Università degli Studi di Roma Tor Vergata
Dipartimento di Medicina Sperimentale

1st Mini-Symposium on Nanomedicine

Thursday, June 16th, 2022

University of Rome Tor Vergata
Room: School of Engineering, Aula Convegni

AGENDA	
9:30 – 9:35	Welcome to the 1st Mini-Symposium on Nanomedicine **Massimo Bottini** – University of Rome Tor Vergata (Rome, Italy)
9:35 – 10:20	*Plenary Lecture* Matching the physi-chemical characterizations of nanostructures with their biomedical functions in vitro and in vivo **Xing-Jie Liang** – Chinese Academy of Sciences Center for Excellence in Nanoscience (Beijing, P. R. China)
10:20 – 10:50	Hydrogel based 3D-cell cultures: From tissue regeneration to disease modeling **Silvia Buonvino** - University of Rome Tor Vergata (Rome, Italy)
10:50 – 11:10	**Coffee break**
11:10 – 11:40	Cationic polymer materials to inhibit the autoimmune disorders induced by cell-free DNAs **Yongming Chen** - Sun Yat-sen University (Guangzhou, P. R. China)
11:40 – 12:10	Exploring the biological impact of engineered nanomaterials using in vitro model systems **Bengt Fadeel** - Karolinska Institutet (Stockholm, Sweden)
12:25 – 12:40	Matrix vesicles: A special class of mineralizing extracellular vesicles **Emanuela Frustaci** – University of Rome Tor Vergata (Rome, Italy)

Contact: Prof. Massimo Bottini (massimo.bottini@uniroma2.it)

Matching the physi-chemical characterizations of nanostructures with their biomedical functions *in vitro* and *in vivo*

Xing-Jie Liang
Chinese Academy of Sciences Center for Excellence in Nanoscience (Beijing, P. R. China)

Compared to traditional drug delivery systems, nanostructures have greater potential in many areas, such as precise targeting functionalization, in vivo enhanced imaging, combined drug delivery, longer circulation time and systemically controlled release. Nanostructures incorporating stimulus-responsive biomaterials have remarkable properties which allow them to bypass biological barriers and achieve targeted intracellular drug delivery. Exploring the mechanisms of the interactions between nanostructures and biosystems is an urgent need for future applications of the nanostructures. The interaction of nanostructures with biosystems was well studied at different biological levels, such as: 1. the modifications of bio-macromolecules (protein, gene, lipid, polysaccharide et al); 2. the interactome of subcellular organelles (lysosome, autophagosome, ER, nuclei et al); 3.the fate of single cell and population (spheroid, organoid); 4. the ADMET of nanostructures in vivo (the physiological barriers). The parameters are critical to determine the unique bioeffect of nanostructures behind interaction with biosystems. The optimized parameters will be employed to support the efficient translation of nanostructures from the bench to clinical applications and the approval by the Food and Drug Administration (FDA) for treatment of various diseases. With the exploration of interaction of nanostructures with biosystems, it might be feasible to design even more promising nano-systems synergistic for drug delivery and cancer therapy in the future.

Hydrogel based 3D- cell cultures: from tissue regeneration to disease modeling

Silvia Buonvino
University of Rome Tor Vergata (Rome, Italy)

3D cell cultures are widely used *in vitro* model systems for improving our understanding of cell biology, mechanisms of diseases, drug effects and for the development of tissue engineering and regenerative medicine tools and in this regard the design and the optimization of 3D hydrogel-based cellular scaffolds is a relevant and challenging issue. Herein we retrace our efforts in this research field optimizing 3D cell cultures using hybrid PEG-protein hydrogels (PEG-fibrinogen PFHy, PEG-silk fibroin PSFHy) as scaffold in order to favour the growth and the initial commitment of mesenchymal stem cells (MSCs) for potential applications in tissue repair. We developed a new protocol to produce hydrogel-based cell microspheres as both cell microcarriers for tissue repair and as *in vitro* models for studying diseases and analysing drugs effects using MDA-MB 231 breast cancer cells and cell co-cultures. These 3D cell culture systems represent good 3D-models for studying 3D cell migration/invasiveness of different kinds of cells and as *in vitro* platform for drug screening. In this context, we have analysed the effects of GSGa, a H_2S slow-releasing donor, on cell growth and invasiveness using these 3D cell culture systems.

Cationic polymer materials to inhibit the autoimmune disorders induced by cell-free DNAs

Yongming Chen
Sun Yat-sen University (Guangzhou, P. R. China)

Rheumatoid arthritis (RA) is a chronic autoimmune disease afflicting approximately 1 % of world population. Its symptoms include swollen and deformed joints due to inflammatory damage of the bone and cartilage. Recently, it was reported that that cell-free DNA (cfDNA), released from dead and apoptotic cells, plays a critical role in RA development, like elevated cfDNA level in serum of patients and extremely high level of the cfDNA in the synovial fluid of patients. It is known that the nucleic acids are damage-associated molecular patterns (DAMP) molecules of immune cells. We proposed that blocking the Toll like receptor (TLR) activation by cfDNA using synthetic materials may reduce inflammation in RA. We applied cationic polymers to scavenge the cfDNA as a new strategy to treat RA. We focused on cationic polymeric nanoparticles (cNP) instead of soluble polycations because of a higher nucleic acid scavenging capacity and a more favorable biodistribution in the inflamed joints. We have showed that cNPs can scavenge cfDNA derived from RA patients to inhibit the activation of primary synovial fluid monocytes (SFMC) and fibroblast-like synoviocytes (FLS). We showed that intravenously injection of cNPs into a CpG-induced or collagen-induced arthritis (CIA) rat model can relieve RA symptoms with respect to ankle and tissue swelling as well as bone and cartilage damage. Furthermore, we have applied various cNPs with tailored structure to increase the therapeutic efficacy while to decrease the toxicity of materials. This work suggests a new direction of nanomedicine in treating inflammatory diseases.

Exploring the biological impact of engineered nanomaterials using *in vitro* model systems

Bengt Fadeel, M.D., Ph.D.
Institute of Environmental Medicine, Karolinska Institutet, 171 77 Stockholm, Sweden

The present lecture will address the safety assessment of various classes of nanomaterials using *in vitro* model systems including models of the human immune system.
We have studied the impact of metal/metal oxides on human cells using conventional toxicity assays complemented with transcriptomics and/or proteomics approaches. We observed nanomaterial surface chemistry-dependent perturbations of specific pathways at low doses using human monocyte-like cells as a model. Specifically, for CuO nanoparticles, evidence was provided for a metal detoxification response, as expected, as well as an unfolded protein response. Moreover, CuO nanoparticles triggered the misfolding of SOD1 in a murine macrophage model. We also studied the cellular responses to a panel of amorphous silica nanoparticles with varying surface chemistries and found that bare silica nanoparticles trigger a pro-inflammatory cell death in monocytes that is distinct from other known modes of cell death (apoptosis, necroptosis, ferroptosis) while surface modification served to mitigate these effects. Finally, studies using Fe-doped nanomaterials revealed that nanomaterials could potentially be exploited for the selective killing of cancer cells while sparing normal cells. Funding: This work was supported by the European Commission through FP7-NANOSOLUTIONS, grant agreement no. 309329; H2020-BIORIMA, grant agreement no. 760928, and Swedish Foundation for Strategic Environmental Research (MISTRA).

Matrix vesicles: A special class of mineralizing extracellular vesicles

Emanuela Frustaci
University of Rome Tor Vergata (Rome, Italy)

Mineralizing cells, including hypertrophic chondrocytes and mature osteoblasts, release a special class of extracellular vesicles, named matrix vesicles (MVs), that bind to the collagenous matrix and produce apatite at the sites of ossification. MVs are also released by mineralizing vascular smooth muscle cells at the sites of medial vascular calcification. Current knowledge describes MVs as released by mineralizing cells by outward budding of apical microvilli and mineralize through a mechanism regulated by the vesicles' biochemical machinery. However, these studies have been mostly carried out on vesicles released from 2D cultures of primary cells (chondrocytes, osteoblasts, and vascular smooth muscle cells) as well as cell lines (e.g., MC3T3-E1 and Saos-2), whereas few studies have used MVs isolated from tissues (e.g., growth plate and calvaria). This has made difficult to draw a clear picture of the biochemical, biophysical, and biological properties of the MVs acting during physiological and pathological calcification processes. The final goal of my project is to fully characterize MVs acting during physiological calcification by using tissue-isolated vesicles. In my talk I will describe the results I have obtained by isolating MVs from the growth plate of chicken embryos and characterizing the vesicles by means of both microscopic (atomic force and fluorescence microscopies) and spectroscopic (dynamic light scattering) techniques. In my talk I will also discuss about future experiments. The development of this project will translate into a better understanding of how MVs drive physiologic and ectopic calcifications.

Xing-Jie Liang

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SHORT BIOGRAPHY

Professor Xing-Jie Liang got Ph.D at National Key Laboratory of Biomacromolecules, Institute of Biophysics, Chinese Academy of Sciences. He finished his postdoc with Dr. Michael M. Gottesman (member of NAS and Deputy Director of NIH, USA) for 5 years at Laboratory of Cell Biology, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, Maryland. Then, he worked as a Research Fellow at Surgical Neurology Branch, NINDS (National Institute of Neurological Diseases and Strokes, NIH). He was an Assistant professor at Department of Radiology, School of Medicine, Howard University. Professor Liang currently is deputy director of Key Laboratory for Biomedical Effects of Nanomaterials and Nanosafety, National Center for Nanoscience and Technology of China and a principal investigator at Center for Excellence of Nanoscience, Chinese Academy of Sciences. Professor Liang was granted by NSFC (National Natural Science Foundation of China) and awarded with Department of Education and many other prizes. Professor Liang is the elected Fellow of American Institute for Medical and Biological Engineering and Faculty Member of F1000 Research (Pharmacokinetics & Drug Delivery). He is also a founder member of International Society of Nanomedicine and president of Chinese Association of Nanobiology. He is the associated director of nanobiomaterial-related committees and council members of scientific associations, such as China Society of Biomaterials (CSBM), Chinese Medicinal Biotechnological Association (CMBA), Chinese Pharmaceutical Association (CPA) and Biophysical Society of China (BSC). Professor Liang is current Editor-in-Chief of Exploration, Associate Editors of Biomaterials and Biophysics Report; Advisory editorial board member of ACS Nano and Advanced Therapeutics; Editorial member of Bioconjugate Chemistry and Theranostics. His research interests are in elucidating mechanisms to improve drugability and nanomedicinal bioavailability by nanotechnology in vitro and in vivo, and novel strategies to increase therapeutic efficiency on cancers and infective diseases. Developing drug delivery strategies for prevention/circumvent of clinical adaptive treatment tolerance (ATT) are current programs ongoing in Professor Liang's lab based on understanding of basic physio-chemical and biological processes of nanomedicine. Prof. Liang has successfully developed “Injectable Nanomicelles Powders with Irinotecan” approved with CFDA for clinical trials with China Resources Pharmaceutical Group.

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Silvia Buonvino	
	University of Rome Tor Vergata (Rome, Italy)

SHORT BIOGRAPHY

In 2020 she obtained the master's degree in Chemistry with laude, and she is currently attending the second year of Ph.D in Biochemistry and Molecular Biology at the University of Rome Tor Vergata. In 2021 she has been awarded of the Mariano Paliotta prize for the best master thesis in Chemistry by University of Rome Tor Vergata. In the same year she attended the international congress "Italy-China Joint Symposium" (University of Rome Tor Vergata-Soochow University) organized by Springer Nature Group and CDD Press with the oral presentation "H_2S donors for Optimization of 3D Culture Systems for Stem Cell Therapy in Tissue Regeneration". She is co-author of 3 publications on peer reviewed journals and of 2 publications in submission. Her field of interest is the biochemical and mechanophysical optimization of 3D cell culture systems based on PEG-protein hydrogels for both mesenchymal stem cells and breast cancer cells cultures. In particular, her research is focused on the study of the effects of H_2S-slow releasing agents on these systems and on more 3D complex systems of co-cultures.

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5. Buonvino, S., Ciocci, M., Nanni, F., Cacciotti, I., Melino, S. New vegetable-waste biomaterials for tissue growth by Lupin albus L. *Biomaterials*, Submitted.

Yongming Chen

PhD, Professor
School of Materials Science and Engineering
Sun Yat-sen University, Guangzhou, China

SHORT BIOGRAPHY

Yongming Chen received his Master degree of chemistry in 1990 from Northwest University, Xian. In 1993, he obtained his Ph.D. on polymer science from Nankai University, Tianjin. From 1994 to 1998, he was Postdoctoral Researcher and later Research Assistant at the Institute of Chemistry, CAS. Then he spent the period 1998−2001 as Postdoctoral Researcher in University of Düsseldorf and University of Mainz. Since 2001, Chen was Professor at the Institute of Chemistry CAS. He moved to Sun Yat-sen University in 2013. He obtained "Distinguished Young Scholars" by National Science Foundation of China (2006) and "Wang Bo-Ren Polymer Research Award" by Chinese Chemistry Society (2011). He served for Polymer, an Elsevier journal as an Associate Editor during 2007 to 2018. He also was in Advisory Board Panel of Macromolecules and ACS Macro Letters, the ACS Publication. Professor Chen's research interests are in the areas of synthesis methodology of polymers and polymer application in nanomedicine on biologics delivery, immune activation and inhibition. He has published over 260 research articles.

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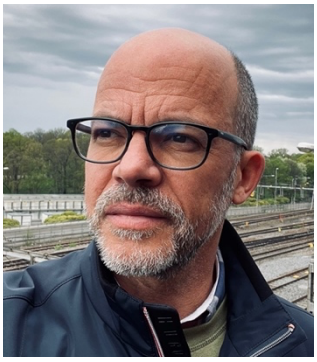
Bengt Fadeel, MD, PhD



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SHORT BIOGRAPHY

Bengt Fadeel is a Full Professor of Medical Inflammation Research at the Institute of Environmental Medicine, Karolinska Institutet, Stockholm, Sweden. He obtained his M.D. and Ph.D. from Karolinska Institutet. He has participated actively in several EU-funded nanosafety projects including NANOMMUNE, MARINA, NANOREG, SUN, NANOSOLUTIONS, and BIORIMA, and he is a current member of the Graphene Flagship Project (2013-2023). Dr. Fadeel served previously as chair of the expert panel of the national nanosafety platform, SweNanoSafe, and he is currently the chair of the platform. He also serves on the editorial board of several academic journals including *Current Opinion in Toxicology*, *Frontiers in Toxicology*, and *Toxicological Sciences*. He has authored or co-authored 275 papers.

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Emanuela Frustaci

University of Rome Tor Vergata (Rome, Italy)

SHORT BIOGRAPHY

She obtained the master's degree in Biotechnologies at the University of Rome Tor Vergata in December 2021. She is currently working in the Laboratory of Biochemical Nanotechology of Prof. Bottini at the University of Rome Tor Vergata on a project focused on the characterization of mineralizing extracellular vesicles by using both microscopic and spectroscopic techniques.

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