemblies of cationic lipid and gramicidin as microbicidal agents"</i>	10:00 - 10:20	NANO-186: Samir Iqbal , University of Texas at Arlington, USA <i>"Isolation and Typing of Tumour Cells from Images of Aptamer-Functionalized Chips"</i>
10:20 - 10:40	NANO-153: Margaret Holme , University of Basel, Switzerland <i>"Shear stress sensitive nanocontainers with tunable release properties"</i>	10:20 - 10:40	NANO-28: Jiunn-Der Liao , National Cheng Kung University, Taiwan <i>"SERS-based DNA detection using inverted multi-angular Au nano-cavity array-embedded microfluidic device"</i>
10:40 - 11:00	NANO-179: David Cramb , University of Calgary, Canada <i>"Critical factors in nanoparticle drug delivery design"</i>	10:40 - 11:00	NANO-31: Kevin Critchley , Molecular and Nanoscale Physics Group, UK <i>"Cadmium Free Quantum Dots "</i>
11:00 - 11:30	Refreshments break		

Time	Topic: Tissue Engineering & Biomedical Sciences Chair: Dr Brian Cousin (UK) Room: Old Refectory	Time	Topic: Diagnosis and Imaging Chair: Prof. Ueli Aebi (Switzerland) Room: Chadwick Lecture Theatre
11:30 - 11:50	NANO-149: Volker Mailänder , Max Planck Institute for Polymer Research, Germany <i>"Specific targeting by (oligo)mannose functionalized hydroxyethyl starch nanocapsules: en route to drug delivery systems with targeting properties"</i>	11:30 - 11:50	NANO-55: Manlio Tassieri , University of Glasgow, UK <i>"Measuring the viscous and elastic properties of single cells using particle tracking microrheology"</i>
11:50 - 12:10	NANO-32: Angel Millan , Universidad de Zaragoza, Spain <i>"Multifunctional Nanoplatfrom for Biomedical Applications"</i>	11:50 - 12:10	NANO-58: Alessandra Bestetti , The University of Melbourne, Australia <i>"A Versatile and Widely Applicable Strategy for the Conjugation of Quantum Dots to Biomolecules through Click Chemistry"</i>
12:10 - 12:30	NANO-17: Vesselin N Paunov , University of Hull, UK <i>"Encapsulation of Living Cells into Sporopollenin Microcapsules"</i>	12:10 - 12:30	NANO-63: E. Castro , University of Minho, Portugal <i>"Could anisotropic iron oxide nanoparticles lead to further enhancing in magnetic resonance imaging?"</i>
12:30 - 12:50	NANO-194: Raffaella Aversa , Second University of Naples, Italy <i>"Mechanical and Swelling Behaviour of New Hybrid Ceramo-Polymeric bio-nanocomposites"</i>	12:30 - 12:50	NANO-82: Jérémy Paris , Université de Bourgogne, France <i>"Bimodal Contrast Agents for the in Vivo Imaging: The Elaboration of Functionalized SuperParamagnetic Iron Oxide Nanoparticles"</i>
12:50 - 14:00	LUNCH		
Time	Topic: Tissue Engineering & Biomedical Sciences Chair: Prof. Jawwad A. Darr (UK) Room: Old Refectory	Time	Topic: Diagnosis and Imaging Chair: Dr Nasar Ali (UK) Room: Chadwick Lecture Theatre
14:00 - 14:20	NANO-25: Mohd Zobir Hussein , Universiti Putra Malaysia, Malaysia <i>"Zinc Layered Hydroxide-Salicylate Nanohybrid and Its Effect on Vero3 Cells Viability"</i>	14:00 - 14:20	NANO-85: Julien Boudon , Université de Bourgogne, France <i>"Biodistribution Study of a Novel Theranostic Versatile Platform Composed of Surface-modified Titanate Nanotubes"</i>
14:20 - 14:40	NANO-16: Vesselin N Paunov , University of Hull, UK <i>"Triggered Cell Release from Shellac-Cells Composite Microcapsules"</i>	14:20 - 14:40	NANO-86: John Wang , National University of Singapore, Singapore <i>"Multifunctional Hybrid Nano Core@shells via Bioinspired Silification for Targeted Diagnosis"</i>
14:40 - 15:00	NANO-52: Cynthia Wong , Deakin University, Australia <i>"Potential of electrospun polyurethane blended with elastin and collagen as vascular graft"</i>	14:40 - 15:00	NANO-96: Yang Liu , Loughborough University, UK <i>"AFM Measurement of Single Cell Mechanical Properties of Live, Membrane-Impaired and Dead Human Mesenchymal Stem Cells"</i>

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**Certificate of Participation at NanoMED-2012 held during 7-9 November 2012 at University College
London, London (UK)**

This is to certify that **Sandy Budi Hartono** of *The University of Queensland, Australia*, attended and participated in the **International Conference on Nanotechnology in Medicine (NanoMED)**, held at the University College London (UCL) in London, United Kingdom during 7-9 November 2012.

We would like to thank you for your participation and for supporting NanoMED 2012.

Yours Sincerely,

A handwritten signature in black ink, appearing to read 'Jawwad Darr'.

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