Institut de Nanociència i Nanotecnologia

UNIVERSITAT DE BARCELONA

Department of Biomedical Sciences - IN2UB Meeting

July 9th 2019 at Aula Magna Faculty of Medicine and Health Sciences (Campus Clinic)

A BRIEF DESCRIPTION OF THE PRESENTATIONS FROM IN2UB

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NOTE: The information in this document has been provided by researchers from the IN2UB in the frame of the meeting between the Department of Biomedical Sciences and IN2UB (July 9th 2019).

1. Water soluble iron oxide nanoparticles

A brief description of the talk: We have worked for a few years in functionalization of iron oxide nanoparticles with complex systems. This work was aimed towards spintronics and devices. We have now used our expertise to prepare size homogeneous, water soluble magnetic iron oxide nanoparticles that can be used as drug delivery devices. The system presented here are iron oxide NP with dopamine/hyaluronic acid shells functionalized with drugs for immunotherapy.

Name and web of the research group Grup de Magnetisme i Molècules Funcionals GMMF, http://www.gmmf-ub.com

Name of the speaker and mail E. Carolina Sañudo; esanudo@ub.edu

2. Implantable Sensors for Tissue Ischemia Monitoring

A brief description of the talk: Free flaps are commonly used on all kind of reparative surgeries. The main risk of failure for such operations is microvascular complications on the anastomotic sites, which causes blood irrigation shortage and tissue necrosis. Thus, the control of tissue ischemia is a primary aim during the postoperative care. The standard procedure for such control is based on frequent clinical observation. However, on deep/buried flaps, clinical observation cannot be done, and blood perfusion complications are detected too late, when the free flap salvage rate is very low. We have developed a micrometric array of sensors for the minimally invasive control of post-operative tissue ischemia. The sensors were tested in blood and intramuscular tissue in adult rabbits model and sheep foetus model. The hypoxia was induced by restriction of the breathing oxygen in the adult animal and umbilical cord occlusion in the foetus showing successful response.

Name and web of the research group Nanobioengineering Group at Institute for Bioengineering of Catalonia (IBEC); http://www.ibecbarcelona.eu/nanobioengineering

Name of the speaker and mail Dr. Mònica Mir; mmir@ibecbarcelona.eu

3. Nanoparticles for photothermal ablation: A challenging strategy for cancer theranostics.

A brief description of the talk: Taking into consideration that laser-induced photothermal ablation has shown satisfactory results for the removal of tumors, a new generation of nanoparticles (NP) aimed for photothermal therapy (PTT) will be presented. These NP are light-absorbing materials, namely photothermal agents (PA) that can convert absorbed light into heat. The result is the ablation of malignant areas noninvasively by heating the tissue locally above 42 ˚C while keeping the temperature of the surrounding tissue at a normal level. In laser ablation, the spectral ranges of the used wavelengths are located in the Near Infrared region, the so called biological windows, where tissues become partially transparent as a result of a simultaneous reduction in both absorption and scattering. We have designed and developed PA that generate heat after irradiation at the second biological window which offers improved light penetration, lower background signal, and higher maximum permission exposure compared to the traditional first window. The developed nanoparticles will also be designed to be directed by an external magnetic field or to be used as image probe, therefore as theranostic agents.

Name and web of the research group: Colloidal group.

Name of the speaker and mail: Maria Antònia Busquets; mabusquetsvinas@ub.edu

4. Bacterial inclusion bodies for anti-amyloid drug discovery: Current state and future perspectives

A brief description of the talk: Amyloid aggregation is linked to an increasing number of human disorders from non-neurological pathologies such as type-2 diabetes to neurodegenerative ones such as Alzheimer or Parkinson's diseases. Thus, thirty-six human proteins have shown the capacity to aggregate into amyloid structures. To date, it is widely

accepted that amyloid folding is a universal process present in eukaryotic and prokaryotic cells. In the last decade, several studies have unequivocally demonstrated that bacterial inclusion bodies -insoluble protein aggregates usually formed during heterologous protein overexpression in bacteria- are mainly composed of overexpressed proteins in amyloid conformation. This fact shows that amyloid-prone proteins display a similar aggregation propensity in humans and bacteria, opening the possibility to use bacteria as simple models to study amyloid aggregation process and the potential effect of both anti-amyloid drugs and pro-aggregative compounds.

Name and web of the research group: Conformational Diseases Group

Name of the speaker and mail: Dr. Raimon Sabate; rsabate@ub.edu

5. Micro and nanotechnologies for biomedical applications

A brief description of the talk: We have been working for quite some time on the micro and nanofabrication of advanced surfaces and devices and the development of their required measurement system for various applications. For this, we have access to state-of-the-art nanofabrication facilities. We will present results on:

Surface plasmon resonance (SPR) grating couplers for chemical and biomedical detection. We are now working on the extension towards antigen-antibody detection.

Miniaturized gas sensors and gas sensor systems (electronic noses) based on metal oxides. We have been using these devices and systems for environmental applications and we are now moving towards their use in breath analysis.

Pillar-based nanosystems for the determination of mechanical stresses in living tissues under the tumoral growth or wound healing conditions.

Name and web of the research group MIND, Dept. of Electronic and Biomedical Engineering and SIC, Dept. of Electronic and Biomedical Engineering

Name of the speaker and mail: Mauricio Moreno (mauricio.moreno@ub.edu) and Albert Romano (albert.romano@ub.edu)

6. From Nanomaterials to Perspectives for Brain Cancer Treatments

A brief description of the talk Recently in vitro and in vivo studies have shown that it is possible to increase the ability to cross the Blood-Brain-Barrier (BBB) for engineered nanoparticles (NPs) carrying a loose layer of proteins. Nevertheless, the NP-protein corona composition—and, as a consequence, the cellular biological response to the NP—change over time due to the competition among the plasma proteins in the blood stream [O. Vilanova, J. J. Mittag, P. M. Kelly, S. Milani, K. A. Dawson, J. O. Rädler, G. Franzese, ACS Nano 10, 10842 (2016)]. In collaboration with experimental groups, we develop a multiscale approach for the study of bio-membranes, proteins, NPs and nanomaterials in aqueous solution oriented to applications to the BBB-crossing for oncological treatments. We model the kinetics of NP interaction with proteins [P. Vilaseca, K. A. Dawson, G. Franzese, Soft Matter 9, 6978 (2013); O. Vilanova, V. Bianco, G. Franzese, in 'Design of self- assembling materials', ed. I. Coluzza (Springer Publishing, New York), 2017], of proteins with water, and of water with membranes and nanomaterials, with the aim of finding how to optimize the NP-protein corona formation to cross the BBB.

Name and web of the research group http://www.ffn.ub.es/gfranzese

Name of the speaker and mail Giancarlo Franzese; gfranzese@ub.edu

7. Stimulus Triggered Delivery Systems for Chronic Wound Healing

A brief description of the talk Chronic wounds represent a silent epidemic that affects a large fraction of the world population and poses major and gathering threat to the public health and economy of developed countries. Developing delivery techniques that minimize toxicity and improve efficacy offers great potential benefits, and opens up new markets for pharmaceutical and drug delivery systems. Chronic wounds are encountered in every specialty and the

occurrence of non-healing wounds will continue to rise as the population ages, people continue to live longer with chronic diseases, and the nutritional needs of the body are not met. The pH value within the wound-milieu influences indirectly and directly all biochemical reactions taking place in the process of healing. Both acute and chronic wounds with an elevated alkaline pH have demonstrated lower rates of healing. Recent studies in our lab have demonstrated that the gelification properties of gelatin as well as the strong dependence of gelatin ionization with pH makes this compound an interesting candidate to be used to the effective delivery of active biomacromolecules in chronic wound conditions. The goal of the present project is the preparation and characterization (physicochemical and biological properties) of new therapeutic-containing NPs for the sustainable delivery under chronic wound conditions

Name and web of the research group Cellular Responses to Xenobiotics (CEREX)
https://www.ub.edu/portal/web/dp-bioquimicaifisiologia/respostes-xenobiotics

Name of the speaker and mail: M. Carmen Morán Badenas (mcmoranb@ub.edu)
Departament de Bioquímica i Fisiologia- Secció Fisiologia
Facultat de Farmàcia i Ciències de l'Alimentació
IN2UB- Nanopharmaceutics and Nanomedicine

13. LEDs, lasers, illumination and Raman spectroscopy for biomedical applications

A brief description of the talk: The Group of Optoelectronics and Photonics devices (GOP) is a research unit of the Laboratory of Micro/NanoTechnologies for Electronic and Photonic Devices (MIND). Our main research activities are devoted to the design, fabrication and test of electronic, optoelectronic and photonic devices, integrated circuits and systems. There is a broad field of applications including physics, engineering, chemistry and biomedicine. Research line: 1) Devices for Optoelectronic and Photonic Integrated Circuits (OEICs and PICs). 4) LED and laser light sources for general lighting and also for dermatology, neuropsychiatry and

aesthetic medicine; 3) Efficient and intelligent lighting for laboratories, experiments and operating theatres; 4) Raman spectroscopy for detection of analytes, biopsies, and trace elements, contaminants, quantitative composition, etc..

Name and web of the research group “GOP – MIND”; https://www.ub.edu/web/ub/es/recerca_innovacio/recerca_a_la_UB/grups/fitxa/M/MINDELFO/informacioGeneral/index.html

Name of the speaker and mail “Blas Garrido and Sergi Hernandez” (blas.garrido@ub.edu, shernandez@ub.edu)

14. Dynamics of active materials from suspensions of cytoskeletal proteins

A brief description of the talk: Many intracellular processes are orchestrated by the action of molecular motors, proteins that transform surrounding energy sources into directed mechanical action. A recent approach to understand the dynamics in these complex systems is to prepare minimal in-vitro reconstitutions that can exhibit self-sustained motion. In our research group, we study these active soft materials, in particular those formed by the combined action of fibers of condensed tubulin microtubules that are actively cross-linked by ATP-consuming kinesin molecular motors. Spontaneously, this material self-assembles into a configuration where the permanently evolving fibers have long-range orientational order and organize into a seemingly disordered regime that has been termed active turbulence. A close inspection has revealed the presence of intrinsic length and time scales, that we have learnt to characterize, analyze and even control, both in boundary-free and in microfluidic confinement. Some of the approaches used here to control the geometry and dynamics of these active biomimetic materials might be of interest to study the evolution of simple tissue growth.

Name and web of the research group Self-Organized Complexity and Self-Assembled Materials, www.ub.edu/socsam

Name of the speaker and mail: Jordi Ignés Mullol; jignes@ub.edu

15. Multifunctional nanomaterials suitable for bio-applications

A brief description of the talk: Our group has an extended expertise in the synthesis and characterization of nanomaterials for technological and health approaches. Within the framework of bio-applications, our research addresses two main goals:

1) The synthesis by chemical routes of magnetic iron oxide nanoparticles (NP) with a good control of the particle size within 5 to 100 nm, a tunable shape and a good stability in aqueous media. Those features make those iron oxide NP very attracting for Magnetic Resonance Imaging (MRI), controlled drug delivery, cell separation and purification, and local heating through magnetic hyperthermia, among others. In addition, we are developing hybrid systems combining iron oxide either with gold or bismuth sulfide NPs in order to enhance their functionality for medical approaches. For example, hybrid iron oxide-bismuth sulfide NPs have proved to be excellent contrast agents in both MRI and X- ray tomography.

Suggested reference: *Liver and brain imaging through dimercaptosuccinic acid-coated iron oxide nanoparticles*. Mejías, R. et al; Nanomedicine **5**, 397 (2010).

2) The fabrication by physical lithographic techniques of gold nanostructures composed by nanoelements of tunable shapes (cups, stars, discs,…) and sizes, over macroscopic areas up to 1 cm^2. We have demonstrated their ability to detect very small amounts of organic molecules (down to ≈ 10^{-12} g), such as crystal violet or 4-mercaptopyridine. In addition, the ulterior combination of those gold nanostructures with magnetic materials may allow for enantiomer detection using the chiral response of biomolecules.

Suggested references: (1) *Nanoparticles with tunable shape and composition fabricated by nanoimprint lithography,* Alayo, N.; et al, Nanotechnology **26**, 445302 (2015); (2) *Geometric frustration in ordered lattices of plasmonic nanoelements*. Conde-Rubio, A. et al, Scientific Reports **9**, 3529 (2019).

Name and web of the research group:

Group of Magnetic Nanomaterials (GMN), Condensed Physics Department and IN2UB. Web page: https://magneticnanomaterialsub.wordpress.com/

Name of the speaker and mail:

Group Contact: Xavier Batlle (xavierbatlle@ub.edu).

16. Polypurine Reverse Hoogsteen Technology for Therapeutic Gene Silencing

A brief description of the talk: We developed a new type of specific gene silencing molecules termed Polypurine Reverse Hoogsteen hairpins (PPRH) which are DNA oligonucleotides. PPRHs are formed by two stretches of polypurines of about 25 nucleotides linked by a penthamydine group. The two antiparallel polypurine stretches bind to each other intramolecularly by Hoogsteen bonds, and the resulting structure is very stable. PPRHs then bind in a sequence specific manner to stretches of polypyrimidines in the double stranded DNA. This binding occurs by Watson and Crick bonds and thus forms a triplex. As a result, the fourth strand of the genomic dsDNA is displaced. Finally, the expression of the gene, either by altering transcription or splicing, is decreased. The stretches of polypyrimidines can be found mostly in gene regulatory sequences in practically all genes. We use as targets stretches of about 25 nucleotides, conferring great sensitivity and absence of off-target effects. We used PPRHs on cancer related genes with very good results, in terms of cytotoxicity, by decreasing mRNA and protein levels of the target. https://en.wikipedia.org/wiki/Polypurine_reverse-Hoogsteen_hairpin

Name and web of the research group http://www.ub.edu/terapiamol/cancer/Welcome.html

Name of the speaker and mail: Verònica Noé <vnoe@ub.edu>

17. Nanodelivery and Nanodiagnostics

A brief description of the talk: 1) Drug carriers: gold nanoparticles offer a suitable means of transporting active molecules to diseased cells or tissues. Hence, we are developing AuNPs exhibiting a thermolabile group allowing the attachment and posterior release of a drug/prodrug. 2) Crossing the Blood-Brain Barrier (BBB): we are using the unique BBB-crossing properties of AuNPs to address the alteration of metallostasis (Cu, Zn and Fe) and the aggregation of amyloid proteins observed in some neurodegenerative diseases. Thus, NPs containing (i) metal-chelating groups, or/and (ii) fluorescent probes to detect amyloid aggregates or/and (iii) anti-aggregation agents are being designed. 3) Diagnosis: we are developing diagnostic tools based on different types of NPs for the detection of specific "biomarkers". For example, we are functionalizing magnetic NPs with antibodies for a specific disease and AuNPs with other antibodies for the same disease. The AuNPs also contain a DNA barcode for the quantification of the "biomarker". The combination of the Au and magnetic NPs through interaction with the target produces a "complex" that can be isolated magnetically.

Name and web of the research group Bioinorganic Chemistry (QBI); www.bio-inorganic-chemistry-icrea-ub.com

Name of the speaker and mail Patrick Gamez; patrick.gamez@qi.ub.es

18. EELS analysis of transition metals in biological tissue

A brief description of the talk: Electron Energy Loss (EELS) Spectroscopy in the Transmission Electron Microscope (TEM), in particular when carried out in an aberration corrected instrument, can be used to map the spatial distribution not only of chemical composition but also of oxidation state in a given nanostructure, with atomic column resolution. Interestingly, EELS experiments have been recently applied to address the role of the oxidation state of transition metals present in biological tissue in the mechanisms underlying several diseases. In

particular, in neurological diseases (Alzheimer's disease (AD), Parkinson's disease, Pick's disease, Huntington's disease, Progressive supranuclear Palsy (PSP), and Hallervorden-Spatz syndrome) iron accumulation is observed in brain regions associated with decreased function and cell loss, coupled with significant changes in the Fe oxidation state (Fe2+ is found). The availability of Fe2+ for redox reactions, and the magnetic fields created by the magnetite nanoparticles are believed to play a crucial role in neurodegenerative diseases.

Name and web of the research group

MIND-LENS-IN2UB (http://www.lens.el.ub.edu/)

Name of the speaker and mail: Sònia Estradé (sestrade@ub.edu)

19. FIB-SEM methods for biological Applications

A brief description of the talk: Focused ion beam scanning electron microscopy (FIB-SEM) consists in a scanning electron microscope (SEM) with an attached gallium ion column and both electron beam and ion beam (FIB) are focused on one coincident point. The main application is the acquisition of three-dimensional data, which is known as FIB-SEM tomography.

FIB, previously restricted to the materials sciences and semiconductor fields, is becoming a powerful tool for ultrastructural imaging of biological samples. Cell and tissue architecture can be investigated in three dimensions by scanning electron microscopy imaging of surfaces that result from the progressive removal of material using the focused ion beam.

The instrument can also be used to cut open biological structures to get access to internal structures or to prepare thin lamella for imaging by transmission electron microscopy (TEM). High-resolution structural and chemical information is attainable from FIB-prepared TEM samples.

Name and web of the research group

MIND-LENS-IN2UB (http://www.lens.el.ub.edu/)

Name of the speaker and mail: Gemma Martín (gmartin@el.ub.es)

20. Electron Microscopy at organic-inorganic interfaces

A brief description of the talk: Charged Particle Microscopy is a well stablished group of techniques that includes Scanning Electron Microscopes (SEM), Focused Ion Beam Microscopes (FIB) and Transmission Electron Microscopes (TEM) with outstanding applications for the quantitative characterization in both material and bio sciences. Among them, TEM offers the highest capabilities in terms of both spatial resolution (up to tens of pm) and spectrometry (up to 0.8eV). Historically, an exchange of TEM applications between bio and material science has been produced. As an example, the tomographic reconstructions at the nanoscale started in bioscience and then jumped to material science. Similarly, there are many imaging modes usually associated with material science problems that in fact are also very interesting for biomedical applications, like Electron Energy Loss Spectroscopy (EELS), Electron Holography (EH), Precession Electron Diffraction (PED), in-situ TEM and the use of Corrected TEM (CTEM). In this talk we will present the state of the art of these traditional material science TEM techniques applied to biomedical problems where they are becoming routine tools for nowadays research.

Name and web of the research group

MIND-LENS-IN2UB (http://www.lens.el.ub.edu/)

Name of the speaker and mail: José Manuel Rebled Corsellas (jmrebled@el.ub.es)

21. Biological activity of organometallic gold and platinum complexes

A brief description of the talk: This talk is divided in two main parts: the first dedicated to gold and the second to platinum derivatives. The different studies developed by our group, in collaboration with experts on the biological properties, will be presented mainly based on antitumoral activity.

Name and web of the research group Supra and Nanostructured systems group. http://www.ub.edu/inorgani/recerca/suns/index.html

Name of the speaker and mail Laura Rodríguez (laura.rodriguez@qi.ub.es)

22. Bioengineering for Medicine: Tissue models and Organ-on-a-Chip for theragnostics and regeneration

A brief description of the talk: The group "Unitat Bioelectrònica del Laboratori de Nanobioengenieria" at the Department of Electronics and Biomedical Engineering is devoted to the engineering of new strategies for the improvement of diagnostics and therapies in medicine. To do that, the group is participated by experts in microfluidics, modelling, electronics and biomaterial engineers in order to create a multidisciplinary ecoenvironment to integrate all these disciplines towards successful approaches with an important translational goal.The main research activities of the group are focused on the development of: 1) Microfluidic Organ-on-Chip devices to mimic organ-level functions and disease, 2) Tissue models for regenerative therapies and, 3) Lab-on-a-Chip devices for clinical diagnosis applications.

Name and web of the research group Unitat Bioelectrònica del Laboratori de Nanobioengenieria; https://webgrec.ub.edu/cgi-bin/3DADREC/crfitgrup.cgi?PAR=SICBIOIN; http://www.ibecbarcelona.eu/nanobioengineering

Name of the speaker and mail Dr. Romen Rodríguez (romen.rodriguez@ub.edu)