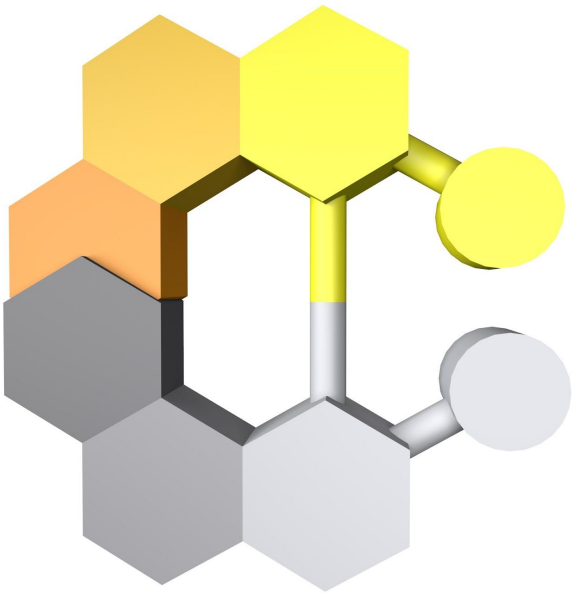

II EDICIÓ DEL CONGRÉS ANUAL DE NANOCIÈNCIA I NANOTECNOLOGIA

Dijous, 19 de novembre de 2020

Book of Abstracts

II EDICIÓ DEL CONGRÉS ANUAL DE NANOCIÈNCIA I NANOTECNOLOGIA

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Speakers

Dr. Daniel Closa (IIBB-CSIC) *Will nanotechnology become the next "sack man" of pseudoscience and conspiracy theories?*

Dr. Imma Ratera (ICMAB-CSIC) *Impact of Stimuli-Responsive and Hierarchical RGD Nanostructured Surfaces on Integrin-mediated Cell Guidance*

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Dr. Salvador Borrós Gómez (IQS) *Stable and efficient generation of poly(β-aminoester)s for RNAi delivery*

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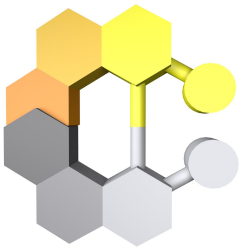
Dr. Pere Santamaría (IDIBAPS) *Peptide-Major Histocompatibility Complex-based nanomedicines for the treatment of autoimmune disease: engineering, mechanisms, diseases*



II EDICIÓ DEL CONGRÉS ANUAL DE NANOCIÈNCIA I NANOTECNOLOGIA
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Poster contest

Coral García-Fernández (IQS) *Novel mRNA vaccination strategies: use of poly(betaaminoesters) to achieve selective dendritic cells delivery*

Lídia Ballell (Nanomol Technologies SL + ICMAB-CSIC) *DELOS nanovesicles for drug delivery: an example of reformulation of a protein to treat complex wounds*

Poster Gallery

Marina Llenas Martínez (ICMAB-CSIC) *Microwave-Assisted Synthesis of SPION-Reduced Graphene Oxide Hybrids for Magnetic Resonance Imaging (MRI)*

Mingyue Wang (UAB) *Different anions doped polypyrrole molecularly imprinted polymer based electrochemical sensor for detection of acetaminophen, uric acid and ascorbic acid*

Marina Parra-Robert (Service of Biochemistry and Molecular Genetics, Hospital Clinic Universitari) *Mesoporous silica-coated nanoceria reduce metabolic alterations associated with obesity*

Teodora Andrian (IBEC) *Correlating super-resolution microscopy and transmission electron microscopy to study multiparametric heterogeneity in nanoparticles*

Anna Herrera (UAB) *Molecularly Imprinted Polymers biosensing for enhanced detection of Tryptamine*

Meritxell Perramon (IDIBAPS) *Engineered poly(beta-aminoester) nanoparticles (PBAE NPs) containing pituitary transforming gene 1 (PTTG1) siRNA selectively target the liver and spleen in fibrotic*
rats

Munmi Sarma (UAB) *Application of nanoparticles modified epoxy-graphite electrodes for electochemical detection of capsaicin*

Will nanotechnology become the next "sack man" of pseudoscience and conspiracy theories?

Daniel Closa

IIBB-CSIC

All scientific and technological advances have been accompanied by movements of rejection by a part of society. This is now more visible than ever thanks to the use that these movements made of social media. It may seem difficult to understand that in the middle of the 21st century it is debated whether the Earth is flat, whether the Moon was reached, or whether vaccines will contain microchips activated by 5G technology, but these debates are very real in certain environments. Although we often take it as a joke, it is still a burden for the advancement of science and sometimes a danger to human health. A rapidly evolving field, such as nanotechnology, has all the numbers to become the next scarecrow of these movements, and it's worth thinking about how to respond to them a little in advance.

Impact of Stimuli-Responsive and Hierarchical RGD Nanostructured Surfaces on Integrin-mediated Cell Guidance

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[4] *Institute for Bioengineering of Catalonia (IBEC), 08028, Barcelona, Spain*
[5] *Institut de Química Avançada de Catalunya (IQAC-CSIC), 08034, Barcelona, Spain*
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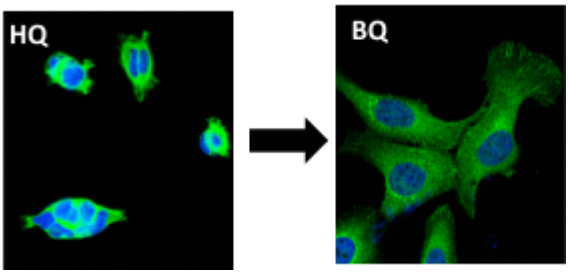
In tissue engineering, biological, physical, and chemical inputs are combined to mimic cellular environments designed to fulfill different biomedical needs. [1] Protein nanoparticles (pNPs) can simultaneously provide such physical and biochemical stimuli to cells when attached to surfaces. [2] To provide a stable anchoring, a covalent binding of pNPs will be presented featuring a robust nanoscale topography with unprecedented mechanical stability and availability to influence cell morphology and orientation. [3]



Dynamic molecular interfaces that allow temporal control of cell behavior using an external stimulus, are also very relevant for applications in biology, material sciences and medicine. Here we will present a cell adhesion study with spatio temporal control using stimuli-responsive self-assembled monolayers (SAMs) of an electroactive hydroquinone-benzoquinone (HQ-BQ) molecule that are used as a dynamic interface to immobilize pegitaled RGD functionalized peptides via interfacial reactions upon the application of a low electric potential. [4]

Density and spacing of RGD peptide at the nanoscale has already shown a significant influence on cell adhesion but its hierarchical nanostructuration effect is still rather unexplored. Here we present a versatile colloidal system based on fluid nanovesicles as a novel template for the hierarchic nanostructuration of RGD, anchoring it on the fluidic vesicle membrane. The engineered RGD-based nanovesicles are covalently anchored to surfaces. Such hierarchical substrates significantly enhance cell adhesion capabilities opening new pathways for the hierarchical immobilization of biomolecules on surfaces.

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[2] (a) W. I. Tatikewicz, J. Seras-Franzoso, E. Garcia-Fruitós, E. Vazquez, A.R. Kyvik, J. Guasch, A. Villaverde, J. Veciana, I. Ratera, *ACS Appl. Mater. Inter.*, **2018**, 10, 30; (b) W. I. Tatkiewicz, J.Seras-Franzoso, E. García-Fruitós, E. Vazquez, A. R. Kyvik, N. Ventosa, J. Guasch, A. Villaverde, J. Veciana, I. Ratera, *ACS Biomater. Sci. Eng.* **2019**, 5, 5470−5480
[3] M. Martinez-Miguel, A. R. Kyvik, L. M. Ernst, A. Martinez- Moreno, O. Cano-Garrido, E. Garcia-Fruitos, E. Vazquez, N. Ventosa, J. Guasch, J. Veciana, A. Villaverde, I, Ratera, *J. Mater. Chem. B*, **2020**, 8, 5080
[4] A. R. Kyvik, C. Luque-Corredera, D. Pulido, M. Royo, J. Veciana, J. Guasch, I. Ratera, *J. Phys. Chem. B.,* **2018**, 122, 4481−4490

Biomaterials to promote in situ regeneration microenvironments

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Biomaterials have been used in regenerative medicine for years, but they have been mainly used as scaffolds to support and guide cells or as cell and signaling delivery carriers. Our research has focused in how the biomaterials interact with the host environment. We have determined that no biomaterial is inert and that all of them can affect cell behavior. Understanding how cells interact with the biomaterials and how the degradation products can activate metabolically the cells allows the creation of microenvironments that can induce cell reprograming and activation of stem and progenitor cells.

Cells are susceptible to change their phenotype and function in response to the designed scaffolds. The selected material, topography, scaffold structure and degradation products have to be optimized to fulfil the requirements for each tissue (1,2). We have demonstrated that biomaterials themselves can activate stem cells at their niche and can either differentiate them or dedifferentiate adult cells towards a more precursor phenotype. This is perfect for in situ tissue engineering applications.

The way how we can translate and transfer the technology into products will have a lot to do in how they are fabricated and how is the interaction with the cells and tissues.

Nanoscale Coordination Polymers as Novel Bioimaging Probes

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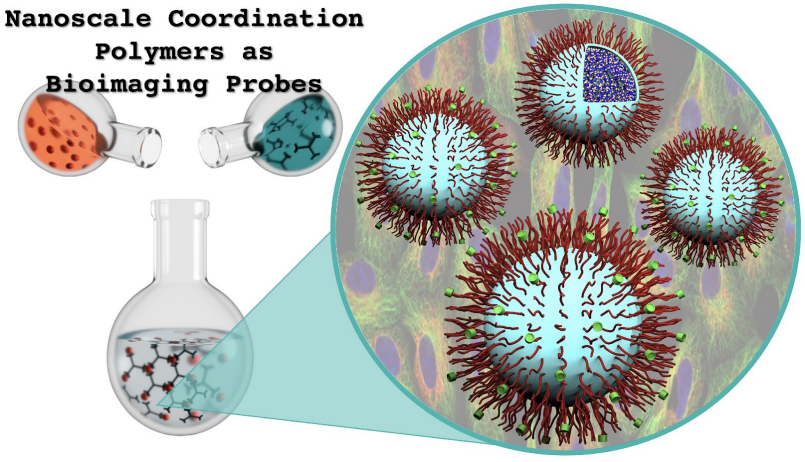
The success in nanomedicine research is based on the interaction of a multitude of disciplines including material science and engineering, cell biology and translational clinic. Over the next decades, nanotechnology will fundamentally transform science, technology and society, offering a significant opportunity to enhance human health. In this sense, many efforts are being focused on the development of novel approaches for the formation of advanced materials that enable early disease diagnosis, as well as precise and effective therapy tailored specifically to each patient.
Nanomaterials have an essential role in the development of biomedical imaging. Among all of them, coordination polymers and its rational design let the formation of nanostructured materials with a wide variety of properties. The multiple combinations between metal ions and organic ligands as precursors of self-assembled materials have fascinated scientists for decades. The application of coordination chemistry at the nanoscale is considered one of the most versatile approaches for the development of new nanostructured materials due to the infinite possibilities endowing unprecedented properties. Specifically, nanoscale coordination polymers (NCPs) provide an added value thanks to their pre-designed nature, increasing the interest for their application in several imaging techniques, including magnetic resonance imaging, optical imaging and radioimaging, among others. During the last few years, NCPs have reported exceptional features and advantages over other nanomaterials allowing to overcome some of the current challenges in the diagnosis of diseases. The study and development of novel imaging probes based on NCPs have promoted an exponential growth in the field thanks to their versatility, structural and chemical diversity and tailoring capacity. Moreover, incorporating simultaneously diagnostic and therapeutic functionalities in NCPs provides entities that can be used to deliver diagnostic imaging agents and therapeutic drugs at the same time, the so-called theranostic nanomedicines.



Stable and efficient generation of poly(β-aminoester)s for RNAi delivery

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Cationic polymers are promising delivery systems for RNAi due to their ease of manipulation, scale-up conditions and transfection efficiency. However, some properties, such as stability and targeting, remain challenging to overcome. In this work, different modifications in poly(*β*-amino ester) (pBAE) structure have been explored to overcome these limitations. Recent studies have demonstrated that hydrophobicity plays a key role in controlling electrostatic interactions of plasma proteins with nanoparticles. Results show that a slight increase in the polymer hydrophobicity increases its siRNA packaging capacity, stability, and transfection efficiency. In this work, we have addressed one of the main limitations of synthetic vectors, which is their reduced stability in the presence of serum proteins. For that, we have synthesized hydrophobized versions of previously reported top performing poly(beta-amino ester) formulations using hexylamine, hexadecylamine, and cholesterol, making the resulting polyplexes stable against plasma proteins for more than 48 hours, which is really high for this class of transfection vectors. For RNAi complexation, the polymers were designed with terminated oligopeptides. Thus, the strategy chosen to attach the hydrophobic moieties was through the polymeric backbone, leaving the terminated oligopeptides free to complex with the RNAis. Moreover, the newly developed polymers present higher transfection efficiency than previously described pBAEs. Specifically, C6-50 and Cchol-50 polymers (figure 1) are promising delivery systems with improved stability, which may be useful for in vivo applications. Therefore, tailoring the hydrophilicity–hydrophobicity ratio of top performing polymer formulations developed in this work may result in significant advances with a high impact on the particle stability, packaging capacity and transfection efficiency of RNAi

Therefore, it can be concluded that these newly optimized pBAE polymers present great potential as delivery vectors to specifically drive therapeutic RNA-based nucleic acids in a cell-specific manner under physiological conditions.

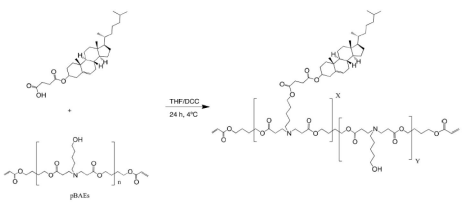

Fig. 1 Cchol oligopeptide-end PBAE

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Nanochaperones: A hopeful therapeutic approach to fight conformational diseases?

Ana B. Caballero
Universitat de Barcelona

Conformational pathologies, including neurodegenerative ones, are characterized by misfolded proteins called amyloids, which lose their physiological role and acquire toxicity. The accumulation and spread of amyloids is related to an impaired proteostasis network. Chaperones, as key actors of proteostasis, have thus become promising drug targets and models.
At nanoBIC, we explore how nanoparticles can be used to either emulate or help chaperones against amyloid accumulation. I will present how the nascent concept of *nanochaperone* may set future directions toward the development of cost-effective, disease-modifying drugs to treat conformational disorders.

Polyurea/polyurethane Nanocapsules Targeting the Acidic Tumoral Microenviroment as Smart Drug Delivery Vehicles

Marta Pérez
Idibell, UB

Cancer is one of the leading causes of mortality worldwide and this fact is due, in part, to limited success of some current therapeutic approaches. The clinical potential of many promising drugs is restricted by their systemic toxicity and lack of selectivity towards cancer cells, leading to insufficient drug concentration at the tumor site. To overcome these hurdles, we have developed a new drug delivery system based on robust polyurea/polyurethane nanocapsules (NCs) which present amphoteric characteristics that facilitate their accumulation into acidic tissues, such is the tumor microenvironment, presenting thus, selectivity for tumor cells. Moreover, these NCs have the potential to protect the drug from premature inactivation and release it only inside cancer cells through reductive conditions involving GSH. We have demonstrated that the drug loaded into these nanocarriers maintains its cytotoxic activity against cancer cells, which is increased in slightly acidic conditions and corresponds with a better cellular internalization. Moreover, the systemic toxicity of the loaded drug is reduced in *in vivo* when it is nanoencapsulated, maintaining its anticancer activity. As an added value of this work, these nanocarriers are synthesized through an industrially scalable method, which can be applicable to several commonly used hydrophobic drugs, becoming a powerful tool to improve the performance of current cytotoxic molecules used in cancer treatment.

Novel mRNA vaccination strategies: use of poly(beta aminoesters) to achieve selective dendritic cells delivery

Coral García-Fernández*, Marta Guerra-Rebollo*, Cristina Fornaguera*, Salvador Borrós**
** Institut Químic de Sarriá*

Advances in immunotherapy highlight the importance of the immune system as a valuable factor in the treatment and cure of a wide range of diseases, including cancer and infectious diseases. Given the paradigm with the current crisis triggered by coronavirus disease, the development of vaccines is more than ever a crucial research goal. Vaccine design has evolved towards the use of genetic material, particularly mRNA, as the active principle to activate the patient's immune system. However, the labile nature of this molecule represents a major obstacle, as the encapsulation of RNA is required. Besides, the mRNA must target specific cell populations, usually Antigen Presenting Cells (APCs), to activate the immune response. Thus, it is necessary to design vectors for efficient delivery of the oligonucleotides. Here, we highlight the excellent results obtained in our group regarding the design of poly-beta amino ester nanoparticles. These vectors, easily tunable for the encapsulation of genetic material and adjuvants, stand out for their versatile nature in terms of application, being easily scalable under GMP conditions.

DELOS NANOVESICLES FOR DRUG DELIVERY: AN EXAMPLE OF REFORMULATION OF A PROTEIN TO TREAT COMPLEX WOUNDS

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***Center for Genetic Engineering and Biotechnology (CIGB), Cuba*
****ICMAB-CSIC and CIBER-BBN*

The growing interest in active reformulation with therapeutic efficiency has been transforming the field of drug delivery. Then, the idea of using nanotechnology as a strategy to develop nanovehicles can be a feasible strategy to provide protection together with the effective delivery of the active molecules in the site of action.
In the frame of Nanomol Technologies SL, a spin-off of the Nanomol group from the Institute of Materials Science of Barcelona (ICMAB-CSIC), develops and commercialize a new one-step and scalable technology called DELOS-susp for the production of unilamellar and homogeneous nanovesicles, which can encapsulate active compounds, present remarkable physicochemical properties and also meet the quality standards required in pharmaceutical formulations.
Using this promising platform, a new nanomedicine based on the reformulation of a human recombinant epidermal growth factor (rhEGF), which is a small polypeptide that promotes epidermal regeneration but its bioavailability and effectiveness can be affected by the proteolytic environment present in the complex wounds, was successfully developed using DELOS-susp methodology to treat complex wounds such as diabetic foot ulcers and chronic venous ulcers.
This nanomedicine was profoundly characterized to determine their physicochemical properties (size and zeta potential by dynamic light scattering, morphology by cryo-TEM, entrapment efficiency and protein loadings by an enzyme-linked immunosorbent assay) and their biological properties (bioactivity, resistance to proteases, and in vivo efficacy).
It should be pointed out that the development of the new re(nano)formulation presented astonishing characteristics in terms of physicochemical and biological properties. Not only, rhEGF integrated into DELOS vesicles presented encapsulation efficiencies higher than 90% but also the biological activity of the encapsulated protein increased 3-fold in relation to the free protein. Furthermore, the stability against protease action was clearly enhanced

and the pharmacological efficacy of the formulation was successfully demonstrated in a rat model of chronic ulcer as well as when used for the compassionate treatment in patients, showing outstanding results in the cicatrization of the treated complex wounds.

Microwave-Assisted Synthesis of SPION-Reduced Graphene Oxide Hybrids for Magnetic Resonance Imaging (MRI)

Marina Llenas*, *Stefania Sandoval*, Silvia Lope-Piedrafita**, Khuloud T. Al-Jamal***, Gerard Tobias**
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***Servei de Ressonància Magnètica Nuclear, Universitat Autònoma de Barcelona, Campus UAB, 08193 Bellaterra (Barcelona), Spain / Centro de Investigación Biomédica en Red-Bioingeniería, Biomateriales y Nanomedicina (CIBER-BBN), Universitat Autònoma de Barcelona, Campus UAB, 08193 Bellaterra (Barcelona), Spain*
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Magnetic resonance imaging (MRI) is a useful tool for disease diagnosis and treatment monitoring. Superparamagnetic iron oxide nanoparticles (SPION) show good performance as transverse relaxation (T2) contrast agents, thus facilitating the interpretation of the acquired images. Attachment of SPION onto nanocarriers prevents their agglomeration, improving the circulation time and efficiency. Graphene derivatives, such as graphene oxide (GO) and reduced graphene oxide (RGO), are appealing nanocarriers since they have both high surface area and functional moieties that make them ideal substrates for the attachment of nanoparticles. A fast, simple, and environmentally friendly microwave-assisted approach for the synthesis of SPION-RGO hybrids has been demonstrated in this study. Different iron precursor/GO ratios were used leading to SPION, with a median diameter of 7.1 nm, homogeneously distributed along the RGO surface. Good relaxivity (r2*) values were obtained in MRI studies and no significant toxicity was detected within in vitro tests following GL261 glioma and J774 macrophage-like cells for 24 h with SPION-RGO, demonstrating the applicability of the hybrids as T2-weighted MRI contrast agents [1].

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Different anions doped polypyrrole molecularly imprinted polymer based electrochemical sensor for detection of acetaminophen, uric acid and ascorbic acid

Mingyue Wang*, *Xavier Cetó Alseda**, *Manel del Valle**
Department of Chemistry, Universitat Autònoma de Barcelona

Molecularly imprinted polymers (MIPs) are synthetic receptors with complimentary cavities towards a chosen template molecule (the target analyte), able to rebind it with high affinity and specificity. Those interactions are similar to the ones between the antibodies and antigens, but with superior chemical, mechanical, thermal and pH stability, and reusability. Thus, with the goal of obtaining of low-cost artificial receptors with high selectivity towards a desired analyte, highly suitable for applications in diverse fields, such as the environmental, medical or agro-alimentary. In this regard, MIPs have become a significant research hotspot in the development of electrochemical sensors given their ability to selectively rebind to the target analytes with high specificity even in the presence of complex matrix; thus simplifying the analysis process and improving chemosensors performance.
In this work, MIP films are in-situ electro-synthesised from a monomer (pyrrole) solution, in the presence of the template molecule and different doping anions as a facile approach for the tunability of the MIP morphology. A systematic evaluation on the effect of a series of anions as counter ion dopant integrated into the polypyrrole (PPy) backbone is carried out, including perchlorate (ClO4-), p-toluene sulfonate (pTS-), dodecyl sulfonate (DS-) and dodecyl benzene sulfonate (DBS-). The target compounds being evaluated are acetaminophen (AP), uric acid (UA) and ascorbic acid (AA), and the performance of the resulting MIPs modified electrodes is evaluated by means of cyclic voltammetry (CV) and differential pulse voltammetry (DPV).

Mesoporous silica-coated nanoceria reduce metabolic alterations associated with obesity

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Background: Low-grade inflammation and oxidative stress are intertwined mechanisms linking the highly prevalent condition of obesity with metabolic comorbidities. Despite lifestyle and diet changes, there is currently no effective therapeutic approach to treat obesity. CeO2 nanoparticles (CeO2NPs) show an auto-regenerative antioxidant effect that overcomes the limitations of classical antioxidants. The objectives of this study were to assess whether mesoporous silica-coated CeO2 nanoparticles (CeO2@mSiO2) are able to maximize the antioxidant effect of CeO2NPs and redress the low-grade inflammation associated with obesity in obese Zucker rats.
Methods: CeO2@mSiO2 (4 nm cores) were synthesized in aqueous media and at room temperature through a rational process with easy implementation, at low cost, sustainable and scalable. Cell viability and ROS production was assessed in HepG2 cells. Animal study consisted of lean Zucker rats treated with vehicle (n=10) and obese Zucker rats treated with CeO2NPs (0.1 mg/kg, n=10), CeO2@mSiO2 (0.1 mg/kg, n=10) or vehicle (TMAOH 0.48 mM, n=10), twice a week on week 8 and 9, and euthanized on week 14.
Results: The encapsulation of CeO2NPs maximized the antioxidant effects and maintained the cellular protection in HepG2 cells. In obese Zucker rats, CeO2@mSiO2 were well tolerated and their presence in non-targeted organs was reduced. This was translated into a higher decrease of hyperlipidemia and inflammation through reduction of circulating levels of TNF-α, triglycerides (TG) and LDL-cholesterol in obese Zucker rats. The lipidomic profile of obese Zucker rats treated with CeO2@mSiO2 revealed an enhanced reduction of palmitic acid and TG-derived saturated fatty acids. Finally, CeO2@mSiO2 improved liver and adipose tissue dysregulation of genes related to metabolic and inflammatory signals in obese Zucker rats.

Conclusion: These results altogether establish CeO2@mSiO2 as a promising therapeutic approach to treat obesity and its metabolic comorbidities addressing the low-grade chronic inflammation and oxidative stress as well as ameliorating the associated metabolic alterations.

Correlating super-resolution microscopy and transmission electron microscopy to study multiparametric heterogeneity in nanoparticles

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The use of nanoparticles for the delivery of therapeutics is a promising research area, with a myriad of different formulations being developed. A common characteristic is the decoration of the nanoparticles with ligands to target biomarkers of interest. The interplay between size and ligand number and distribution is crucial for the formulation performance and need to be properly characterized to understand nanoparticle structure-activity relations. Yet, particle-to-particle heterogeneity poses a serious challenge due to the lack of methods able to measure both size and ligand distribution at the same time and at the single particle level.
We address this issue by developing a correlative super-resolution microscopy (SRM) and transmission electron microscopy (TEM) imaging technique (super-resCLEM). SRM reveals the number and distribution of surface ligands with single-molecule sensitivity, whilst TEM shows the nanoparticle size and morphology. Supe-resCLEM techniques proved their potential in structural biology but, to the best of our knowledge, they have not yet been explored for the structural characterization of nanoparticles. Here we used our method to characterize PLGA-PEG-Maleimide nanoparticles with varying maleimide contents and PEG block lengths. We demonstrated how PEG architecture can influence ligand conjugation efficiency and accessibility, and its interplay with particle size. Moreover, we investigated NP multiparametric heterogeneity highlighting the presence of multiple ligand populations.
Overall, we believe that our super-resCLEM technique is applicable to a wide range of nanomaterials, sizes, formulation strategies and morphologies. Its implementation in nanoparticle characterization would allow the community to explore the relationship between various parameters and unveil the relationship between them, bringing us a step closer to the successful design of nanomaterials.

Molecularly Imprinted Polymers biosensing for enhanced detection of Tryptamine

A. Herrera-Chacon*, C. Muñoz-Borrego*, M. del Valle**
** Universitat Autònoma de Barcelona*

Molecularly Imprinted Polymers (MIPs) are plastic polymers -also named nanoplastics-, which can improve the voltammetric sensor response due to their capacity to act as an artificial receptor. This material is designed and synthesized to have tailored-made binding cavities, which are complementary to the analyte in shape, size and functionality -also named recognition cavities-. Biogenic amines (BAs) are considered a hazard from a biological and a chemical point of view as they are indicators of improper or poor food preservation. Tryptamine is a good candidate for being used in imprinting technique and sensing field, as it may provide proper structural features for a good imprinting and because it has electroactive properties. Once the polymer is obtained, a template removal is performed in order to clear the template out of the abovementioned cavities and allow its usage as a recognition element. Prior to modifying electrodes surface, the polymer morphology and homogeneity is checked through scanning electron microscopy (SEM), achieving data about its size and distribution. Afterwards, this polymer is deposited onto the surface of a graphite epoxy composite (GEC) via drop-casting sol-gel immobilization to provide selectivity to the unspecific chemosensor. The electrochemical response is finally characterized in comparison with the control material, the non-imprinted polymer. The response to different biogenic amines is assayed, and a Principal Component Analysis (PCA) data treatment is done in order to check the biosensor selectivity among this family of chemicals. As feature perspective, its applicability will be checked with a sensory array embedded in real samples. Accordingly, MIPs biosensors will be used against different BAs aimed to their identification and/or quantification.

Engineered poly(beta-aminoester) nanoparticles (PBAE NPs) containing pituitary transforming gene 1 (PTTG1) siRNA selectively target the liver and spleen in fibrotic rats

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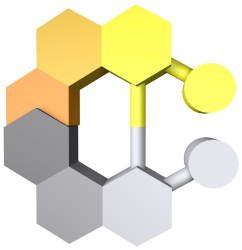
Background: Recent studies have shown that PTTG1, a multifunctional protein with roles in differentiation, proliferation, and gene regulation, plays an important role in liver fibrogenesis. Here we assessed whether a targeted nanoparticle RNA interference strategy is useful as a novel antifibrogenic strategy.
Methods: The study was performed in male fibrotic C57BL/6 wild type (WT) and Pttg1 knock out (KO) mice and in Wistar rats. Fibrosis was induced by intraperitoneal injection or inhalation of CCl_4 in mice and rats, respectively. Fibrotic rats were transfected with Pttg1 small interfering RNA (siRNA) using Invivofectamine (4 intravenous doses of 0.25 mg/kg body weight). Hepatic fibrosis was assessed by morphometric quantification after Sirius red staining and gene expression by Real time PCR. PBAE NPs with retinol moiety containing siRNA Pttg1 were synthesized and organ biodistribution was determined in fibrotic rats. Moreover, cultured human-derived hepatocytes were infected with PBAE NPs to evaluate whether the functionalized NPs were able to efficiently transfect human cells.
Results: Liver fibrosis was associated with an increase of Pttg1 transcript in rats. When Pttg1 was interfered resulted in lower portal pressure and hepatic collagen content. In line with



these results, the transcription of profibrogenic genes including Col1α2, Pdgfrß, Mmp2, Timp1, and Timp2 was diminished. Furthermore, Pttg1 KO mice showed significantly decreased collagen content than wild type mice. Functionalized PBAE NPs targeted the liver and the spleen but not the heart, lung or brain. Finally, after 24 hours of infection the human hepatocyte cell line was efficiently transfected with the functionalized PBAE NPs. Conclusions: Pttg1 knock out and interference attenuates liver fibrosis in mice and rats. Functionalized PBAE NPs specifically target the liver and spleen and successfully transfect human liver cells. These results suggest that functionalized PBAE NPs containing siRNA Pttg1 could be therapeutically useful to mitigate or reverse hepatic fibrosis.

APPLICATION OF NANOPARTICLES MODIFIED EPOXY-GRAPHITE ELECTRODES FOR ELECTOCHEMICAL DETECTION OF CAPSAICIN

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The present research focuses on the electrochemical determination of capsaicin, a lipophilic alkaloid which is responsible for hotness in chili peppers. An electrochemical sensor based on epoxy-graphite composite with the modification of Titanium dioxide (TiO2) nanoparticles is developed for the determination of capsaicin

To overcome the fouling effect in the cyclic voltammetric measurements of capsaicin, extensive search of electrode modifiers, mainly of nanotechnological origin, has been carried out. We observed good behavior in TiO2 modified electrode. TiO2 nanoparticles were incorporated into the sensor by adding the nanoparticles into the mixture of epoxy graphite composite during the fabrication of the sensor.

As capsaicin gives two oxidation peaks during electrochemical measurements. Two linear concentration ranges were obtained from 6 to 75 µM (R=0.99) and from 12 to 138 µM, with a detection limit of 5.34 µM and 11.3 µM capsaicin, for 1st and 2nd oxidation peak, respectively. The main advantage of developed sensor is its repeatability with a relative standard deviation (RSD) value of 2.53 after 10 repeating measurements. To the best of our knowledge, our proposed nanoparticles modified sensor is the first sensor to be developed which does not show fouling effect with capsaicin and can be applied in the repeated measurements of capsaicin samples without renewing the electrode surface between consecutive measurements. This voltammetric platform has successfully been applied to quantify capsaicin in various real samples such as hot chili sauce and pharmaceutical preparations.