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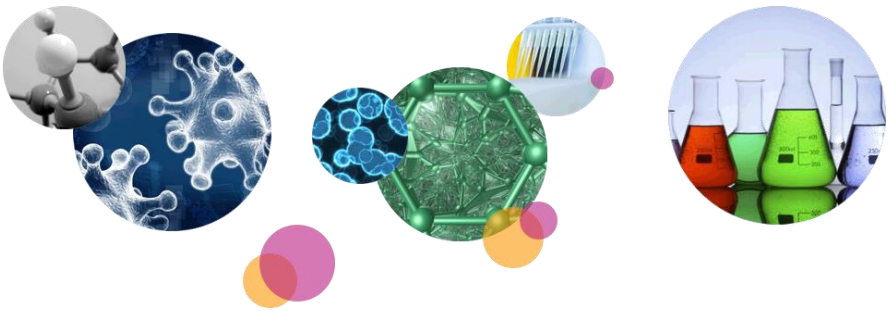

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foreword

On behalf of the Organising Committee we take great pleasure in welcoming you for the 1st edition of the NanoBioMed Online Conference (NBMO2020).
This one-day event will present the most recent international developments in the field of Nanobiotechnology and Nanomedicine and will provide a platform for multidisciplinary communication to participants from both science and industry.

11 high profile talks from worldwide most influential experts in the NanoBioMed sector will present speeches in this international event on how Biotechnology and Nanomedicine can impact positively our daily life.

NBMO2020 means to gather the key players of the BioMed Community and promote constructive dialogue between business and public leaders, putting a specific emphasis on the technologies and applications in the nanoBioMed sector. This event is launched following the success of previous NanoBioMed editions and considering that all major scientific and technological conferences are being cancelled or postponed worldwide until the end of 2020.

We are indebted to the following Institution for the financial support: Institute for Bioengineering of Catalonia (IBEC) – Spain.

We also would like to thank all the speakers and participants that join us this year.

Hope to see you in the next edition of the NanoBioMed International Conference in Barcelona (November 17-19, 2020).

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Speakers list:

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Abstracts

Delivery of biologicals using nanotechnology

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Antigen and therapeutic proteins, including monoclonal antibodies, are normally being administered by injection. To prolong the duration of their effects, a number of strategies, including long-acting injectables have been developed. Despite these advances, the difficulties of these macromolecules for overcoming biological barriers and reach the intracellular targets have limited their full exploitation.

Fortunately, the continuously improved understanding of the biological barriers and the molecular biology associated to pathological conditions is paving the way for a more comprehensive and rational design of protein formulations based on the use of nanotechnology. Our laboratory, with a long-track experience in the formulation of macromolecules using polymer nanoparticles, has significantly contributed to this field. As an example, in the 90's we were the first to report that nanoparticles made of either PLA-PEG or chitosan were efficient vehicles for the transmucosal delivery of proteins and antigens. The result of our subsequent efforts is an array of nanotechnologies that can be used to deliver proteins across mucosal surfaces, and, also, to facilitate their intracellular delivery following parenteral administration.

In my presentation, I will focus on the design of protein carriers that could be used in different therapeutic areas: (i) oral delivery of peptides intended to treat either local or systemic diseases, (ii) delivery of mAb targeted to intracellular onco-proteins, as new oncological treatments, (iii) nanovaccines designed to prevent diseases, i.e. HIV.

Overall, our experience in this field has benefited from integrative approaches adopted by specifically designed consortia. Hopefully, the results of these cooperative efforts will help to accelerate the progress of a rational design of protein-based nanomedicines.

More information about these projects can be found at: http://www.usc.es/grupos/mjalonsolab/

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Oral Drug delivery: Matilde Duran, Sulay Tovar, Carlos Dieguez

Anticancer drug delivery: Desirée Teijeiro, Ana Cadete, Ana Olivera and Dolores Torres from the USC, Spain and Gema Moreno and Angela Molina from the "Universidad Autónoma de Madrid", Spain.

Vaccine delivery: Jose Crecente, Tamara Gómez from the USC and Ma Luo and Francis Plummer from University of Manitoba, Canada.

The research activity has been founded by the European Comision, Horizon 2020 Program (# 646142 – NANOPILOT and #21058- B-SMART), by MINECO- PCIN-2017-129/ AEI, under the frame of EuroNanoMed III, and by The National Institutes of Health (NIH) (#R01AI111805),

Multivalent and multiplexed interaction in nanomedicine

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Abstract

Each cell of our body exerts a unique function as a consequence of its distinctive phenotype, i.e. the cell's proteins and genes collective that defines its identity. Each cell so 'expresses' a unique combination of proteins on their membrane that distinguish them from their neighbours.
We use such information to engineer multivalent and multiplexed nanomedicines that comprise unique ligands combinations. We tune each ligand/receptor interaction to be weak enough that only when combined, they can bind to its complementary phenotype [1]. Ergo, each nanomedicine interacts with a high level of precision, enabling to target defined cell populations. Such a precision nanomedicine increases anticancer drugs therapeutic efficiency of several orders of magnitude allowing for personalised treatment down to the single cell level to compensate for patient to patient variations.
I'll discuss here how we can apply phenotypic targeting to brain delivery, tumour, immune cells as well as to understand viral infection.

REFERENCES

[1] Tian et al. ***Science Adv.*** 2020, 6,4, eaat0919

Interaction of cancer cells with particles depended on cell deformability

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Growing evidence shows correlation between cancer aggressiveness and the mechanical properties of tumor cells. For many cancer diseases it was found that the deformability of the cells is higher in cancer compared to normal cells, and further raises with the degree of cell malignancy. The talk will discuss the effects of physical properties of particles on their interaction with cells and their capacity to penetrate non-cancer and cancer cells of varying malignancy potential.
Methods - The method(s) of study or data collection employed. .
A wide range of biological and physical models are presented and mechanistic insights provided theoretically and experimentally will be discussed. Moreover, a microfluidic based methodology to produce highly controlled nanoparticles is presented for the development of tunable drug delivery.

In a comprehensive study, we found a Triangular Correlation (TrC) between cell deformability, phagocytic like capacity, and cancer aggressiveness. We found that the uptake of inert sub-micron and micro-beads was massively higher in cancer cells compared with normal originated cells. Moreover, cells with a higher malignancy potential had greater uptake capacity. Importantly, in a reciprocal approach, we sorted either human bladder cancer cells or melanoma cells into subpopulations, solely based on their phagocytic capacity. The more phagocytic subpopulations showed elevated phenotypes of cancer aggressiveness ex vivo and in vivo. The uptake potential was found to be an imprinted feature preserved genetically and enriched over the sorting cycles. A gene expression profile revealed differences in gene sets associated with regulation of cell-cell and extracellular matrix adhesions and epithelial-to-mesenchymal transition. In all cases, enhanced phagocytic and aggressiveness phenotypes were correlated with greater cell deformability.

Our multidisciplinary approach provides the proof of concept that phagocytic measurements can be applied can be a surrogate marker for detecting malignancy of cancer cells based on mechanical properties and be used for rational design of drug delivery systems.

REFERENCES

[1] Brill-Karniely Y.*, Dror D.*, Duanis-Assaf T., et al. Correlation (TrC) between cancer aggressiveness, cell uptake capability and cell deformability. Science Advances, 2020, Vol. 6, no. 3, eaax2861
[2] Amoyav B, Benny O. Microfluidic Based Fabrication and Characterization of Highly Porous Polymeric Microspheres.Polymers. 2019 Mar 5;11(3). pii: E419
[3] Amoyav, B. & Benny, O. Controlled and tunable polymer particles' production using a single microfluidic device. Appl Nanosci.
[4] Stern T*, Kaner I*, Laser Zer N, Shoval H, Dror D, Manevitch Z, Chai L, Brill-Karniely Y, Benny O. Rigidity of polymer micelles affects interactions with tumor cells. J Control Release. pii: S0168-3659(16)30783-0. 2016

FIGURES

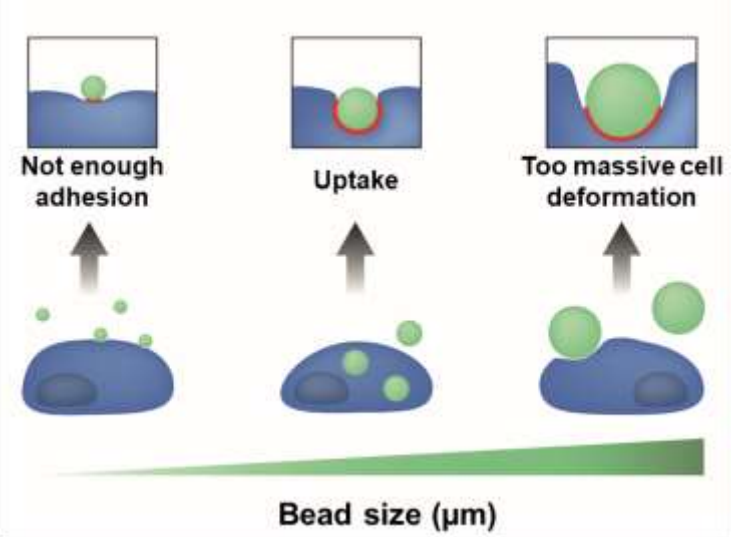

Figure 1: Illustration showing cell deformation effect on cell uptake

Multifunctional 2D materials for cancer therapy and bioimaging

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Two-dimensional materials are considered unique systems for many applications in different fields including biomedicine [1, 2]. They are offering the possibility of original chemical functionalization and design of complex multifunctional systems that allow further their exploitation in therapy, imaging and diagnosis [2]. In this webinar, I will present the chemical strategies to functionalize graphene and other 2D nanomaterials with appropriate functional groups and therapeutic molecules in view of their biomedical applications [3-6]. I will present few examples of their use in cancer therapy and imaging [7-10]. I will also describe how it is possible to enhance the biodegradability and tune the toxic effects of these different materials [11, 12].

REFERENCES

[1] Martìn, C., Kostarelos, K., Prato M., Bianco, A. Chem. Commun. 55 (2019) 5540-5546.
[2] Reina, G., González-Domínguez, J. M., Criado, A., Vázquez, E., Bianco, A., Prato, M. Chem. Soc. Rev. 46 (2017) 4400-4416.
[3] Vacchi, I. A.; Spinato, C.; Raya, J.; Bianco, A.; Ménard-Moyon, C. Nanoscale, 8 (2016) 13714-13721.
[4] Vacchi, I. A.; Raya, J.; Bianco, A.; Ménard-Moyon, C. 2D Mater., 5 (2018) 035037.
[5] Guo, S.; Nishina, Y.; Bianco, A.; Ménard-Moyon, C. Angew. Chem. Int. Ed., 59 (2020) 1542-1547.
[6] Lucherelli, M. A.; Raya, J.; Edelthalhammer, K. F.; Hauke, F.; Hirsch, A.; Abellán, G.; Bianco, A. Chem. Eur. J., 25 (2019) 13218-13223.
[7] Reina, G., Ruiz, A., Murera, D., Nishina, Y., Bianco, A. ACS Appl. Mater. Interfaces 11 (2019) 7695-7702.
[8] Lucherelli, M.A., Yu, Y., Reina, G., Abellán, G., Miyako, E., Bianco, A. Angew. Chem. Int. Ed., 59 (2020) doi:10.1002/anie.201916112.
[9] Martín, C., Ruiz, A., Keshavan, S., Reina, G., Murera, D., Nishina, Y., Fadeel, B., Bianco, A. 25 (2019) 1901761.
[10] Russier, J.; Léon, V.; Orecchioni, M.; Hirata, E.; Virdis, P.; Fozza, C.; Sgarrella, F.; Prato, M.; Vazquez, E.; Bianco, A.; Delogu, L. G. Angew. Chem. Int. Ed., 56 (2017) 3014-3019.
[11] Kurapati, R.; Mukherjee, S. P.; Martín C.; Bepete, G.; Vazquez, E.; Pénicaud, A.; Fadeel, B.; Bianco, A. Angew. Chem. Int. Ed., 57 (2018), 11722-11727.
[12] Kurapati, R.; Bonachera, F.; Russier, J.; Sureshbabu, A. R.; Ménard-Moyon, C.; Kostarelos, K.; Bianco, A. Covalent chemical functionalization enhances the biodegradation of graphene oxide. 2D Mater., 5 (2018) 015020.

Personalized nanomedicine for improved anticancer therapeutics

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The identification of druggable targets in metastasis is a promising strategy to improve the outcome and overall survival of metastatic cancer. Metastasis is indeed the major cause of death in cancer patients with solid tumors, and, as a matter of that, for Non-Small Cell Lung Cancer (NSCLC), the 5-year mean survival is lower than 5% in a metastatic setting. Following a patient-driven approach, we have identified TAS1R3, a novel and druggable oncology target that plays a role in the metastasis of NSCLC and has potential in other cancers (1). We have obtained solid evidence regarding the role of TAS1R3 in cancer progression and metastasis, using patient derived samples, *in vitro* 3D cultures, and *in vivo* animal models. This new biomarker has additionally the potential for patient stratification, providing a highly valuable tool for interpretable decision making and advancing towards the concept of personalized medicine.
We aim to develop nanomedicines targeted to TAS1R3, to specifically deliver anticancer drugs to early-stage metastasis, to interrupt progression to overt metastasis, and to ultimately improve survival.
In out research group, we have developed stable nanometric emulsions, with a simple composition based on natural lipids, which are non-toxic and can be tailored to accommodate different kind of molecules, such as miRNA, plasmids, peptides, proteins, and antibodies (2, 3). As summarized in Figure 1, we are now working on the surface-decoration of the nanosystems with targeted ligands, antibodies and/or aptamers against TAS1R3, on the loading of anticancer drugs to eliminate metastatic resistant cancer cells, and on their radiolabelling with ^{89}Zr for *in vivo* PET/CT diagnosis. These multifunctional nanosystems will be valuable tools for allowing early detection of TAS1R3 positive metastatic cells and simultaneous treatment, to ultimately interrupt metastasis progression in specific patient subpopulations.

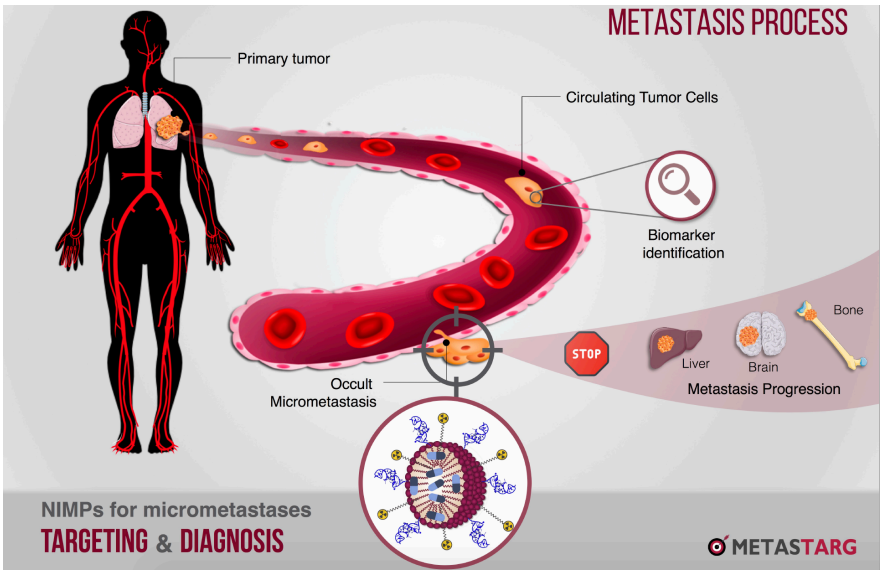

Figure 1: Following a patient-driven approach we aim to develop anticancer nanomedicines specifically targeted to metastasis.

REFERENCES

(1) WO2019138140, filed on January 15th, 2018 before the OEPM, and entitled “Use of the protein TAS1R3 as a therapeutic, diagnostic and/or prognostic biomarker, in tumors that express the protein thereof”; (2) WO2019138139, filed on January 15th, 2018 before the OEPM, and entitled “Nanosystems as selective vehicles”; (3) Bouzo BL, Calvelo M, Martín-Pastor M, Garcia-Fandiño R, de la Fuente M. In Vitro-in Silico Modelling Approach to Rationally Design Simple and Versatile Drug Delivery Systems, J. Phys. Chem. B 2020, In Press.

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SERS Detection of Tumor-Related Metabolic Alterations

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The tumor microenvironment, where numerous cell types interact to create a distinctive physiology, is characterized by deregulated metabolic features. In the recent years, 3D cancer models have been optimized to more accurately recreate and study the complex mechanisms behind tumor metabolism which supports cancer invasion, progression, and response to treatment. Because of the growing interest in studying in situ these complex systems, the development of novel technologies is critical to overcome the existence difficulties. In this context, surface enhanced Raman scattering (SERS) appears as a useful tool for label-free detection and imaging of diverse molecules of interest among the extracellular components. Herein, we present the application of nanostructured plasmonic substrates comprising micropatterned Au nanoparticle superlattices to the precise SERS detection of selected tumor metabolites which shape the cancer landscape, such as kynurenine, tryptophan and purine derivatives. Moreover, we employed this plasmonic substrate to study in situ the tumor response to different stress conditions in 3D cellular models with no need of sample preparation.

REFERENCES

[1] J. Langer et al., ACS Nano 2020, 14, 28-117.
[2] J. Plou, I. García, M. Charconnet, I. Astobiza, C. García-Astrain, C. Matricardi, A. Mihi, A. Carracedo, L.M. Liz-Marzán, Adv. Funct. Mater. 2020, 30, 1910335.

Nanobiosensors for point of care applications

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Abstract

There is a high demand to develop innovative and cost effective devices with interest for health care beside environment diagnostics, safety and security applications. The development of such devices is strongly related to new materials and technologies being nanomaterials and nanotechnology of special role. We study how new nanomaterials such as nanoparticles, graphene, nano/micromotors can be integrated in simple sensors thanks to their advantageous properties. Beside plastic platforms physical, chemical and mechanical properties of cellulose in both micro and nanofiber-based networks combined with their abundance in nature or easy to prepare and control procedures are making these materials of great interest while looking for cost-efficient and green alternatives for device production technologies. Both paper and nanopaper-based biosensors are emerging as a new class of devices with the objective to fulfil the “World Health Organization” requisites to be ASSURED: affordable, sensitive, specific, user-friendly, rapid and robust, equipment free and deliverable to end-users. How to design simple paper-based biosensor architectures? How to tune their analytical performance upon demand? How one can couple nanomaterials such as metallic nanoparticles, quantum dots and even graphene with paper and what is the benefit? How we can make these devices more robust, sensitive and with multiplexing capabilities? Can we bring these low cost and efficient devices to places with low resources, extreme conditions or even at our homes? Which are the perspectives to link these simple platforms and detection technologies with mobile communication? I will try to give responses to these questions through various interesting applications related to protein, DNA and even contaminants detection all of extreme importance for diagnostics, environment control, safety and security.

Surprising Charge Transport in DNA and Properties of Novel DNA-Based Molecules

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Abstract (Arial 11)

Charge transport through molecular structures is interesting both scientifically and technologically. To date, DNA is the only type of polymer that transports significant currents over distances of more than a few nanometers in individual molecules. Nevertheless, and in spite of large efforts to elucidate the charge transport mechanism through DNA a satisfying characterization and mechanistic description has not been provided yet. For molecular electronics, DNA derivatives are by far more promising than native DNA due to their improved charge-transport properties.
In recent years we have invested great efforts to address the above issues. Measuring the charge transport in DNA was elusive due to great technical difficulties leading to various results. We recently devised an experiment in which double-stranded DNA is well positioned between metal electrodes. Electrical measurements give surprisingly high currents over 100 base-pairs (~30 nm) elevated from the surface. The temperature dependence indicates backbone-related band-like transport.
In collaboration with the Kotlyar group, we were also able to synthesize and measure long (hundreds of nanometers) DNA–based derivatives that transport significant currents when deposited on hard substrates. Among the molecules, metal containing DNA, which is true metal-organic hybrid, a smooth and thin metal coated DNA and G-quadruplex DNA.
Step by step we improve the synthesized constructs and the measurement methods of single DNA-based molecules. I will present new and surprising results on dsDNA molecules. I will present new DNA-based molecules and report on our measurements of their properties.

REFERENCES

[1] "Direct measurement of electrical transport through DNA molecules", Danny Porath, Alexey Bezryadin, Simon de Vries and Cees Dekker, Nature 403, 635 (2000).
[2] "Long Monomolecular G4-DNA Nanowires", Alexander Kotlyar, Nataly Borovok, Tatiana Molotsky, Hezy Cohen, Errez Shapir and Danny Porath, Advanced Materials 17, 1901 (2005).
[3] "Electronic structure of single DNA molecules resolved by transverse scanning tunneling spectroscopy", Errez Shapir et al., Nature Materials 7, 68 (2008).
[4] "Long-range charge transport in single G4-DNA molecules", Gideon I. Livshits et. al., Nature Nanotechnology 9, 1040 (2014).
[5] "Synthesis and Properties of Novel Silver containing DNA molecules", Gennady Eidelshtein et. al., Advanced Materials 28, 4839 (2016).
[6] "Highly conductive thin uniform gold-coated DNA nanowires", Avigail Stern et. al., Advanced Materials 30, 1800433 (2018).
[7] "Advances in Synthesis and Measurement of Charge Transport in DNA-Based Derivatives". R. Zhuravel, A. Stern, N. Fardian-Melamed, G. Eidelshtein, L. Katrivas, D. Rotem, A. Kotlyar and D. Porath, Advanced Materials 30, 1706984 (2018).
[8] "Scanning Tunneling Microscopy and Spectroscopy of Novel Silver-Containing DNA Molecules", Natalie Fardian-Melamed, et al., Advanced Materials, Article Number: 1902816 (2019).
[9] "Backbone Charge Transport in Double Stranded DNA", Roman Zhuravel et. Al., Nature Nanotechnology, In press (2020)

FIGURES

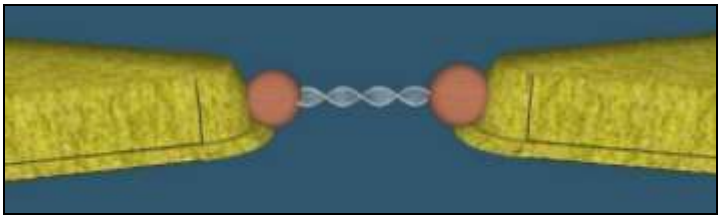

Figure 1: A DNA Dimer between metal nanoelectrodes.

Medical Nanoparticles II*: driving new pharmaceutical substances into the medical praxis

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The majority of drugs are small molecules coming from nature. Then there are subtle varitatiosn of them to alter they pharmacokinetics and indications. New pharmaceutical substances are large biomolecules, such as proteins and antibodies, which are totally biological. This means that introducing xenobiotic substances into the medical praxis is going to be challenging. Fortunately we have a precedent sucess with high energy physics, which has made its place in radiology for diagnostics and therapeutics. Medical Nanoparticles, MedNPs, is the term here used to describe the features that nanoparticles may have in order to make actual clinical work for the benefit of the patient, framed in the innovation, production, and regulation limits of our societies. This means that the proposed MedNPs have to be able to be transferred to society: that they can be produced as stable and reliable products and that they can enter the regulatory process which determines which substances can be applied in humans. This means that in another context, where there was more funding available to develop in-depth new ideas, with an industry (more) capable of mass (and competitive) production of nanomaterials, and a regulatory framework designed to accompany development of nanodrugs (and not small or biomolecules) will inevitably bring a brighter and sooner future for nanomedicine. But as far as we are concerned, if today, we want to develop medical nanoparticles (not just the mere exploration of the interactions of inorganic matter with biological systems at the nanoscale) in order to improve life quality and span of patients, we should adapt/subordinate our nanotechnology knowledge, tools, and abilities to the current medical practice and practitioners. These considerations have consequences in which materials are used to treat which disease and in which form.

Swarming hybrid nanobots and their imaging in vitro and in vivo

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The combination of biological components and artificial ones emerges into what we called hybrid bots. Alike bacteria or small swimmers found in nature, these *artificial nanobots* convert bio-available fuels to generate propulsion force to swim at the nanoscale. One of the dreams in nanotechnology is to engineer small vehicles which can eventually be applied *in vivo* for medical purposes. In my talk, I will present how we bioengineer hybrid nanobots combining the best from the two worlds: biology (enzymes) and (nano)technology (nano- micro-particles) providing swimming capabilities, biocompatibility, remote control, multifunctionality and actuation. I will present some of the proof-of-concept applications such as the efficient transport of drugs into cancer cells and spheroids, sensing capabilities and the use of molecular imaging techniques for their tracking and localization both in vitro and in vivo in confined spaces like mice bladder.

Supramolecular Antivirals

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Viral infections are among the main causes of death in the world. When prevention is not an option, antiviral drugs are the last resort to prevent the spread and the mortality of these infections. There are only a few effective drugs on the market, for the most part they prevent intracellular viral replication. Unfortunately, they are too few when compared to the many viruses that threaten humans.
In this talk, I will show a new design rule to achieve drugs that fight viruses extracellularly by irreversibly inhibiting their infectivity, i.e. I will show how to create virucidal compounds. The design of these macromolecular virucidal agents starts by a bio-mimic approach and is characterized by the limited toxicity towards host cells that one would expect from such compounds. Yet, I will demonstrate that the multivalent binding to the viruses, coupled with a large hydrophobic contact between the compounds and the virus leads to a loss of integrity of the virion that obviously leads to an irreversible loss of infectivity. Results in and ex-vivo will be illustrated especially for the cases of influenza, herpes, and respiratory syncytial virus.

SERS and microdroplets for multiplex phenotyping of cancer single cells

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The reason behind the high mortality of cancer is that it is a heterogeneous and dynamic disease, and that an average of 60 % of patients diagnosed with a primary tumour will relapse, having other tumours spread in their body[1,2]. Metastasis accounts for 90 % of cancer related deaths and due to the complicated nature of cancer, a panoply of different inherent factors have been defined as the hallmarks of metastasis: motility and invasion, ability to modulate the secondary site or local microenvironments, plasticity, and ability to colonise secondary tissues[3]. In the context of personalised medicine, the analysis of single cells is key in order to understand the origin and evolution of cancer to provide accurate prognosis.[4] Microfluidics and microdroplets have been increasingly used for the handling and understanding of the behaviour of single cells, as they offer the perfect isolated environment. Herein, we developed a protocol for fast phenotyping of different cancer cells types, based on surface-enhanced Raman scattering (SERS) spectroscopy and microdroplets. In this optofluic based platform, gold nanostars were used as SERS tags to identify the phenotypic characteristics of the cells that were previously encapsulated in microdroplets to allow single-cell analysis. The signal corresponding to the SERS tags paired to the expression of EpCAM, even at low expression levels, was identified for two different cancer cells lines (SK-BR-3 and MDA-MB-435). This integrated optofluidic platform paves the way towards the multiplex and automated characterisation of cell populations in cancer patients.

REFERENCES

[1] World Health Organization - Cancer.
[2] A. S. B. Primeau, Cancer Recurrence Statistics **2018**.
[3] D. R. Welch, D. R. Hurst, *Cancer Res.* **2019**, *79*, 3011.
[4] P. Bheda, R. Schneider, *Trends Cell Biol.* **2014**, *24*, 712.
[5] A. Teixeira, J. L. Paris, F. Roumani, L. Diéguez, M. Prado, B. Espiña, S. Abalde-Cela, A. Garrido-Maestu, L. Rodriguez-Lorenzo, *Materials (Basel).* **2020**, *13*, 1934.
[6] R. J. Best, J. J. Lyczakowski, S. Abalde-Cela, Z. Yu, C. Abell, A. G. Smith, *Anal. Chem.* **2016**, *88*.

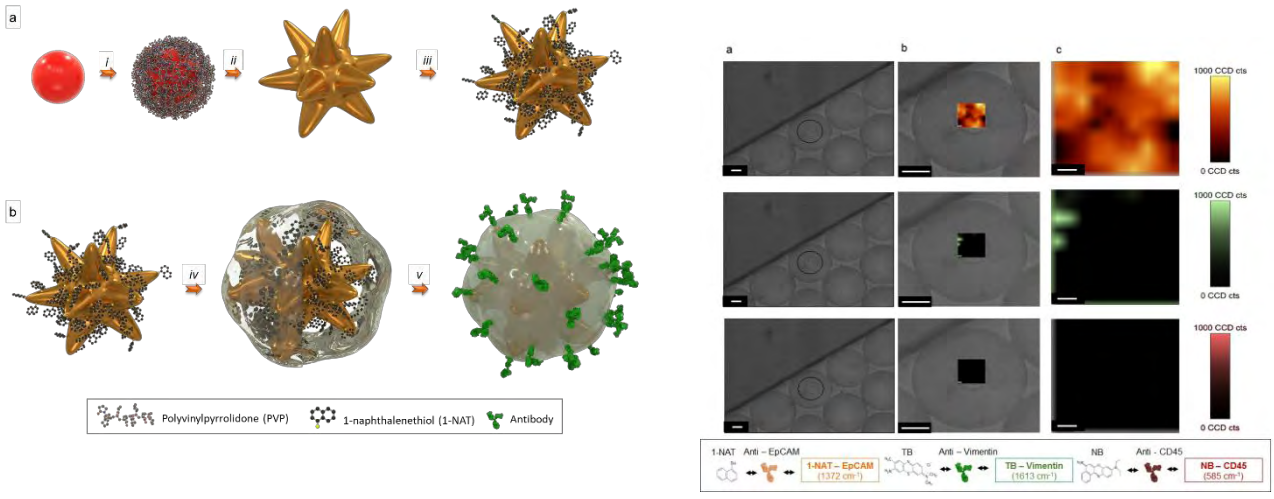

Figure 1: Left: Scheme depicting the synthesis of SERS tags; right: single cancer cells in droplets and corresponding SERS mapping.

Scanning probes for enzyme nanopatterning and for the spatial mapping of collagen micro-stiffness in tissue sections

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Scanning probe microscopy makes use of small probes, with size from tens of nanometers to few micrometers, scanned over the sample surface to obtain topographical and mechanical information with spatial resolution and force sensitivity. In a different application, scanning probes can be used as nanometric pens to locally modify the sample surface in contact with the probe. This second approach provides lithographic capabilities and it is called scanning probe lithography (SPL)1. In SPL, different inputs are used to generate the desired surface modification. In particular, when heatable cantilevers are employed to locally induce chemical reactions, the technique is called thermochemical nanolithography (tc-SPL)2. Both approaches can be of great interest for biological applications, to provide functional (nano and micro-mechanical) markers in biological surfaces (AFM) or for patterning purposes (tc-SPL). In my presentation, I will show the use of force volume AFM for the spatial mapping of collagen distribution in mammalian tissues with affordable timescales. This study points to the use of AFM as a routine tool in the biomedical research, to provide micromechanical data that correlate with outputs from other (optical, biochemical, histological) techniques3. I will also describe tc-SPL for the fabrication of nanoscale patterns in polymer films. These patterns can be used for enzymes anchoring with high throughput, high reproducibility and spatial control, till the single molecule level. Tc-SPL allows for the fabrication of 3D surfaces with independent control of topography and chemistry, and in my work it is employed to generate pockets (< 10 nm in size) that accomodate single enzymes4,5. References

REFERENCES

[1] Garcia, R., Knoll, A. W., Riedo, E., Nat. Nanotechnol. 9 (2014) 577-587.
[2] Szoszkiewicz, R., Okada, T., Jones, S. C., Li, T.-D., King, W. P., Marder, S., Riedo, E., Nano Lett. 7 (2007) 1064-1069.
[3] Calò, A., Romin, Y., Sroujib, R., Zambirinis, C. P., Fan, N., Santella, A., Feng, E., Fujisawa, S., Turkekul, M., Huang, S., Simpson, A. L., D'Angelica, M., Jarnagin, W. R., Manova-Todorova, K. (submitted).
[4] [4] Xiangyu, L., Kumar, M., Calò, A., Albisetti, E., Zheng, X., Manning, K., Elacqua, E., Weck, M., Ulijn, R., Riedo, E. (accepted in ACS Appl. Mater. Interfaces).
[5] [5] Xiangyu, L., Kumar, M., Calò, A., Albisetti, E., Zheng, X., Manning, K., Elacqua, E., Weck, M., Ulijn, R., Riedo, E., Faraday Discussion 2019 (doi: 10.1039/C9FD00025A).

FIGURES

Figure 1: Enzyme patterning through tc-SPL.

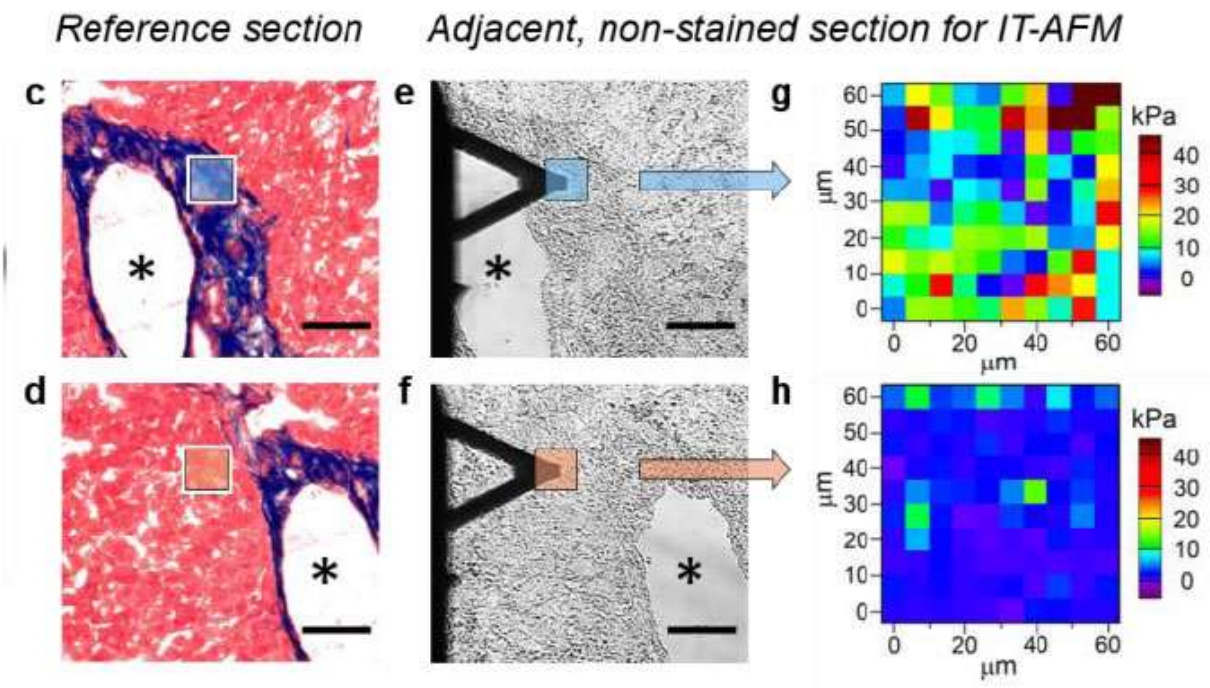

Figure 2: Force volume AFM in tissue sections from human liver.

Stealth magnetoliposomes based on calcium-substituted magnesium ferrite nanoparticles for curcumin transport and release

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The phytochemical curcumin has been showing a wide range of promising pharmacological properties, including anticancer action [1]. However, it is characterized by a low water solubility, rapid metabolism and elimination, limiting its biomedical use and therapeutic effect. The development and optimization of functionalized nanocarriers for curcumin aim to improve curcumin ADMET (absorption, distribution, metabolism, excretion and toxicology) and specificity for targeted therapies. In this work [2], stealth (aqueous and solid) magnetoliposomes containing calcium-substituted magnesium ferrite nanoparticles, $Ca_xMg_{1-x}Fe_2O_4$ (with x = 0.25, 0.50, 0.75) were developed as nanocarriers for curcumin, following previously developed work [3]. Magnetic nanoparticles were synthesized by coprecipitation method and characterized on their colloidal stability and optical, magnetic and structural properties. Their superparamagnetic properties and crystalline structure, with sizes below 10 nm, make them suitable to act as magnetic mediators for magnetoliposomes guidance and hyperthermia action. The magnetoliposomes based on these nanoparticles have hydrodynamic diameters around or below 150 nm, a low polydispersity and the ability to encapsulate hydrophobic drugs, as the potential antitumor drug curcumin. Considering the leaky nature of tumor blood vessels, as a result of the presence of gaps within the range of 100 to 780 nm between the endothelial cells of tumor capillaries and the lack of lymphatic drainage, the synthesized magnetoliposomes are an effective strategy for curcumin passive targeting. Magnetoliposomes were sterically stabilized with polyethylene glycol (PEG) to reduce in vivo opsonisation. The influence of an alternating magnetic field (AMF) on drug release over time (in PEGylated and non-PEGylated solid magnetoliposomes) was evaluated and compared with curcumin release by diffusion (Figure 1). The results suggest the potential of drug-loaded magnetoliposomes as nanocarriers that can be magnetically-guided to the tumor sites and act as agents for a synergistic effect combining magnetic hyperthermia and controlled drug release.

REFERENCES

[1] Goel, A.; Kunnumakkara, A.B.; Aggarwal, B.B. Curcumin as 'Curecumin': from kitchen to clinic. Biochem. Pharmacol. 2008, 75, 787–809

[2] Cardoso, B.D.; Rodrigues, A.R.O.; Almeida, B.G.; Amorim, C. O.; Amaral, V. S.; Castanheira, E.M.S.; Coutinho, P.J.G. Stealth Magnetoliposomes Based on Calcium-Substituted Magnesium Ferrite Nanoparticles for Curcumin Transport and Release. International Journal of Molecular Sciences, 2020. 21(10): p. 3641.

[3] Cardoso, B.D.; Rio, I. S. R.; Rodrigues, A.R.O.; Fernandes, F.C.T.; Almeida, B.G.; Pires, A.; Pereira, A.M.; Araujo, J.P.; Castanheira, E.M.S.; Coutinho, P.J.G. Magnetoliposomes containing magnesium ferrite nanoparticles as nanocarriers for the model drug curcumin. Royal Soc. Open Sci. 2018, 5, 181017

Stem cell condensation and gap junctional communication on nanopatterned substrates for improved cartilage formation

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Mesenchymal condensation is a prevalent morphogenetic transition, regulated by cell adhesion, in which mesenchymal stem cells (MSCs) migrate towards each other. In osteochondral development, this is concurrent to the formation of an extensive gap junctional intercellular communication (GJIC) network. Little is known about the way the environment modulates the formation of this network and its implications in tissue architecture and function. We previously developed substrates nanocoated with the cell adhesive arginine-glycine-aspartic acid (RGD) peptide to tailor local surface adhesiveness at the nanoscale. Substrates were characterized with Atomic Force Microscopy, and local areas with a mean interparticle distance shorter than 70 nm were considered as adherent. We showed that substrate ligand density modulates the expression of chondrogenesis markers [1,2].
Here we studied the influence of local ligand density on mesenchymal condensation and the establishment of a functional GJIC network, by assessing expression and spatial disposition of GJ protein Cx43 and by a tracer intake assay in cell condensates. Substrates with a high percentage of cell-adherent area (90%) promote stable cell condensation, differentiation and Cx43 expression. Cx43 expressed in these condensates forms a tighter communication network than in other substrates of lower ligand density, as shown by the tracer intake assay. To understand the effect of ligand density on tissue formation after condensation, formed condensates were transplanted to new substrates of either the same or a different ligand density, and Cx43 expression was quantified. Transplantation of formed condensates to fresh optimal substrates further increased Cx43 expression, which does not occur in condensates transplanted to low ligand density substrates. We therefore conclude that nanoscale ligand density regulates not only the process of mesenchymal condensation, but also concurrent protein expression and its spatial disposition during differentiation, affecting the functionality of developing tissue [3].

REFERENCES

[1] Lagunas *et al*. Nano Research (2017) 10(6): 1959-1971
[2] Casanellas *et al*. Journal of Visualized Experiments (2018) 131: e56347
[3] Casanellas *et al.* ACS Applied Materials & Interfaces (2020) In revision

Gold Nano-assemblies as SERS–NIR–PTT theranostic agent: Tentacles more powerful than Satellites

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Theranostics has been a key research area in the past decade and is growing in importance as researchers around the world are able to effectively bridge diagnostic and therapeutic strategies. Light-mediated optical theranostic i.e., diagnostic and therapeutic agents based on gold nanostructures have become increasingly popular.[1] Thus, designing gold nano-assemblies for efficient surface-enhanced Raman (SERS) detection and high light-to-heat conversion for photothermal therapy (PTT) is crucial towards realizing the goal of optical theranostics. Multi-branched polymeric linkers have been effective in controlling gold nano-assembly morphologies.[2]

Here we report on low plasmon enhancers such as 15 nm and 5 nm spherical gold nanoparticles (NPs) fashioned into a unique colloidal gold nano-assembly morphology that features intensive NIR plasmon coupling. The developed nano-assembly morphology mimics multiple tentacles, each composed of multiple 5 nm NPs, anchored randomly onto a 15 nm core that is held together by a flexible branched polymeric linker (fig 1, left). We show that this morphology is the key to such continuum near-infrared (NIR) broadband localized surface plasmon resonance (LSPR) profile. The LSPR extends into the tissue transparency region and surpasses the plasmon behaviour of a typical core satellite nano-assembly made from the same building blocks (fig 1, right).[3] Furthermore, its approximate size of 70 nm, composition of nano-gold and polyethylene glycol polymer, and demonstrated biocompatibility towards human non-cancerous cell line Wi-38 makes it an ideal candidate for in vivo nanomedicine applications. SERS (830 nm laser excitation) of labelled core multi-tentacle nano-assemblies could be detected with the SERS label concentration below 50 nM with high SNR (comparable to larger 100–200 nm gold nanostars which have limited in vivo use), as well as having enhanced photothermal heat conversion. Thus, the high SERS amplification of the multi-tentacle nano-assemblies, coupled with its improved PTT potential and lower toxicity towards human cancerous cell line MCF7, suggests its potential as an optical NIR–SERS–PTT theranostic agent.

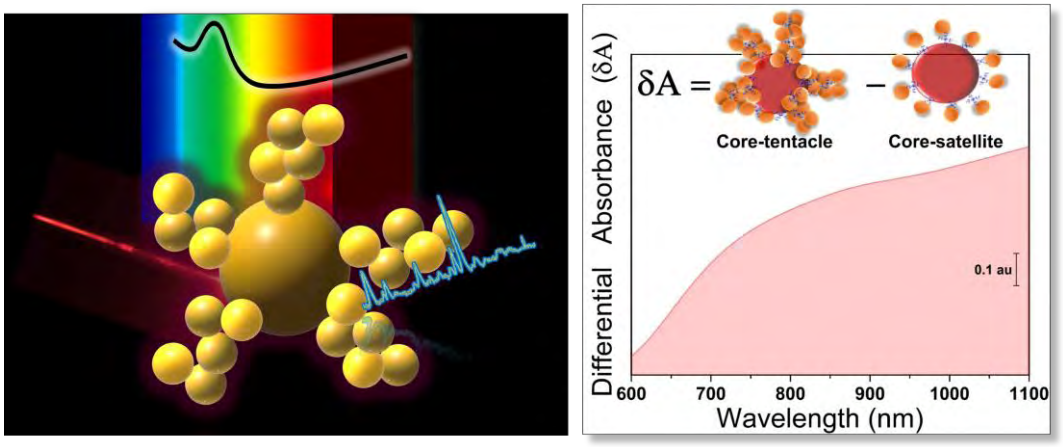

Figure 1: (Left) Cartoon depiction of core multi-tentacle gold nano-assemblies and (Right) the boost in NIR plasmon coupling of tentacles as compared to satellites, resulting in improved SERS and PTT performance.

REFERENCES

[1] T. A Tabish, P. Dey, S. Mosca, M. Salimi, F. Palombo, P. Matousek, N. Stone, *Advanced Science* (2020); 1903441.
[2] P. Dey, I. Blakey, K.J Thurecht, P. M Fredericks*, Langmuir* (2013); **29,** 523.
[3] P. Dey, T. A Tabish, S. Mosca, F. Palombo, P. Matousek, N. Stone*., Small* (2020); 1906780.

Lipid Biomimetic Models as an Alternative Platform to Guide the Drug Design Process

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In a rational drug design, the modulation of the chemical structure based on its pharmacokinetic profile could be the solution to avoid bigger investments in non-promising drugs. The transport of drugs across cell membranes is a highly complex biological process involving the interaction of drugs with lipid barriers. The need to understand this interaction is often neglected when the drugs' effects are studied, since systematic investigations are hindered by the complexity and dynamic nature of membranes.[1] Biomimetic membrane models provide an alternative platform with very well defined and controlled conditions to help researchers from the drug discovery field to predict drugs' pharmacokinetic properties with therapeutic efficacy implications, such as their transport, biodistribution, bioaccumulation, toxicity.[2-4] In this regard, biophysical techniques have emerged as essential tools to unveil such interactions.[2-4] In the present study several biomimetic membrane models (cell membrane and epithelial membrane of blood-brain barrier) were used and different biophysical techniques (derivative spectroscopy; quenching of steady-state and time-resolved fluorescence; dynamic light scattering; differential scanning calorimetry and small and wide angle x-ray diffraction) were applied to characterize the pharmacokinetic profile of a newly synthesized drug in order to support drug screening process decisions.

REFERENCES

[1] Lúcio, M., *et al*., Current Medicinal Chemistry,17 (2010) 1795-1809
[2] Fernandes, E., *et al*., International Journal of Molecular Sciences, 19 (2018) 3411
[3] Fernandes, E., *et al*., Frontiers in Chemistry, 6 (2018) 323
[4] Carvalho, A., *et al.,* International Journal of Pharmaceutics, 580 (2020) 119222

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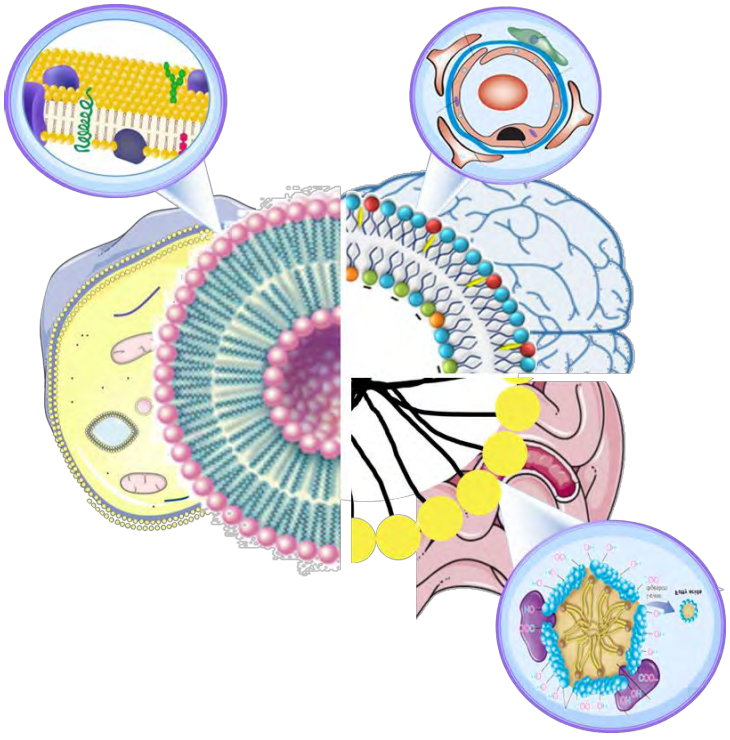

Figure 1: Figure illustrating the several biomimetic models used to predict drug pharmacokinetic profiling

Development of C75-CoA-loaded polymeric nanomedicines to inhibit CPT1 in specific brain cells

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Carnitine palmitoyl transferases are a family of proteins involved in the metabolism of fatty acids. CPT1A in the mitochondria catalyses the conversion of long-chain fatty acids into acylcarnitines. It is expressed in peripheral tissues but also in the hypothalamus, where it is involved in energy homeostasis. Inhibition of hypothalamic CPT1A reduces feeding, whereas overexpression increases food intake and adiposity. Furthermore, CPT1A and CPT1C are overexpressed in glioblastoma, and CPT1C is upregulated in glucose depletion and hypoxia, suggesting a protecting role under these conditions [1,2]. Pharmacological manipulation of CPT1 proteins activity in specific brain cells could therefore be useful in treating diseases such as obesity or glioblastoma.
C75 is a racemic lactone originally described to inhibit FASN. Later it was described that (+)-C75 inhibits CPT1A, while the physiologically formed adduct (-)-C75-CoA inhibits FASN [3,4]. However, peripheral inhibition of CPT1A leads to undesired side effects. To overcome this problem, we have developed a strategy involving polymeric nanoparticles targeted to hypothalamic neurons or glioblastoma cells [5]. We have prepared PEG-PLL nanoparticles which can encapsulate racemic C75 and its enantiopure forms, and can be modified with ligands designed to overcome the blood-brain-barrier and target hypothalamic neurons and glioblastoma cells.

REFERENCES

[1] Sierra AY, Gratacós E, Carrasco P, et al. Journal of Biological Chemistry. 11(2008) 6878-6885.
[2] Casals N, Zammit V, Herrero L, Fadó R, Rodríguez-Rodríguez R, Serra D. . Progress in Lipid Research. 61(2016)134-148.
[3] Mera P, Bentebibel A, López-Viñas E, et al. Biochemical Pharmacology. 6(2009)1084-1095.
[4] Makowski K. PhD Thesis (2012)
[5] Quader S, Liu X, Chen Y, et al. Journal of Controlled Release. 258(2017)56-66.

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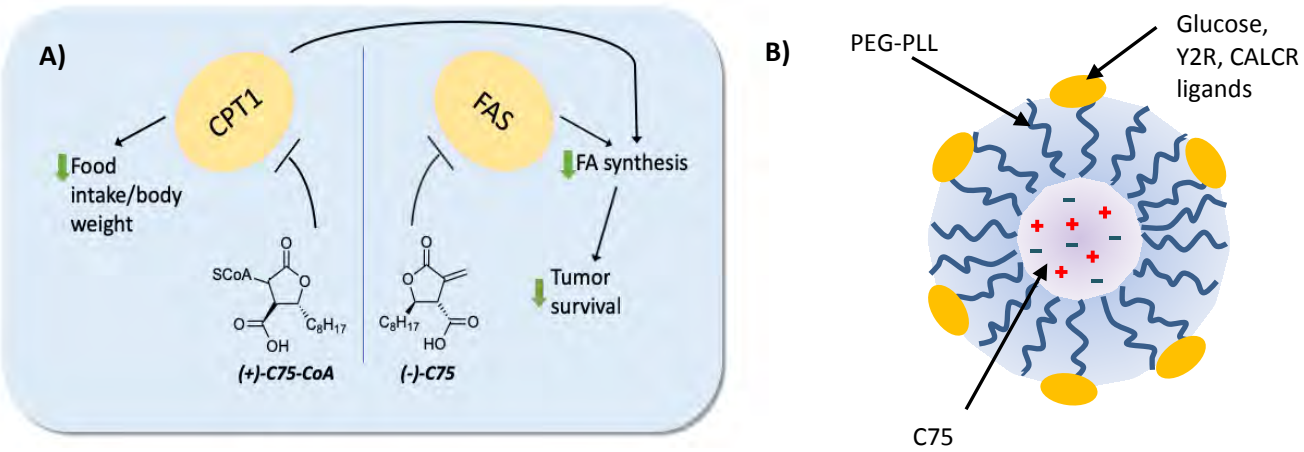

Figure 1: A) C75 action summary. B) Nanoparticle model

Plasmonic Scaffolds for 3D SERS sensing

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Bioprinting has emerged as a promising tool for the rapid fabrication of scaffolds for supported tissue or tumour growth [1]. Numbers of biopolymer and hydrogel-based inks have been developed for the design of ever increasing complex 3D cell models. However, there is still a lack of detection tools able to precisely monitor cell behaviour within 3D microenvironments over long periods of time [2]. This issue can be addressed by incorporating additional functionalities to 3D printable inks to prepare scaffolds with sensing properties, able to monitor tissue growth or disease evolution. In this work, we evaluate the potential of a series of surface-enhanced Raman scattering (SERS) active inks for the detection of relevant analytes within a plasmonic hydrogel 3D-printed scaffold. SERS is an advantageous technique not only for *in situ* biosensing, but also for bioimaging of 3D cell cultures [3]. This technique takes advantage of the remarkable optical properties of noble metal nanoparticles due to their Localized Surface Plasmon Resonances (LSPR) that result in strong absorption and scattering of light at specific wavelengths, creating high local electric fields at the surface [4]. These electric fields enhance the Raman scattering of the molecules adsorbed to the metal surface and allow for extremely low detection limits. Furthermore, the excitation wavelength can be tuned to the near infrared range (NIR) matching the so-called biological transparency window (650-1350 nm) and, thus, improving light penetration in tissues. To produce SERS sensing scaffolds, different biopolymers have been combined and incorporated to plasmonic nanoparticle suspensions, such as gold nanorods (AuNRs) or gold nanostars (AuNSs). The applicability of SERS spectroscopy for the detection of model molecules such as 4-mercaptobenzoic acid (MBA) as well as relevant bioanalytes such as adenosine is demonstrated. These 3D printed plasmonic scaffolds show great potential for advanced 3D biosensing of cell-secreted molecules over extended periods of time.

REFERENCES

[1] P. S. Gungor-Ozkerim, I. Inci, Y. S. Zhang, A. Khademhosseini, M. R. Dokmeci, Biomaterials Science, 6 (2018) 915.
[2] C. S. Hansel, M. N. Holme, S. Gopal, M. M. Stevens, Biomaterials, 226 (2020) 119406
[3] E. Lenzi, D. Jimenez de Aberasturi, L. M. Liz-Marzán, ACS Sensors, 4 (2019) 1126
[4] S. Schlücker, Angewandte Chemie, 53 (2014), 4756

Neurotransmitter's encapsulation on Bipyridinium-functionalized polysilicon microparticles by supramolecular interactions

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Abstract

Neurotransmitters are biomolecules that play a pivotal role in communication between cells. Generally, an imbalance of these neurotransmitter levels could cause psychiatric and neurological disorders [1,2]. The development of effective methods for neurotransmitter's encapsulation is a topic of great importance in neuronanomedicine because of the prolongation of the overall efficiency of the neurotransmitter as well as their delivery in the target area in a controlled way. In parallel, Bipyridinium salts are π-acceptor and redox-responsive molecules that strongly interact with π-donor compounds. These properties have promoted us toward the immobilization of bipyridinium salts ($1{\cdot}4PF_6$- $4{\cdot}4PF_6$) on polysilicon surfaces and microparticles for encapsulating and releasing of catecholamines and indolamines, π-donor neurotransmitters. First, the formation of the supramolecular complex was performed and characterized in solution as proof of concept. Second, the immobilization of bipyridinium salts on polysilicon surfaces and the subsequent neurotransmitter incorporation was corroborated by contact angle measurements. Furthermore, the quantification of neurotransmitter encapsulated and released from the microparticles by reducing the bipyridinium moiety using ascorbic acid was also performed using high-performance liquid chromatography. Thus, the combination of biocompatible microfabricated polysilicon-based devices with bipyridinium salts as hosts for a controllable encapsulation and release of π-donor biomolecules can open new opportunities for the delivery of drugs, whose physicochemical properties difficult their administration.

REFERENCES

[1] Sou, K.; Le, D.L.; Sato, H., Small 15 (2019) 1–12.
[2] Si, B.; Song, E. Chemosensors 6 (2018) 1–24.

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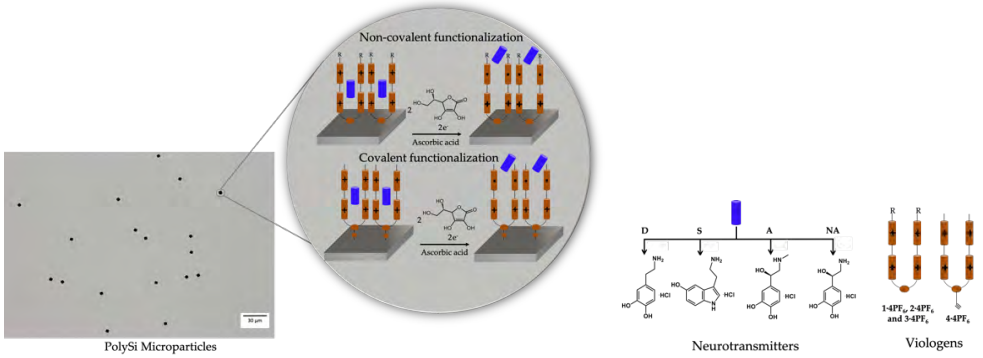

Figure 1: Representation of the covalently and non-covalently functionalized microparticles and their release using ascorbic acid as triggering agent.

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Compliant 3D scaffold as self-training skeletons for bio-hybrid robots

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Biomimetic soft robotic systems aim to design advanced functional robotic platforms able to perform gentle actuation by resembling some of the mechanisms and designs of their biological counterparts [1]. Some of the desired unique from this living entities include self-healing, energy efficiency, power-to-weight ratio, adaptability, or bio-sensing capabilities [2]. Although most of the designs resemble the well-known structures in nature (i.e. medusoid that mimics a jelly-fish motion dynamic [3]), simpler structures have served to stablish key design rules for efficient bio-robotic platforms. Some examples are a cantilever structure where cardiac cells where immobilized [4] or a system based on two legs joined by a beam where a 3D skeletal-muscle cell construct is assembled [5].

In our case, we developed a skeleton-muscle based bio-robot with an integrated compliant skeleton whose design is based on a spring serpentine. Such configuration not only provided mechanical integrity to the bio-robot system, but also allowed an on-demand bending and a mechanical self-stimulation in absence of any external electrical input. Corresponding finite element analysis were done to both find the optimal geometrical stiffness to achieve the desired asymmetry/ buckling effect for efficient motion and the mechanical self-stimulation for an enhanced output force.

REFERENCES

[1] T. Patino, R. Mestre, S. Sánchez, Lab Chip. 16, 2016, 3626–3630.
[2] C. Appiah, C. Arndt, K. Siemsen, A. Heitmann, A. Staubitz, C. Selhuber-Unkel, Adv. Mater. 31, 2019, 1807747.
[3] J. C. Nawroth, H. Lee, A. W. Feinberg, C. M. Ripplinger, M. L. McCain, A. Grosberg, J. O. Dabiri, K. K. Parker, Nat. Biotechnol. 30, 2012, 792–7.
[4] J. Park, J. Ryu, S. K. Choi, E. Seo, J. M. Cha, S. Ryu, J. Kim, B. Kim, S. H. Lee, Anal. Chem. 77, 2005, 6571–6580.
[5] C. Cvetkovic, R. Raman, V. Chan, B. J. Williams, M. Tolish, P. Bajaj, M. S. Sakar, H. H. Asada, M. T. A. Saif, R. Bashir, Proc. Natl. Acad. Sci. U. S. A. 111, 2014, 10125–30.

Exploring the Biophysics of Bacterial Growth and Division with Time-lapse Optical and Atomic Force Microscopy

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Observing bacterial growth at the single cell level is inherently challenging due to the diffraction limit. We built a dedicated platform for long-term, correlated Atomic Force Microscopy (AFM) and fluorescence microscopy[1] and obtained time-lapses of mycobacterial growth[2] with high resolution. We observed a biphasic growth pattern, where a new cell pole initiates fast growth only after a lag phase of slow growth. Surprisingly, this growth dynamics was different from what was previously reported, resembling instead the growth dynamics of fission yeast (*new end take off* or NETO)[3]. While it is possible to measure NETO dynamics in fission yeast using optical microscopy, AFM was required to capture the subtle variations of elongation for bacteria, which are three orders of magnitude smaller in volume. Using AFM micromanipulation of the cells, we found that pole-to-pole contact forces were not the reason for the initial slow growth at the new poles. On the contrary, we showed, using a combination of AFM and fluorescence photoconversion, that the lag phase corresponds to the relocalization of a molecular factor involved in growth from the old to the new cell pole. AFM shed light on a previously unknown degree of similarity between organisms that are far apart in the evolutionary tree (one is a eukaryote, the other a prokaryote). Our results hints at global biophysical constraints associated with polar growth that remained unexplored so far.

REFERENCES

[1] P. D. Odermatt *et al.*, "High-Resolution Correlative Microscopy: Bridging the Gap between Single Molecule Localization Microscopy and Atomic Force Microscopy," *Nano Lett.*, vol. 15, no. 8, pp. 4896–4904, Aug. 2015, doi: 10.1021/acs.nanolett.5b00572.

[2] H. A. Eskandarian *et al.*, "Division site selection linked to inherited cell surface wave troughs in mycobacteria," *Nat. Microbiol.*, vol. 2, no. 9, p. 17094, Sep. 2017, doi: 10.1038/nmicrobiol.2017.94.

[3] M. T. M. Hannebelle *et al.*, "A biphasic growth model for cell pole elongation in mycobacteria," *Nat. Commun.*, vol. 11, no. 1, 2020, doi: 10.1038/s41467-019-14088-z.

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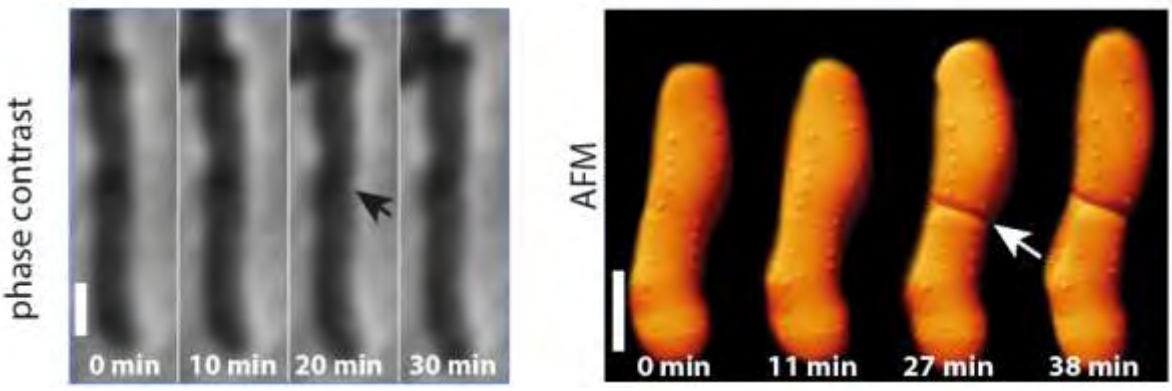

Figure 1: Bacterial division seen with phase contrast optical microscopy and AFM. Scale bar 1um.

Bio-inspired models and biophysical studies applied in ADMET profiling

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Molecular interactions between cell membranes and drugs have a crucial effect on the pharmacokinetics (PK) and therapeutic efficacy of drugs [1]. These interactions determine the partitioning, position and orientation of drugs in membranes and thus play a significant role in the transport, distribution, accumulation and, eventually, in the therapeutic impact of drugs. In addition, drug-membrane interactions can also modify the biophysical properties of the membranes and therefore affect their functionality, which is responsible for the toxic effects of drugs at membrane level [2]. Molecular interactions between cell membranes and drugs are therefore important for the determination of the drug profile ADMET (absorption, distribution, metabolism, elimination and toxicity) that essentially determines the PK of drugs. Herein, we propose to illustrate how some biophysical techniques and bioinspired models may be used in the estimation of specific physicochemical main descriptors and in conjunction with silico models to forecast drug PK characteristics [2].
Interactions of drugs with mimetic models of biological interfaces include: (i) drug partitioning and thermodynamics aspects of drug distribution within membrane mimetic nanosystems studied by derivative spectrophotometry; (ii) drug effect on the biophysical properties of the membrane models studied by dynamic light scattering (DLS), fluorescence anisotropy, atomic force microscopy (AFM) and synchrotron small and wide angle X-ray scattering (SAXS and WAXS); (iii) drug molecular orientation within the lipid bilayer studied by steady-state, time-resolved fluorescence and computer simulations; (iv) drug binding to the blood carrier protein albumin and resulting conformational changes studied by the quenching of intrinsic protein fluorescence, derivative spectrophotometry and dynamic and electrophoretic light scattering (ELS) and (v) drug PK parameters (unbound drug fraction in plasma and tissues; volume of distribution and theoretical off-target distribution). The results obtained *in vitro* were compared with drugs biological effects *in vivo*.

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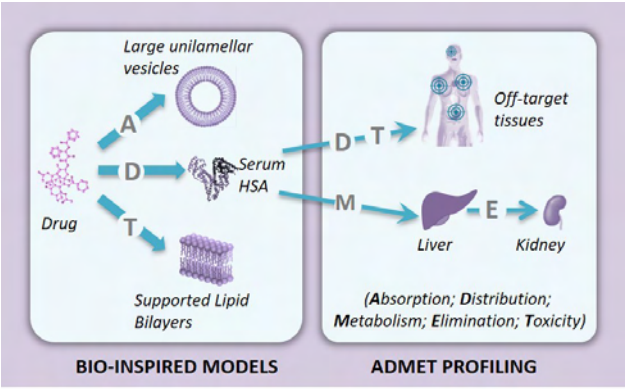

Figure 1: Bio-inspired models applied in ADMET profiling

REFERENCES

[1] A. M. Carvalho, E. Fernandes, H. Goncalves, J. J. Giner-Casares, S. Bernstorff, J. B. Nieder, M. Real Oliveira and M. Lucio, Int J Pharm, 580 (2020) 119222.
[2] E. Fernandes, T. B. Soares, H. Goncalves, S. Bernstorff, M. C. D. R. Oliveira, C. M. Lopes and M. Lucio, Int J Mol Sci, 19 (2018) 3411.

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IRONSperm: Sperm-templated flexible magnetic microrobots

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Biohybrid magnetic microrobots, referred to as IRONSperms, were developed by electrostatic-based self-assembly of non-motile sperm cells and magnetic nanoparticles (Figure 1). Such microrobots are under 100 µm in length and have potential unique applications for therapy and diagnosis in healthcare. IRONSperms consist of a cellular template (bovine sperm cell) with magnetic constituents (maghemite nanoparticles). Incorporating a biological entity into microrobots entails many functional advantages beyond shape templating, such as the facile uptake of DNA, RNA or chemotherapeutic agents to achieve targeted drug delivery. A single-step electrostatic-based self-assembly technique is presented to fabricate IRONSperms, which results in soft magnetic swimmers emulating the motion of motile sperm cells.[1] IRONSperms are actuated by external rotating magnetic fields and we observe out-of-plane wobbling of the head and helical wave propagation along the passive flagellum. It is also demonstrated that the nanoparticle coating increases the acoustic impedance of the sperm cells and enables localization of clusters of IRONSperm using ultrasound feedback.[2] Finally, cytotoxicity tests show the biocompatibility of IRONSperms and the drug delivery capability is demonstrated by loading their organic body with a model anti-cancer drug. This work presents new insights into the development of a biocompatible, controllable, and detectable biohybrid magnetic microrobot for in vivo targeted therapy.

REFERENCES

[1] I. S. M. Khalil, V. Magdanz, J. Simmchen, A. Klingner, S. Misra, *Appl. Phys. Lett.* **2020**, *116*, 63702.
[2] V. Magdanz, I. S. M. Khalil, J. Simmchen, G. P. Furtado, S. Mohanty, J. Gebauer, H. Xu, A. Klingner, A. Aziz, M. Medina-Sánchez, O. G. Schmidt, S. Misra, *Sci. Adv.* **2020**.

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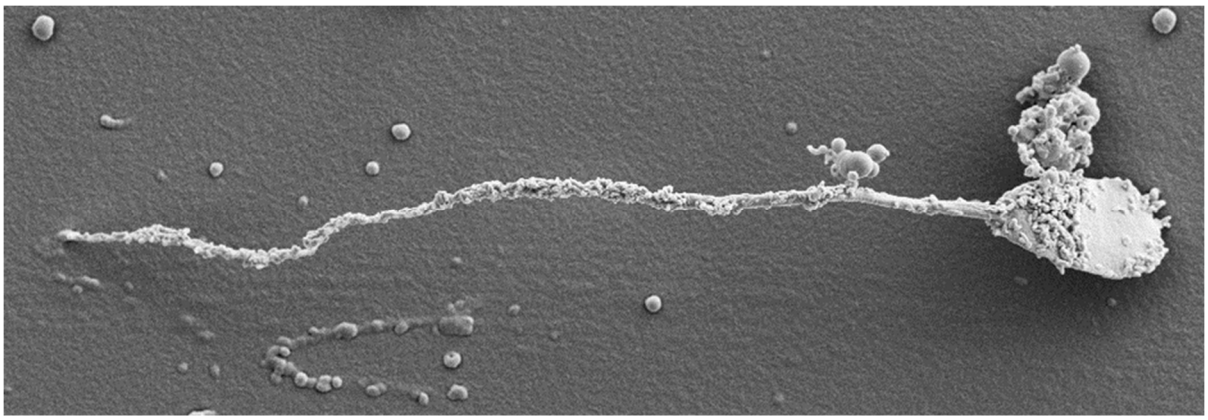

Figure 1: Bovine sperm cell with attached maghemite nanoparticles to create a sperm-templated flexible magnetic microrobot.

Stable Anchoring of Bacteria-based Protein Nanoparticles for Surface Enhanced Cell Guidance

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In tissue engineering, biological, physical, and chemical inputs have to be combined to properly mimic cellular environments and successfully build artificial tissues, which can be designed to fulfill different biomedical needs such as organ donor shortage or the development of in vitro disease models for drug testing. Inclusion body-like protein nanoparticles (pNPs) can simultaneously provide such physical and biochemical stimuli to cells when attached to surfaces.[1-4] However, this attachment has only been previously made by physisorption. To provide a stable anchoring, a covalent binding of lactic acid bacteria (LAB) produced pNPs, which lack the innate pyrogenic impurities of gram-negative bacteria like Escherichia coli, is presented.[5] pNPs can be arranged on the surface at the microscale with microcontact printing, a cost-effective soft lithography technique. Micropatterning of pNPs allow for the study of the influence of the material arrangement on cell adhesion. The reported micropatterns feature a robust nanoscale topography with an unprecedented mechanical stability. In addition, they are denser and are more capable to influence cell morphology and orientation. The increased stability and absence of pyrogenic impurities represent a step forward towards the translation of this material to a clinical setting.[6]

REFERENCES

[1] Diez-Gil, C., et al., Biomaterials, 31 (2010) 5805.
[2] Seras-Franzoso, J., et al., Nanomedicine (Lond), 7 (2012) 79.
[3] Tatkiewicz, W. I., et al., ACS Applied Materials & Interfaces, 10 (2018) 25779.
[4] Tatkiewicz, W. I., et al., ACS Biomaterials Science & Engineering, 5 (2019) 5470.
[5] Cano-Garrido, O., et al., Acta Biomateralia, 43 (2016) 230.
[6] Martínez-Miguel, M., et al., Journal of Materials Chemistry B, 8 (2020) 5080.

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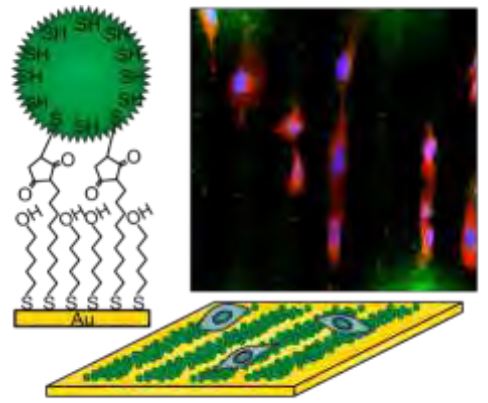

Figure 1: Schematic representation and fluorescence microscopy capture of cells seeded on top of covalently anchored GFP protein nanoparticles, which have been microstructured into striped patterns through microcontact printing.

Gold Nanoparticles Chemiresistors for Selective Potassium Ions Sensing

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The combination of metal nanoparticles (NPs) with ad hoc supramolecular receptors of the analyte of choice represents a powerful strategy for the fabrication of novel hybrid plasmonic sensors.[1] On the one hand, AuNPs are ideal scaffolds because of their highest surface-to-volume ratio combined with their unique optical and electrical properties.[2] On the other hand, supramolecular recognition has proven to be key to the realization of sensors exhibiting detection limits down to ppm/ppb levels with fast response speed combined with unprecedented selectivity.[3] Potassium ion is an essential element and one of the most abundant physiological metal ions in living organisms. In this context, the development of effective methods to detect K^+ concentration is urgently needed and significant because several diseases could be caused referring to the abnormal K^+ levels in living organisms.
Here, we have devised a novel chemiresistor (CR) capable to perform real-time sensing of potassium ions. Such device is based on the use of all-covalent 3D networks obtained by interconnecting AuNPs with dithiolated crown ethers, which act as both molecular linker and supramolecular receptor. In the present case, we have performed the layer-by-layer assembly of AuNPs on a substrate with photolitographically patterned electrodes (See Figure 1). The potassium adsorption/desorption into the AuNP-based network can determine a modification of the network's structure (e.g. via swelling) and/or electronic properties (e.g. via a change in the device capacitance). The performance of such devices was studied and optimized in terms of NPs size as well as the geometry of the gold interdigitated electrodes. The selectivity of the system was analysed against the most common metal cations found in body fluids (K^+, Na^+, Ca^{2+} and Mg^{2+}). Finally, to demonstrate the sensing capabilities of these hybrid nanocomposites we have performed the real time detection of potassium ions in water and in a real body fluid.
The ultimate goal is to develop a point of care technology that can be implemented in portable optoelectronic devices, whose performance can compete with state-of-art devices within this field of interest.

REFERENCES

[1] J Liao, S. Blok, S. Jan van der Molen, S. Diefenbach, A. W. Holleitner, C. Schönenberger, A. Vladykae and M. Calame, Chem. Soc. Rev.,44 (2015), 999
[2] K. Saha, S. S. Agasti, C. Kim, X. Li, and V. M. Rotello, Chem. Rev.,112 (2012), 2739
[3] R. Pinalli, A. Pedrini and E. Dalcanale, Chem. Soc. Rev., 47 (2018),7006

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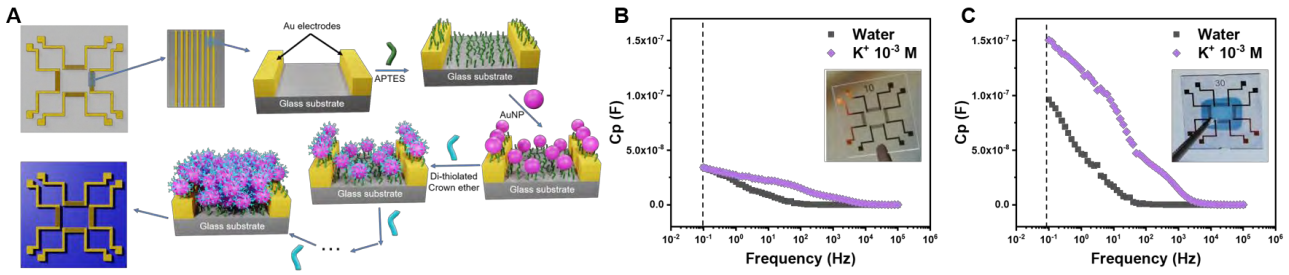

Figure 1: (A) Schematic representation of AuNP-dithiolated crown ethers assemblies fabricated by Layer-by-Layer deposition, (B-C) Capacitance response of devices in water (black curves) or K^+ 10^{-3} M (purple curves) in the absence (B) or presence (C) of the 3D network of AuNPs. The inset show the optical image of the device without (B) and with (C) the 3D network of AuNPs.

FLUORESCENT ORGANIC NANOPARTICLES DEMONSTRATING HIGH FRET EFFICIENCY FOR THEIR USE AS BIOIMAGING PROBES

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In the very recent years, FRET-based nanoparticle for biosensing, bioimaging, and theragnostic applications have experienced an unprecedented upsurge of interest.[1],[2] One of the advantages of FRET over single fluorophores as optical reporters is the relatively larger gap between the excitation and emission maxima and thus can significantly reduce the background while imaging. The use of nanoparticles as nanocarriers for the loading of the organic dyes offers an interesting strategy to bring organic dyes in aqueous media showing photostability, biocompatibility and generally, higher brightness. Considering the challenges for obtaining an ideal fluorescent bioprobe based on FRET, in this work, two carbocyanine molecules (DiI and DiD) were simultaneously loaded into quatsomes (QS), a new class of nanoscopic unilamellar vesicles made by surfactants and sterols.[3] Dye-loaded QSs were prepared by a one-step method using compressed CO_2, named depressurization of expanded liquid organic solution-suspension (DELOS-susp).[4] Indeed, it is a green technology leading to a formation of a highly homogenous dispersion of quatsomes in an aqueous environment (Figure 1, top). The obtained fluorescent organic nanoparticles (FONs) allow the dispersion and stability of the FRET pair organic dyes on aqueous media, ensuring photostability, biocompatibility and attractive spectroscopic properties for their use as bioprobes. Of special interest is their huge brightness displayed, ~100-fold brighter than commercial Quantum Dots emitting at same wavelengths. We anticipate this novel fluorescent organic nanoparticle with tremendous FRET efficiencies, stable during long periods of time, and biocompatible to gain a vast impact and set of applications in different fields, including bioimaging. This kind of nanostructures can be easily functionalized with targeting groups, representing a very promising platform, especially for theragnostic nanomedicine.[5], [6]

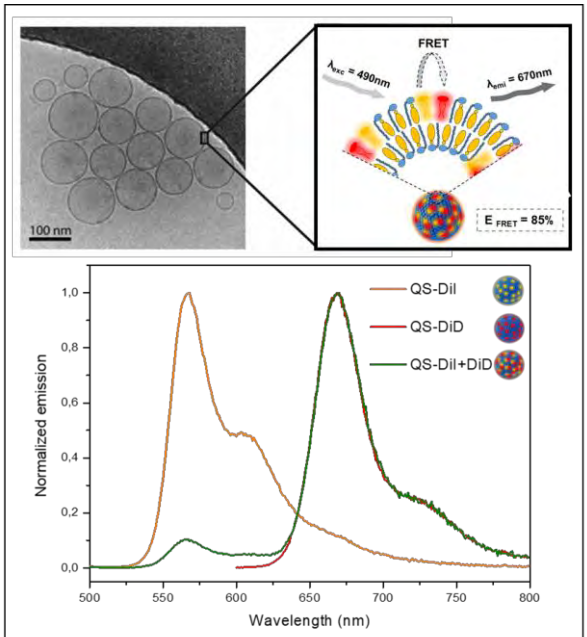

Figure 1. Cryo-TEM image of QS and schematic representation of QS membrane organization with FRET(top) . Emission spectra of QS containing the lipophilic dyes (down).

REFERENCES

[1] J. Shi, F. Tian, J. Lyu, and M. Yang, *J. Mater. Chem. B*, (2015) vol. 3, no. 35, pp. 6989–7005.
[2] R. Andreas and K. A. S., *Small*, (2016) vol. 12, no. 15, pp. 1968–1992.
[3] L. Ferrer-Tasies *et al.*, *Langmuir*, (2013) vol. 29, no. 22, pp. 6519–6528.
[4] A. Ardizzone *et al.*, *Small*, (2018) vol. 14, no. 16, p. 1703851.
[5] I. Cabrera *et al.*, *Nano Lett.*, (2013) vol. 13, no. 8, pp. 3766–3774.
[6] J. Morla-Folch *et al.*, *ACS Appl. Mater. Interfaces*, (2020) 12,18.

CCL21-loaded synthetic 3D hydrogels for T cell expansion and differentiation

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Abstract

Recent achievements in the field of immunotherapy, such as the development of engineered T cells used in adoptive cell therapy, are introducing more efficient strategies to combat cancer. Nevertheless, T cells are challenging to manufacture, manipulate, and control. For example, there are limitations in producing the large amounts of T cells needed for these therapies in a short period of time and in an economically viable manner. In this study, three-dimensional (3D) poly(ethylene) glycol hydrogels (PEG) covalently combined with low molecular weight heparin were engineered to resemble the lymph nodes, where T cells reproduce. In these hydrogels, PEG provides the needed structural and mechanical properties, whereas heparin is used as an anchor for the cytokine CCL21, which is present in the lymph nodes, and can affect cell migration and proliferation. The 3D structure of the hydrogel in combination with its loading capacity result in an increased primary human CD4+ T cell proliferation compared to the state-of-the-art expansion systems consisting of artificial antigen presenting cells. Thus, we present a new tool for adoptive T cell therapy to help achieving the large numbers of cells required for therapy of selected phenotypes targeted against cancer cells, by mimicking the lymph nodes.

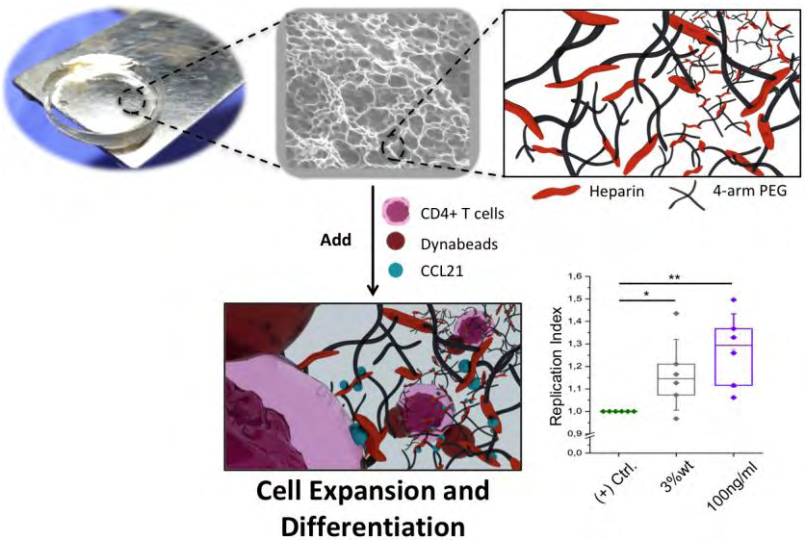

Figure 1: Scheme of the inner hydrogel structure used for the culture of immune cells resulting in an increased cell proliferation in comparison with the state-of-the-art expansion systems.

Synthesis and characterization of magnetoliposomes containing nickel ferrite nanoparticles covered with gold for applications in phototherapy

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Abstract

Currently, cancer is one of the leading causes of death worldwide. Despite the investigations and discoveries to date, there are many difficulties in rapid diagnosis, as well as in target treatments to reduce side effects. Nanotechnology has increasingly allowed the development of new techniques and strategies for application in cancer therapy, for example, using hyperthermia. Magnetic nanoparticles have been increasingly important in this regard, due to their unique characteristics, such as the ability to target a specific therapeutic site using external magnetic field gradients. On the other hand, gold has been used in different applications, from particle coating to prevent agglomeration, to the use of gold nanoparticles for local heating in cancer therapy. In this work, nanoparticles with magnetic/plasmonic properties of nickel ferrite decorated with gold nanoparticles and core/shell nickel ferrite/gold nanoparticles were prepared and characterized. The synthesized nanoparticles were used for the preparation of solid magnetoliposomes (SMLs), these systems being our target of study. The nanosystems were evaluated for the ability to cause local heating upon excitation in the gold plasmonic band. For that, fluorescence quenching of rhodamine B incorporated in SMLs lipid layer was measured [1]. The developed multifunctional nanosystems have shown promising results for application in combined cancer therapy (chemo/phototherapy).

Figure 1. A: Irradiation setup. B: Schematic representation of local heating, by action of the gold-covered magnetic nanoparticles.

REFERENCES

[1] Rio, I.S.R.; Rodrigues, A.R.O.; Rodrigues, C.P.; Almeida, B.G.; Pires, A.; Pereira, A.M.; Araújo, J.P.; Castanheira, E.M.S.; Coutinho, P.J.G. Development of Novel Magnetoliposomes Containing Nickel Ferrite Nanoparticles Covered with Gold for Applications in Thermotherapy. Materials 2020, 13, 815.

Magnetic/plasmonic liposomes as nanocarriers for novel antitumor tricyclic lactones against non-small cell lung cancer

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Multifunctional nanosystems are one of the most promising therapeutic approaches in cancer treatment. The combination of the plasmonic effect with a superparamagnetic behavior results in materials with magnetic guidance, hyperthermia and controlled drug delivery capabilities in a single nanosystem [1]. Therefore, magnetic/plasmonic nanomaterials are promising in cancer therapy for simultaneous chemotherapy and phototherapy, as they can act both as magnetic and photothermal agents, allowing magnetic guidance, local temperature increase and triggered drug release.

In this work, $MnFe_2O_4$/Au core/shell nanoparticles (NPs) and $MnFe_2O_4$ NPs decorated with Au NPs were synthesized and the structural, spectroscopic and magnetic properties evaluated. The prepared NPs were covered with a lipid bilayer, forming solid magnetoliposomes (SMLs) [2,3]. The heating capabilities of the nanosystems were assessed through the fluorescence quenching of Nile Red (incorporated in the lipid bilayer of the SMLs) under irradiation [4]. Two novel antitumor thienopyridine derivatives (tricyclic lactones **1** and **2**, figure 1) were encapsulated in the lipid bilayer of the SMLs and the growth inhibitory activity in human tumour cell line NCI-H460 (non-small cell lung cancer), was evaluated in the presence and absence of a light source. SMLs were also tested in non-tumor cells, under irradiation, for comparison. Low inhibitory concentrations of 0.11 µM and 0.12 µM were observed for SMLs based on $MnFe_2O_4$/Au core/shell NPs loaded with compound **1** and **2**, respectively, pointing these nanosystems as promising therapeutic agents in future applications of combined lung cancer therapy.

REFERENCES

[1] Espinosa, A., Di Corato, R., K.-Tabi, J., Flaud, P., Pellegrino, T., Wilhelm, C., ACS Nano 10 (2016) 2436-2446
[2] Rodrigues, A.R.O., Ramos, J.M.F., Gomes, I.T., Almeida, B.G.; Araújo, J.P., Queiroz, M.-J.R.P., Coutinho, P.J.G., Castanheira, E.M.S., RSC Advances 6 (2016) 17302–17313.
[3] Rodrigues, A.R.O., Almeida, B.G., Rodrigues, J.M., Queiroz, M.J.R.P., Calhelha, R.C., Ferreira, I.C.F.R., Pires, A., Pereira, A.M., Araújo, J.P., Coutinho, P.J.G., Castanheira, E.M.S. RSC Advances 7 (2017) 15352-15361.
[4] Rodrigues, A.R.O., Matos, J.O.G., Nova Dias, A.M., Almeida, B.G., Pires, A., Pereira, A.M., Araújo, J.P., Queiroz, M.-J.R.P., Castanheira, E.M.S., Coutinho, P.J.G., Pharmaceutics 11 (2019) 10.

FIGURES

Compound **1** Compound **2**

Figure 1: Structure of the tricyclic lactones derivatives of thienopyridine.

Design and statistical modelling of fusogenic magnetoliposomes production for a potential antibacterial application

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The growing inefficiency of several classes of antibiotics against pathogenic bacteria, due to resistance mechanisms, is emerging as a major concern worldwide. Regarding this issue, nanotechnology is starting to provide efficient strategies to combat bacterial infections [1], [2]. Recently, superparamagnetic iron oxide nanoparticles (SPIONs) have attracted attention, mainly because of their magnetic properties. Already used in nanomedicine SPIONs have recently showed antibacterial properties through magnetic hyperthermia [2], [3]. Nonetheless, since SPIONs are very small in size and tend to aggregate, toxicity effects, such as obstruction of blood vessels and sequestration in several body systems, represent an important drawback of these particles [4].
In this work, the encapsulation of SPIONs inside fusogenic liposomes was performed, not only to reduce toxicity, but also to achieve a targeted therapy against bacteria. A production method of DOPE:DPPC:CHEMS (4:2:4) vesicles encapsulating SPIONs was designed. Performed lipid mixing assays, using FRET, showed the fusogenic ability of the nanosystem with large unilamellar vesicles, mimicking bacterial cell membranes. Furthermore, cytocompatibility assays revealed that the encapsulation of SPIONs decrease their cytotoxicity against fibroblasts. PEGylation was then carried out, in order to increase stability, as well as prolong liposomes *in vivo* circulation time, using a Box-Behnken design. Statistically relevant equations to model size and the polydispersity index behaviour were obtained (Figure 1), leading to an optimized formulation with mean size of 182 nm and polydispersity index of 0.202, with an associated encapsulation efficiency around 66%.

REFERENCES

[1] S. Singh *et al., International Journal of Nanomedicine,* vol. 14 (2019) pp. 2301–2325
[2] R. M. Pinto, F. A. Soares, S. Reis, C. Nunes, and P. Van Dijck, *Frontiers in Microbiology*, vol. 11 (2020), p. 952
[3] A. B. Seabra, M. T. Pelegrino, and P. S. Haddad, *Nanostructures for Antimicrobial Therapy: Nanostructures in Therapeutic Medicine Series*, Elsevier (2017) pp. 531–550
[4] R. M. Patil *et al.*, *Biochemistry and Biophysics Reports,* vol. 13 (2018) pp. 63-72

FIGURES

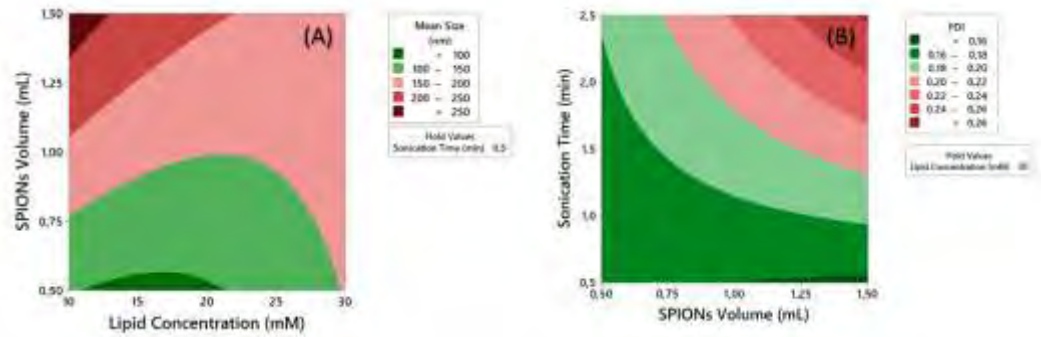

Figure 1: Contour plots of (A) PDI vs sonication time (min) and SPIONs volume (mL) and (B) mean size (nm) vs SPIONs volume (mL) and lipid concentration (mM).

Supramolecular plasmonic magnetic gels for controlled drug delivery

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Abstract

Plasmonic magnetic gels combine the hydrogels' elastic properties with magnetic fluids containing plasmonic entities. Such combination allows the use of complementary strategies to enhance the potential use of magnetic gels in biomedical applications, such as drug delivery, magnetic resonance imaging and hyperthermia [1,2]. In this work, two different magnetic/plasmonic nanoparticle architectures were developed (figure 1), characterized and combined with a naproxen *N*-capped dehydropeptide-based hydrogel. Spectroscopic techniques and rheologic assays were used were used to assess the gel physicochemical properties, the incorporation of a model drug (curcumin), drug transport towards model membranes and controlled drug release. The influence of gold plasmon band excitation on the drug release profiles was assessed. The developed gels showed promising results for tuneable photo-triggered drug release and displayed reversible photothermia (figure 2). The plasmonic magnetic gels bearing gold-decorated nanoparticles showed the best photothermia properties, while the one containing core-shell nanoparticle displayed improved photoinduced drug release.

REFERENCES

[1] S.R.S. Veloso, P.M.T. Ferreira, J.A. Martins, P.J.G. Coutinho, E.M.S. Castanheira, Pharmaceutics, 10 (2018) 145.
[2] S.R.S. Veloso, J.A. Martins, L. Hilliou, C. Amorim, V. Amaral, B. Almeida, P. Jervis, R. Moreira, D.M. Pereira, P.J.G. Coutinho, P.M.T. Ferreira, E.M.S. Castanheira, *J. Mat. Chem. B* 8 (2020) 45-64.

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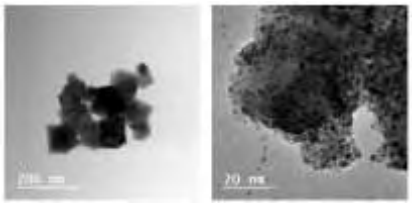

Figure 1: TEM images of the core/shell manganese ferrite/gold nanoparticles (left) and gold-decorated manganese ferrite nanoparticles.

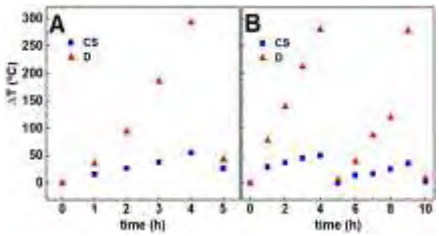

Figure 2: Temperature variation (estimated from curcumin fluorescence variation) upon gold plasmon excitation of curcumin-loaded magnetic gels containing core/shell manganese ferrite/gold nanoparticles (CS) and gold-decorated manganese ferrite nanoparticles (D). (A) First irradiation cycle. (B) Subsequent cycles of 5 hours.

Alginate microparticles produced by atomization system: Biomedical applications

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Nowadays, biomedical technologies must use biocompatible and biodegradable materials in order to avoid side effects. In this context, natural polymers play an important role. Alginate is a biomaterial of great interest to use for biomedical purposes. It has also shown to be an attractive vector for the controlled release of drugs or cells [1], due to its low immunogenicity level, biocompatibility, low toxicity and low cost [2]. Alginate has the ability to form hydrogels under mild aqueous conditions of divalent cations such as Ca^{2+} or Ba^{2+}. Alginate microparticles was produced by atomization system [3]. In this technique, alginate solutions were introduced into a pressurize tank. Two important parameters were liquid and air pressures. Due to the effect of liquid pressure, alginate solution flows from the container through a nozzle. On the other part of the nozzle, air is introduced from an air cylinder and breaks the jet of alginate in small droplets. These droplets are sprayed into a divalent solution under magnetic stirring. The main objective of this study was to compare between two types of alginate gels formed with divalent ions and secondly, production of alginate microparticles with the atomization system. Alginate solutions at different concentrations (0.5% w/v to 2% w/v) and alginate gels were characterized by a rheometer AR 1500 ex (TA Instruments, Spain). Microparticles were produced by electrostatic interactions between barium chloride with sodium alginate. The size (d 0.5) of particles ranges from 40 – 200 µm and Zeta potential was negative (- 8.60 mV). So, these residuals carboxylate groups are responsible of negative charge of particles. In addition, these groups can be used to join drugs or another polymer with polymer charge, such as chitosan [4]. As a result of this research, we showed microparticles more stables in time which may have special interest to the use of them as vectors or in drug delivery formulations.

REFERENCES

[1] Martín del Valle E.M., Herrero E.P., Martins D.A.O., Galán M.A., The Open Tissue Engineering & Regenerative Medicine Journal, 2 (2009), 14 – 19.
[2] Agüero L., Zaldivar-Silva D., Peña L., Dias M.L. Carbohydrate Polymers, 168 (2017), 32-43.
[3] Herrero E.P., Martín del Valle E.M., Galán M.A., Chemical Engineering Journal, 121 (2006), 1-8.
[4] Goycoolea F.M., Lollo G., Remuñán-López C., Quaglia F., Alonso MJ. Biomacromolecules, 10 (2009), 1736 – 1743.

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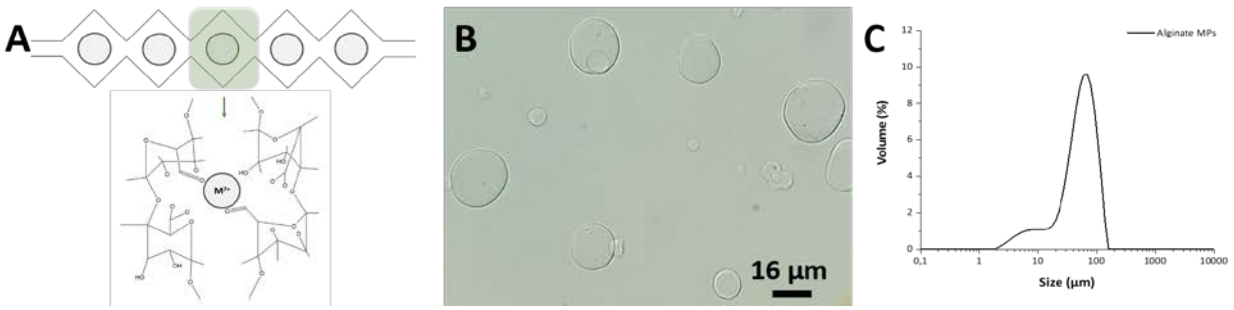

Figure 1: A) Schematic representation of the interactions between alginate and divalent ions; B) Alginate – BaCl2 microparticles produced by atomization system; C) Size distribution obtained by Mastersizer2000.

Investigating the effect of a new contrast agent in an orthotopic mice model

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Cancer is the second most common cause of death in the world after cardiovascular diseases. However, there has been a lack of effective diagnostic tools at an early stage for this malice. Over the years, there have been significant improvements in the diagnostic field such as ultrasound, computed tomography (CT), positron emission tomography (PET) but not without issues. MRI presents itself as an efficient alternative technique but, with the use of gadolinium (Gd) as contrast agent, there is an urgent need to look for improved contrast agents. Gd has been shown to cause some health problems such as nephrotoxicity. Hence, in this work, an iron oxide nanoparticle-based contrast agent is presented and investigated. These nanoparticles were synthesized using thermal decomposition of iron-oleate and characterized using X-ray diffraction (XRD), transmission electron microscopy (TEM). Further, we functionalize the as synthesized nanoparticles with a polyethylene glycol-gallol (PEG-GA) ligand. These nanoparticles are observed to be of biocompatible nature when interacting with non-cancerous cells. 4T1 cell line was used to induce orthotopic tumor in mice and subsequently particles were injected intravenously before following them under MRI. Also, its injection-excretion cycle is determined by various methods. Although not tested here, this contrast agent has the potential to be used as theranostic agent as well using magnetic hyperthermia or by trapping a chemotherapeutic drug in the polymer matrix or both.

REFERENCES

[1] Avasthi, Ashish, et al. "Magnetic Nanoparticles as MRI Contrast Agents." Topics in current chemistry (Cham) 378.3 (2020): 40.
[2] Leal, M. P.; Muñoz-Hernández, C.; Berry, C. C.; García-Martín, M. L., In vivo pharmacokinetics of T 2 contrast agents based on iron oxide nanoparticles: optimization of blood circulation times. RSC Advances 2015, 5 (94), 76883-76891.

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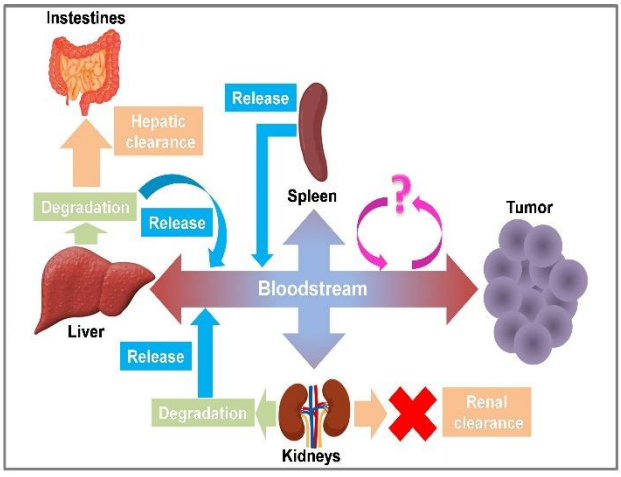

Figure 1: Scheme representing the proposed hypothesis about biodistribution and circulation of nanoparticles

Autism associated shank3 mutations alter skeletal muscle maturation: therapeutic strategies using 3D-bioprinted skeletal muscles

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Abstract
Heterozygous mutations of the gene encoding Shank3, a scaffold protein mainly present at the post synapse, are associated with syndromic forms of autism spectrum disorders (ASD). One of the earliest clinical symptoms of children born with Shank3 associated ASD is neonatal skeletal muscle hypotonia. However, mechanisms underlying this symptom are completely unknown. Here we used induced pluripotent stem cells derived from patients, a well-established Shank3 know-down murine model and muscle biopsies from Phelan Mc Dermid patients to analyse skeletal muscle defects associated with the loss of Shank3. First, we could see Shank3 localisation at the skeletal muscle sarcomere and also at the neuromuscular junctions[1]. Mutations in Shank3 induced ultrastructural alterations of the Z-disc bounding the sarcomere and at the neuromuscular of both our murine and human models. In addition, an impairment of the acetylcholine clustering in our motorneurone skeletal muscle co-cultures derived from induced pluripotent stem cells[2] was also observed. This could be reflected in functional defects in murine muscles giving insight of a very important role of Shank3 not only in the brain but also in the periphery. Providing thus, an open window for therapeutic strategies not only targeting the central nervous system but skeletal muscle. This could be in our hands modelled in 3D-bio-printed functional skeletal muscles[3].

REFERENCES

[1] Lutz AK, Pfaender S, Föhr KJ, Cammerer K, Zoller M, Higelin J, Ioannidis V, Schoen M, Orth M, Liebau S, Barbi G, Grabrucker AM, Delorme R, Bourgeron T, Verpelli C, Demestre M, Tobias M. Boeckers. Autism-associated SHANK3 mutations lead to impaired maturation of hiPSC derived motor units. Science Translational Medicine. 2020, 10;12(547)

[2] Demestre M, Orth M, Föhr KJ, Achberger K, Ludoplh Ac, Liebau S, Boeckers TM#. Formation and characterization of neuromuscular junctions between hiPSC derived motoneurons and myotubes. Stem Cell Resesrch. 2015 . 15 (2).(328)

[3] Mestre R, Patiño T, Barcelo X, Anand S, Pérez-Jiménez A, Sánchez S. Force modulation and adaptability in 3D-bioprinted Biological actuator based on skeletal muscle. Advanced Material Technologies. 2019. 4. (1800631)

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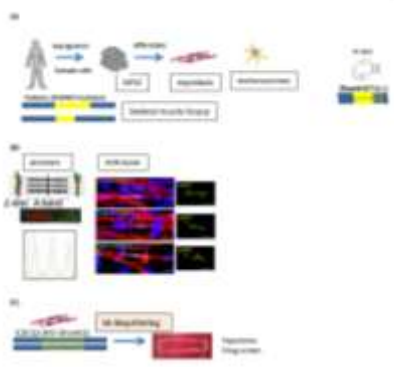

Robust electroactive substrates based on gold-nanoparticle arrays electrodeposited on indium tin oxide for reproducible surface-enhanced Raman spectroscopy

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Detection of low concentration of analytes up to the single-molecule level is becoming increasingly important in nanoscience and technology. Surface enhanced Raman spectroscopy (SERS) is a non-destructive and extremely sensitive technique able to detect trace amounts of substances, providing chemical information from the vibrational fingerprint of each molecule adsorbed on a rough metal surface [1–3]. Therefore, in biomedicine and biosensors SERS is becoming a prominent tool. One of the actual limitations of SERS is the lack of reproducibility of the Raman signal, because the substrates used to hold the molecules are not easy to reproduce in their detection ability [4]. In this work we have developed a conductive type of substrate for reproducible SERS measurements, following an easy and low-cost two-steps methodology. First, we deposit gold nanoparticles on a conductive indium-tin oxide (ITO) substrate by block-copolymer micellar lithography [5], creating a quasi-hexagonal pattern that acts as a template. In a second step, we overgrow these nanoparticles by applying an electrochemical pulse, taking advantage of the conductivity of the ITO. This last step allows for having bigger gold nanoparticles and consequently, smaller gaps between particles, thus increasing the amount of "hot-spots" in the entire surface. These "hot-spots" are responsible for the intensity enhancement of the Raman signal. Here we show that these electroactive substrates, apart from being an improved SERS tool, they can be also used to trigger electrochemical surface reactions. This opens new opportunities for a better understanding of the electrochemical reaction mechanisms in biochemistry, simultaneously allowing the in-situ monitoring.

REFERENCES

[1] R.A. Alvarez-Puebla, L.M. Liz-Marzán, Small. 6 (2010) 604–610.
[2] E. Cortés, P.G. Etchegoin, E.C. Le Ru, A. Fainstein, M.E. Vela, R.C. Salvarezza, J. Am. Chem. Soc. 132 (2010) 18034–18037.
[3] B. Sharma, R.R. Frontiera, A. Henry, E. Ringe, R.P. Van Duyne, Today. 15 (2012) 16–25.
[4] J. Langer, D.J. De Aberasturi, J. Aizpurua, R.A. Alvarez-puebla, B. Auguie, J.J. Baumberg, G.C. Bazan, S.E.J. Bell, A. Boisen, ACS Nano. 14 (2020) 28–117.
[5] R. Glass, M. Möller, J.P. Spatz, Nanotechnology. 14 (2003) 1153–1160.

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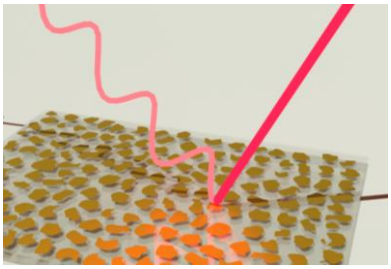

Figure 1. Schematic representation of ITO glass substrate with AuNPs growth by electrochemistry, illuminated by the Raman laser beam.

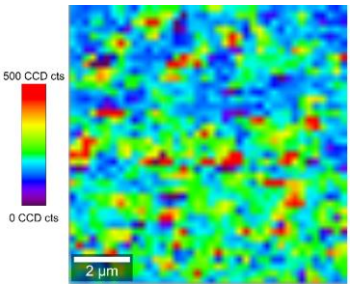

Figure 2. Raman mapping of an ITO substrate, functionalized with 4-MBA molecules, recorded with the 633 nm laser.

Optical analysis on infiltration of Rhodamine dye inside Nanoporous anodic alumina Gradient-index filters

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In the past decade, Nanoporous Anodic Alumina (NAA) has proved itself to be one of the most diversified template to be used in several drug delivery and bio sensing applications [1-2]. This material offers ease of fabrication, mechanical robustness, stable optical signals and tuneable surface chemistries. Light propagation amongst photonic structures (distributed Braggs reflectors, gradient-index filters) can be easily tuned by the precise engineering of their structural components. In order to develop advanced drug delivery systems based on these photonic structures, it is crucial to develop reliable methods to analyze the loading and release mechanism of drug within the nanopores. Pertaining to this, NAA-GIFs serves as one of the promising structures as photonic stopbands can be tuned at desired spectral wavelengths.

In this work, we have demonstrated the use of optical properties of NAA-GIFs to assess the molecular loading profile of Rhodamine 6G dye (serve as a model drug). The structural tuneability of photonic stopbands in NAA-GIFs allows one to obtain one of the bands in the same range as the absorption of the model drug while the second stopband is placed far away from the absorption region. This permits one to obtain a ratio between the reflectance's of both the stopbands while the filling the nanoporous structures with the dye molecules. In addition, drop/dry method has been shown to be a simple and effective strategy to fill the pores.

REFERENCES:

1) Pol L, Eckstein C, Acosta LK, Xifré-Pérez E, Ferré-Borrull J, Marsal LF. Nanomaterials. 2019;9(3).

2) Porta-i-Batalla M, Xifré-Pérez E, Eckstein C, Ferré-Borrull J, Marsal LF. Nanomaterials. 2017;7(8):

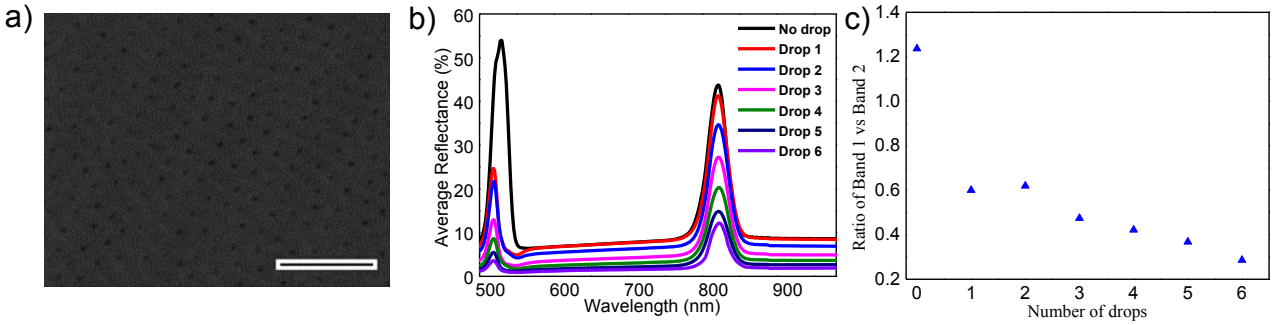

Figure 1. a) ESEM Top view of NAA-GIFs respectively. Scale bar 1µm; b) Reflection spectrum of NAA-GIFs with two photonic peaks after each drop/dry cycle; c) Ratio analysis between stopband 1 & 2.

Anti-biofilm surfaces based on the immobilization of a novel recombinant antimicrobial protein using SAMs

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The increasing appearance of bacteria resistant (and in many cases multiresistant) to antibiotics has become a global health emergency [1]. Far from being a phenomenon that will decrease in the coming years, it is estimated that the emergence of new resistances and the number of pan-resistant microorganisms will continue to grow reaching an increase of 67% in 2030 [2]. The antibiotic resistance is even more complicated when bacteria form biofilms. One of the strategies recently used to provide antimicrobial properties to medical devices is the immobilization of antimicrobial peptides (AMPs) on surfaces. The use of self-assembled monolayers (SAM) strategy to anchor AMPs on surfaces has been shown to be one of the best strategies for a controlled design of antibiofilm surfaces to coat medical devices [3]. SAMs are based on well-organized molecules on surfaces which are easy to be prepared and functionalized and allow a fine control at the molecular level [4]. Here, JAMF1 Host Defense Peptide (HDP), with recently proved effective antimicrcrobial activity, [5] has been successfully anchored on a model gold surface using a mixed self-assembled monolayer (SAM) based on ((1-mercapto-11-undecyl)-(tetra(ethylene glycol)) terminated SAM (PEG-SH), and nitriloacetic acid (NTA) terminated EG4-SAM (NTA-PEG-SH). The immobilized novel antimicrobial protein in its soluble and insoluble (IBs) form [6][7] on S-NTA-Ni surfaces were characterized using a multi-technique approach (XPS, immunostaining, AFM,…). The biofilm assay against *E.Coli* and *Klebsiella Pneumoniae* showed that the antimicrobial protein in both soluble and IBs forms are able to significantly reduce the biofilm formation. This strategy opens up for new possibilities for controlled biomolecule immobilization for fundamental biological studies and biotechnology applications, at the interface of materials science and biology.

REFERENCES

[1] Richard Smith, Joanna Coast, *BMJ* 2013;346:f1493
[2] Van Boeckel et al. PNAS 112 18, (2015) 5649-5654
[3] Monteiro, C., Costa, F., Pirttilä, A.M. *et al. Sci Rep* **9,** 10753 (2019).
[4] Humblot, V. et al. Biomaterials 30, (2009) 3503–3512
[5] Roca-Pinilla R, López-Cano A, Saubi C, Garcia-Fruitós E, Arís A. *Microb Cell Fact*. 2020;19(1):122.
[6] Tatkiewicz, W. I., et al., *ACS Applied Materials & Interfaces*, 10 (2018) 25779
[7] Tatkiewicz, W. I., et al., *ACS Biomaterials Science & Engineering*, 5 (2019) 5470.

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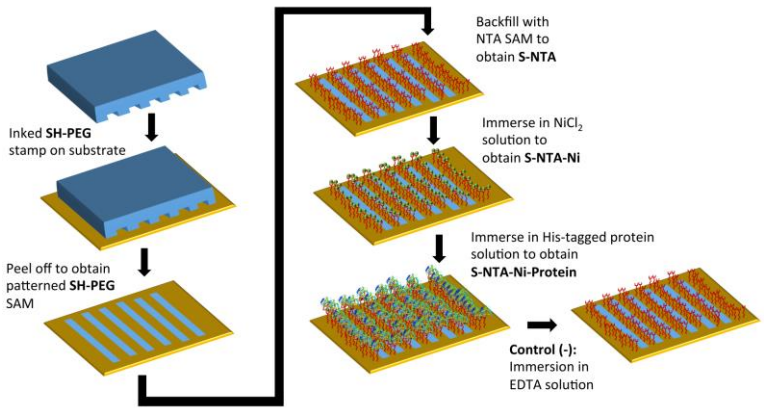

Figure 1: Schematic representation of the experimental procedure followed to prepare patterned SH-NTA and SH-PEG mixed SAMs, using the µCP technique. Subsequent protein immobilization via their His-tag termination led to the protein anchoring. Negative controls were prepared by immersing the substrates in to a EDTA solution (10 or 100 mM).

Dendritic mesoporous silica nanoparticles as self-adjuvants for peptide-based vaccine sustained delivery

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Abstract:

Mesoporous silica nanoparticles have drawn increasing attention as promising candidates in vaccine delivery[1]. Previous studies for evaluating silica-based vaccine delivery systems concentrated largely on macromolecular antigens. In this study, dendritic mesoporous silica nanoparticles (DMSNs) were used to evaluate their effectiveness as delivery platforms for peptide-based subunit vaccines capable of inducing significant levels of protective response without co-injection of adjuvants. An earlier reported foot-and-mouth disease virus (FMDV) peptide vaccine prototype named B_2T[2,3] was employed as antigen model. Our nanoparticle-codelivery system (B_2T@DMSNs) efficiently loaded B_2T and showed long-time sustained release up to 930h in vitro. Besides, B_2T@DMSNs of different sizes were assessed for their in vitro cellular uptake as well as in vivo immunogenicity, eliciting specific immune responses in mice with high IgG production in a particle size-dependent manner. Our results portray DMSNs nanocarriers as an attractive platform for developing peptide-based vaccine delivery.

REFERENCES

[1] K.T. Mody, A. Popat, D. Mahony, A.S. Cavallaro, C. Yu, N. Mitter, Nanoscale. 5 (2013) 5167–5179.
[2] E. Blanco, C. Cubillos, N. Moreno, J. Bárcena, B.G. De La Torre, D. Andreu, F. Sobrino, Clin. Dev. Immunol. 2013 (2013).
[3] E. Blanco, B. Guerra, B.G. De La Torre, S. Defaus, A. Dekker, D. Andreu, F. Sobrino, Antiviral Res. 129 (2016) 74–80.

FIGURES

Figure 1: TEM image of DMSNs-57. b) TEM image of DMSNs-156

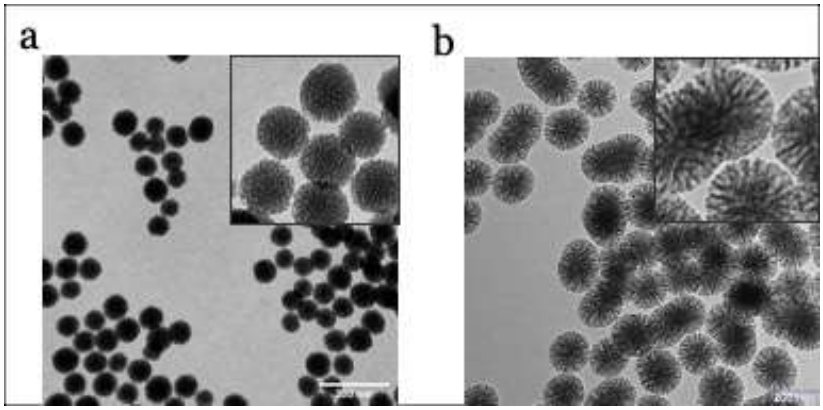
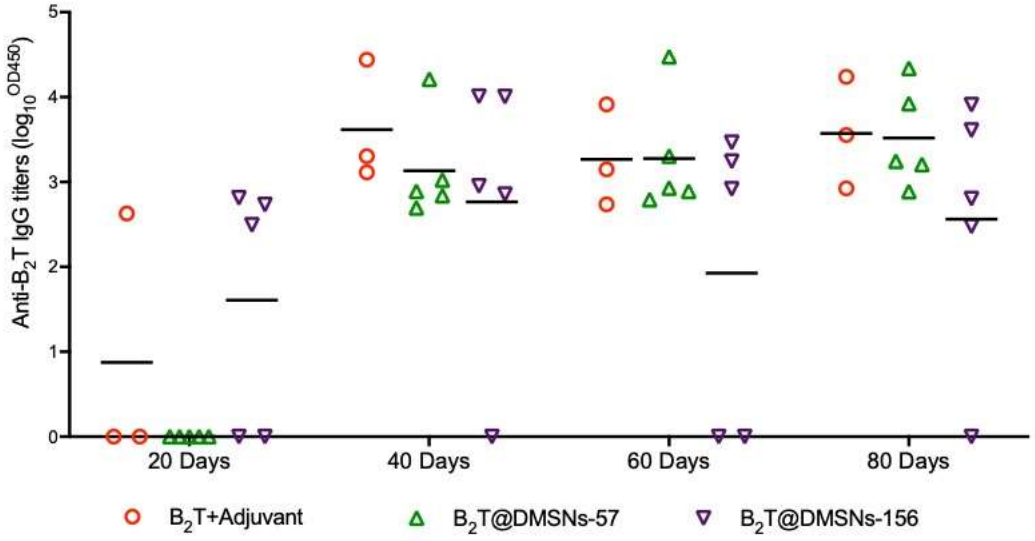


Figure 2: Results of Anti-B_2T IgG titers, measured by ELISA, from sera collected at days 20(pre-boost), 40, 60, and 80 in Swiss Mice immunized with B_2T+Adjuvant (red circle), B_2T@DMSNs-57 (green up triangle) and B2T@DMSNs-156 (purple down triangle).


Anti-B2T IgG titers (log10 OD450)
5
4
3
2
1
0
20 Days
40 Days
60 Days
80 Days
B2T+Adjuvant
B2T@DMSNs-57
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COPPER NANOPARTICLES STABILIZED AS AN ANGIOGENIC STIMULATING POTENTIAL FOR HEALING OF CHRONIC WOUNDS.

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Abstract
The normal process of wound healing[1] involves four successive phases: hemostasis, inflammation, proliferation, and tissue remodelling. One of the relevant phases is proliferation[2], where angiogenesis is triggered, which involves migration, proliferation, and differentiation of endothelial cells, which drives the formation of new blood vessels. Keratinocytes[3], important for tissue re-epithelialization, are responsible for releasing proangiogenic factors[2] such as VEGF-A, PDGF, TGF-α and TGF-β, these act on fibroblasts to induce secretion and remodelling of the extracellular matrix. Studies suggest that copper[4] can stimulate the migration and proliferation of keratinocytes or endothelial cells, but in turn, it is highly cytotoxic. Therefore, it is important to use nanotechnology tools to better these disadvantages, with which, stabilized copper nanoparticles (NpsCu) could be an alternative to reduce cytotoxicity and in turn could allow the release of proangiogenic factors that improve physiological processes such as angiogenesis in wounds. The objective of this work is to determine the effect of NpsCu on the survival and migration of human keratinocytes. For this, cell viability tests were performed using MTS and migration tests at *Transwell*, where keratinocytes are estimated with different concentrations (0.4 - 0.8 and 1 mM) of NpsCu^{o} in the presence or absence of 1% SFB. NpsCu were chemically characterized in a previous work where their main component was also determined to be Cu° and antimicrobial susceptibility tests were performed where it was shown that these NpsCu inhibit gram positive and negative bacteria in concentrations that vary between 7.8 and 125 mM. The results obtained in this work suggest that at a concentration of 0.4 mM NpsCu^{o} + SFB 1%, human keratinocytes (HaCaT) do not undergo significant alterations in relation to their viability, which was determined by measurements of MTS and ATP. The present study has shown in vitro that the stabilized copper nanoparticles (NpsCu^{o}) do not present cytotoxicity in keratinocyte cell cultures at a concentration of 0.4 mM for 24 hours, observing an increase in viability that results in stimulation to initiate the cell migration process, although it remains to be determined if the proliferation of these cells is activated after being stimulated.

REFERENCES

[1] Broughton, G., Janis, J., & Attinger, C. 2006. *Wound Healing: An Overview.* Plastic and Reconstructive Surgery, *117* (SUPPLEMENT), 1e-S-32e-S.
[2] Bennett, N.T. and G.S. Schultz. 1993. *Growth factors and wound healing: biochemical properties of growth factors and their receptors.* Am J Surg. **165**(6): p. 728-37.
[3] Esche, C., A. de Benedetto, and L.A. Bec. 2004. *Keratinocytes in atopic dermatitis: inflammatory signals.* Curr Allergy Asthma Rep. **4**(4): p. 276-84.
[4] Balamurugan, K. and W. Schaffner. 2006. *Copper homeostasis in eukaryotes: teetering on a tightrope.* Biochim Biophys Acta. **1763**(7): p. 737-46.

FIGURES

Fig.1

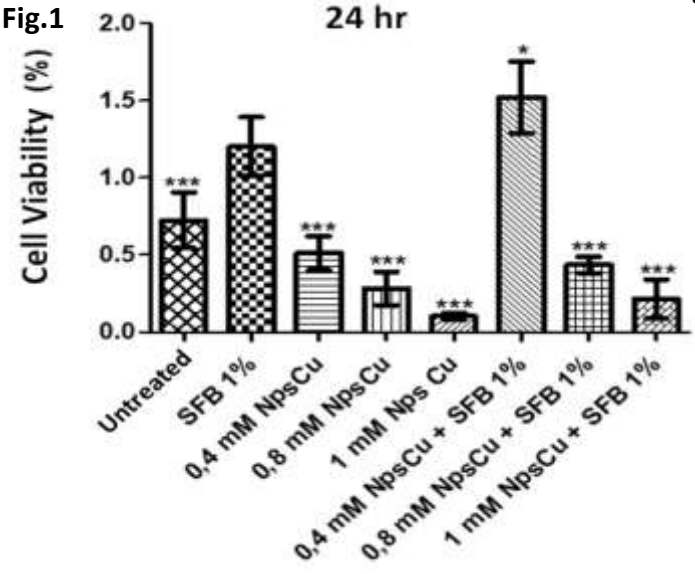

Fig. 2

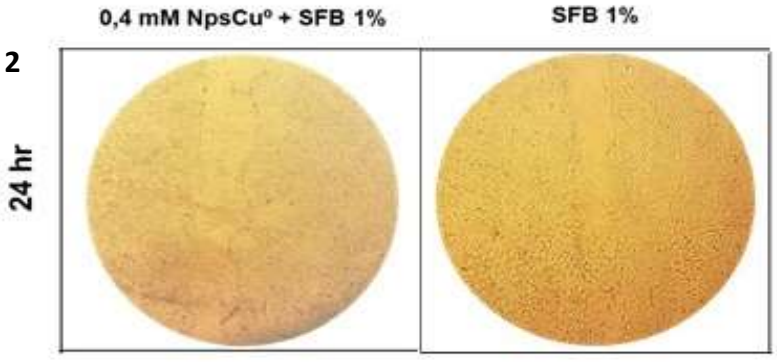

Fig. 1: Evaluation of the effect of different concentrations of NpsCu on the viability of HaCaT keratinocytes, by means of MTS at different concentrations and time, with presence and absence of SFB

Fig. 2: NpsCu increases wound closure in an in vitro test at 24 hours. Migration kinetics; HaCaT cells were stimulated with 0.4 mM NpsCu^{o} + 1% SFB.

The influence of chemical structure in the drug release of two modulated flavanones formulated in a nano system

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Prenylated flavanones include a diverse class of naturally flavonoids oxygen-containing heterocycles that contain prenyl substituents. Nowadays many studies proved their anti-oxidative, anti-obesity, anti-inflammatory and other various biological effects that could apply in the prevention of various pathologies including cancer [1-3]. Recently, the flavanone (2*S*)-5,7-dihydroxy-6-(3-methyl-2-buten-1-yl)-2-phenyl-2,3-dihydro-4H-1Benzopyran-4-one **1** was isolated from a methanol extract obtained from the aerial parts of *E. platycarpa* [4]. The aim of this study was to evaluate a new topical emulsion that contained the prenyl flavanones (8S)-5-hydroxy-2,2-dimethyl-8-prenyl-3,4,7,8-tetrahydro-2H,6H-Benzo[1,2-b:5,4-b']dipyran-6-one **2**; and (8S)-5-hydroxy-2,2-dimethyl-8-phenyl-7,8-dihydro-2H,6H-Benzo[1,2-b:5,4-b']dipyran-6-one **3** (Figure 1) in a nano system formulation through *in vitro* drug release. The nano system formulation of flavanones **2** and **3** (0.5% w/w) were preparated with, labrasol, labrafac, plurol oleique and propyleneglycol as excipients. The particles sizes were measured by Zeta-Sizer, Malvern Instruments. *In vitro* release assays were performed in Franz Diffusion Cells of 2.54cm^2 with dialysis membrane. The receptor phase was ethanol:water (70:30), under temperature of 32 ± 1ºC. Samples were withdrawn at different time point scheme for 89 h and quantified by means a validated HPLC method [5] (water:acetonitrile (20:80) for **2** and (10:90) for **3** as mobile phase; 1 ml/min flow rate; 300 nm; Machery Nagel® C18 5mm, 25x4.6cm column). *In vitro* data were analyzed by GraphPad Prism software with Weibull model. The results showed the average drop size of the nanostructured formulation of **2** and **3** were 340.6 and 383 nm with PI=0,2 and 0.4 respectively. The kinetic release model that best describes the amount of (**2** and **3**) load at any time is representing by the function named as Weibull, $Q_t = Q_\infty \left[1 - e^{-\left(\frac{t}{t_d}\right)\beta}\right]$ where; Q = 1714 ± 556.2 and 48.4 ± 16.1 and t_d = 83.6 ± 25.5 and 41.5 ± 33.2, respectively. Although the similar drop size of both nano structured formulation, the kinetic release of the formulation showed a significant difference. While, Q represents the maximum quantity at which release tends; td is the time at which 63% of the initial amount of flavanone tested has dissolved. The flavanone **2** release more than flavanone **3** maybe due to the absence of double bond in **3**. The nano-structured formulation of flavanones **2** and **3** are promising alternatives to administrate modified drug. Acknowledge to CONACyT, Mexico for the scholarship 709906. The authors would like to thank Gattefossé for supplying excipients for this study.

REFERENCES

[1] M.S. Brewer, Compr. Rev. Food Sci. Food Saf. **2011**, 10: 221–247.
[2] S. Venturelli, *et al*., Nutrition. **2016**, 32: 1171–1178.
[3] X. Yang, *et al*. *Trends Food Sci. Technol*. **2015**, 44: 93–104.
[4] V.Domínguez-Villegas; et al, *Nat. Prod. Comm*, **2013**, 8:177-180.
[5] P. Bustos- Salgado, *et al, Biomolecules*, **2020**, 10(6): 889.

FIGURES

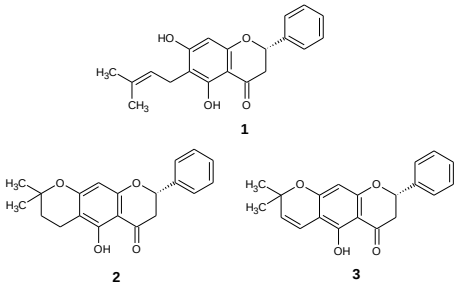

Figure 1: (2*S*)-5,7-dihydroxy-6-(3-methyl-2-buten-1-yl)-2-phenyl-2,3-dihydro-4H-1Benzopyran-4-one **1**; (8S)-5-hydroxy-2,2-dimethyl-8-prenyl-3,4,7,8-tetrahydro-2H,6H-Benzo[1,2-b:5,4-b']dipyran-6-one **2**; and (8S)-5-hydroxy-2,2-dimethyl-8-phenyl-7,8-dihydro-2H,6H-Benzo[1,2-b:5,4-b']dipyran-6-one **3**

CELLULAR TOXICITY OF A NANOSTRUCTURED EMULSION OF AMPHOTERICIN B.

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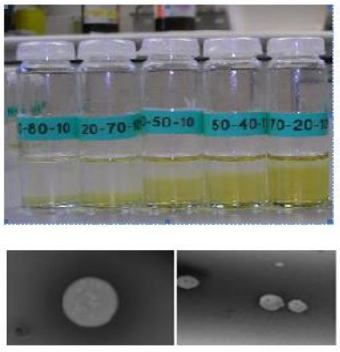
Abstract

Amphotericin B (AmB) is a potent polyene macrolide antibiotic with high molecular weight (924 Da) and broad-spectrum coverage (1). From a physicochemical point of view, AmB is a poorly hydrosoluble, amphoteric, amphiphilic molecule and is difficult to solubilize in organic solvents. For this reason, there is no topical formulation of AmB commercially available at the moment (2). This fact evidences the need to develop new formulations using excipients with permeation-enhancing properties in order to facilitate the penetration of drug into Stratum Corneum (SC) and its distribution from SC to epidermis and dermis. We have developed a AmB nanoemulsion 0,3% (NE) having as composition: Labrasol® / plurol®5: 1, Transcutol® and castor oil® with the following proportions: 55-05-40 (3). To determine the toxicity of this formulation, we have performed cytotoxicity tests through the technique WST-1 on two cell lines: Raw 264.7 and J774, respectively. Cytotoxicity tests were performed with: A solution of AmB dissolved in DMSO, the AmB NE and the blank (NE without AmB). The results obtained indicate that the AmB NE presented lower cellular toxicity than the AmB in solution in both Cell lines and greater toxicity in J774 cells. The NE without drug was not toxic against Raw cells and presented cellular toxicity against J774 cells at a concentration of 38,94 ± 0,20 µg/mL (Table 1). As a future perspective, we will conduct these tests on keratinocytes (HaCaT).

Table 1. Citotoxicity Concentration about AmB solution, AmB NE and NE (blank)

Compounds	CC50 µg/mL	
	RAW	J774
AmB Solution 150-0,14(µg/mL)	56,34 ± 0,29	57,80 ± 0,24
NE AmB 150-0,14(µg/mL)	95,76 ± 0,28	342,13 ± 0,23
Formulation	**CC50 % p/p**	
NE 12,5-0,02 (%)	> 12,50	38,94 ± 0,20



REFERENCES

1. Gray KC, Palacios DS, Dailey I, Endo MM, Uno BE, Wilcock BC, et al. Amphotericin primarily kills yeast by simply binding ergosterol. Proc Natl Acad Sci U SA 2012;109:2234-9.

2. Perez AP, Altube MJ, Schilrre P, Apezteguia G, Celes FS, Zacchino S, et al. Topical amphotericin B in ultradeformable liposomes: Formulation, skin penetration study, antifungal and antileishmanial activity *in vitro*. Colloids Surf. B Biointerfaces **2016**, 139, 190–198.

4. Sosa L, Clares B, Alvarado HL, Bozal N, Domenech O and Calpena AC. Amphotericin B releasing topical nanoemulsion for the treatment of candidiasis and aspergillosis. Nanomedicine **2017**, 13, 2303–2312

SERS Detection of Pathogens using a LAMP–in–Microdroplets platform

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In recent years, cases of listeriosis have been increasing and are considered one of the most serious foodborne diseases under EU surveillance [1], emphasising the need for seeking methodologies for the early detection of this pathogen. Traditional molecular techniques are normally based on the detection of specific DNA or RNA target sequences using amplification processes, like the polymerase chain reaction (PCR) [2]. Nevertheless, isothermal nucleic acid amplification technology, specifically loop-mediated isothermal amplification (LAMP), has been widely proposed as an alternative methodology because it exhibits good performance in ultrasensitive detection and biosensing, as compared to PCR [3]. LAMP has been successfully implemented in lab-on-chip systems, however the low volumes inherent to a microfluidic system force these strategies to be coupled to highly sensitive detection techniques. Microdroplets have been used as laboratory flasks for the detection of pollutants, bacteria and even single cells [4]–[6]. Surface-enhanced Raman scattering (SERS) spectroscopy is an ultrasensitive sensing tool, that when combined with microfluidics/microdroplets offers a great potential for the development of automated and sensitive diagnostic platforms.
Herein, we developed a droplet-based optofluidic system for the detection of foodborne pathogens. Specifically, LAMP was combined with SERS, which offers an excellent method for DNA ultradetection. For this, were prepared multifunctional AuNPs involving three components with key roles: (1) thiolated poly(ethylene glycol) as stabilizing agent, (2) 1-naphthalenethiol (1-NAT) as Raman reporter, and (3) glutathione as a bioinspired chelating agent of magnesium (II) ions. The variation of the SERS signal of 1-NAT was controlled by the aggregation of AuNPs triggered by the complexation of pyrophosphate and glutathione with free magnesium ions. Using this strategy, we detected *Listeria monocytogenes*, not only in buffer, but also in a food matrix (i.e., ultra-high temperature milk) enabled by the massive production of hotspots as a result of the self-assemblies that enhanced the SERS signal. This allowed the development of a microdroplet-LAMP-SERS platform with isothermal amplification and real-time identification capabilities.[7]

REFERENCES

[1] E. F. S. A. and E. C. for D. P. and C. (EFSA and ECDC), “The European Union One Health 2018 Zoonoses Report,” *EFSA J.*, vol. 17, no. 12, p. e05926, 2019.
[2] L. Garibyan and N. Avashia, “Polymerase Chain Reaction,” *J. Invest. Dermatol.*, vol. 133, no. 3, pp. 1–4, 2013.
[3] M. Fakruddin *et al.*, “Nucleic acid amplification: Alternative methods of polymerase chain reaction YR - 2013/10/1,” *J. Pharm. Bioallied Sci.*, 5, 245–252, 2013.
[4] J. Q. Yu *et al.*, “Droplet optofluidic imaging for λ-bacteriophage detection via co-culture with host cell Escherichia coli,” *Lab Chip*, vol. 14, no. 18, pp. 3519–3524, 2014.
[5] X. Zhao and T. Dong, “A microfluidic device for continuous sensing of systemic acute toxicants in drinking water,” *Int. J. Environ. Res. Public Health*, vol. 10, no. 12, pp. 6748–6763, Dec. 2013.
[6] D. Hümmer, F. Kurth, N. Naredi-Rainer, and P. S. Dittrich, “Single cells in confined volumes: microchambers and microdroplets,” *Lab Chip*, vol. 16, no. 3, pp. 447–458, 2016.
[7] A. Teixeira *et al.*, “Multifuntional Gold Nanoparticles for the SERS Detection of Pathogens Combined with a LAMP–in–Microdroplets Approach,” *Materials (Basel).*, vol. 13, no. 8, p. 1934, Apr. 2020.

FIGURES

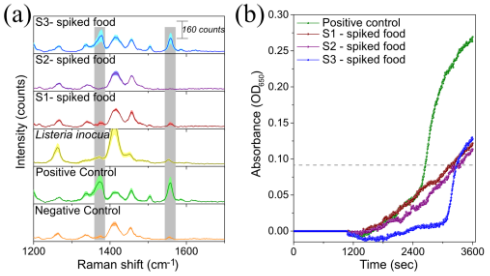

Figure 1: Ability of LAMP-on-a-chip SERS assay to detect L. monocytogenes in UHT milk. (a) SERS (i.e., using LAMP-on-a-chip SERS assay) and (b) turbidity (e.i. LAMP real-time turbidity detection) as reference.

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