# MAD-Nano16

## MADEIRA INTERNATIONAL CONFERENCE

## Emerging Trends and Future of Nanomaterials for Human Health

17-20 November 2016 | **Madeira Island** | PORTUGAL

# ABSTRACTS BOOK


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CQM CENTRO DE QUÍMICA DA MADEIRA

UNIVERSIDADE da MADEIRA

# MAD-NANO16

## MADEIRA INTERNATIONAL CONFERENCE ON EMERGING TRENDS AND FUTURE OF NANOMATERIALS FOR HUMAN HEALTH



# Abstracts Book

17th - 20th November 2016
Funchal, Madeira Island – PORTUGAL

Abstracts Book
MAD-NANO16: Madeira International Conference on Emerging Trends and Future of Nanomaterials for Human Health

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# WELCOME MESSAGE

Dear Colleagues,

It is a great privilege to welcome you to the MAD-Nano 16: Madeira International Conference on Emerging Trends and Future of Nanomaterials for Human Health, in Funchal, Madeira Island. This event is organized by *Centro de Química da Madeira* (CQM) - University of Madeira (UMa) and is sponsored by *Fundação para a Ciência e a Tecnologia* (FCT), the *Agência Regional para o Desenvolvimento da Investigação, Tecnologia e Inovação* (ARDITI) and the *Programa Iberoamericano de Ciencia y Tecnología para el Desarrollo* (CYTED).

Due to the expected impact on improving the quality of life of human beings, nanomaterials for health is a very emerging topic that is attracting several researchers, clinics, companies and supporting agencies in the field.

We aim with this conference to create an alternative forum to share, in an informal manner, with the future independent researchers, the current state of the art, create new networks, present and discuss the most innovative nanomaterials and approaches that can be used to treat different disease that affect the human population.

Madeira Island and the city of Funchal are the perfect places to organize this conference as historically they form a bridge between the past and the future. The islands of Madeira and Porto Santo are considered the first territorial discovery of the period of the "Portuguese Age of Discovery". With a subtropical-Mediterranean climate, a *Laurisilva* forest considered by UNESCO as a natural World Heritage Site and 2170 km of levadas (aqueducts that carry water from the northwest coast of the Island to the agricultural regions in the south), Madeira Island attracts tourists from all over the world throughout the year. It has also become a destination where people come to work and live in a safe and beautiful environment. Well-served by infrastructures (airport, roads, free trade zones and hospitals), Madeira Island, has also developed strong connections to Europe, North and South America, and Africa over the years. With the contribution of University of Madeira and the *Centro de Química da Madeira*, the Region is now also a gateway to Asia, fulfilling the mission of bringing people of different cultures together to share knowledge and innovation in the field of nanomaterials for human health applications.

In the name of the International Advisory Committee and the Organizing Committee, I wish you all a very pleasant and fruitful stay.

Funchal 17th of November 2016

João Rodrigues
Chairman of MAD-Nano16

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# KEYNOTE LECTURES

**Abhay Pandit**

Abhay Pandit is an Established Professor of Biomaterials at the National University of Ireland, Galway. He is the Scientific Director of the Centre for Research in Medical Devices (CÚRAM), a multi-disciplinary academic-industry-clinician translational research centre funded by Science Foundation Ireland (E49M). His research integrates material science and biological paradigms in developing solutions for chronic disease. Prof. Pandit has developed next generation reservoir delivery vehicles with high payload capacity, programmable degradation profiles and inbuilt gradients of physical, chemotropic and protective cues which facilitate spatiotemporal localized sustained delivery of multiple biomolecules to target injury mechanisms at the molecular and cellular levels. He was inducted as an International Fellow in Biomaterials Science and Engineering by the International Union of Societies for Biomaterials Science and Engineering and elected as a Fellow of the Tissue Engineering and Regenerative International Society. He is the first Ireland-based academic to be bestowed with this honor. He has been an elected member of the Council for both the Tissue Engineering and Regenerative Medicine International Society and European Society for Biomaterials Society. Prof. Pandit has published more than 200 papers in peer-reviewed journals, filed numerous patent applications and has licensed four technologies to medical device companies. In recognition of his track record in technology transfer, Prof. Pandit secured the Academic/Emerging Medical Technology Company of the Year – Silver Award for 2013 awarded by the Irish Medical Devices Association, Enterprise Ireland, and IDA Ireland. Prof. Pandit is an Executive Editorial Board of the Tissue Engineering journal, an Associate Editor of the Biomaterials journal. In addition, he serves as an Editorial Board Member for 14 other journals.

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[KN1]

# Biological-basis for designing biomaterials for the injured and degenerated host

Abhay Pandit

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Biomaterials are no longer considered innate structures and using functionalisation strategies to modulate a desired response whether it is a host or implant is currently an important focus in current research paradigms. Fundamentally, a thorough understanding the host response will enable us to design proper functionalisation strategies. The input from the host response need to be weighed in depending on the host disease condition. In addition biomaterials themselves provide immense therapeutic benefits which needs to be accounted for when using functionalisaton strategies. Strategies such as enzymatic and hyperbranched linking systems, we have been able to link biomolecules to different structural moieties. The programmed assembly of biomolecules into higher-order self-organized systems is central to innumerable biological processes and development of the next generation of functionalized scaffolds. Recent design efforts have utilized a developmental biology approach toward both understanding and engineering supramolecular protein assemblies. Structural moieties have taken a variety of different forms such as nanofibers and nanoparticulate. This approach has resulted in functionalisation of micro and nanoparticles with biomolecules that include designed peptide motifs, growth factors and a multitude of gene vector systems. In addition, nature itself has abundant structural complexity that can be harnessed for targetted clinical applications. This talk will elucidate some of these ongoing strategies in our laboratory.



## References

[1] Samal, J.; Hoban, D.B.; Naughton, C.; Concannon, R.; Dowd, E.; Pandit, A. *Nanomedicine*, **2015**, *10*, 765.
[2] Thomas, D.; Fontana, G.; Chen, X.; Sanz-Nougés, C.; Zeugolis, D.; Dockery, P.; O'Brien, T.; Pandit, A. *Biomaterials.*, **2014**, *35*, 8757.
[3] Lang, Y.; del Monte, F.; Collins, L.; Rodriguez, B.J.; Thompson, K.; Dockery, P.; Finn, D.P.; Pandit, A. *Nature Communications.*, **2013**, *4*, 3683 .
[4] Browne, S.; Monaghan, M.G.; Brauchle, E.; Berrio, D.C.; Chantepie, S.; Papy-Garcia, D.; Schenke-Layland, K.; Pandit, A. *Biomaterials*, **2015**, *69*, 133.
[5] Dash, B.C.; Thomas, D.; Monaghan, M.; Carroll, O.; Chen, X.; Woodhouse, K.; O'Brien, T.; Pandit, A. *Biomaterials*, **2015**, *65*, 126.

**Rui L. Reis**

Rui L. Reis is a Full Professor of Tissue Engineering, Regenerative Medicine, Biomaterials, and Stem Cells in the Department of Polymer Engineering, School of Engineering of University of Minho (UMinho). He is the Vice-Rector/President for Research of the University of Minho, Braga & Guimarães, Portugal. He is also the Director of the 3B's Research Group – Biomaterials, Biodegradables and Biomimetics at the University of Minho in Portugal (www.3bs.uminho.pt), and the Director of the PT Government Associate Laboratory ICVS/3B´s. Rui L. Reis is the CEO of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine (TERM) that has 22 partners from 13 different countries, and will be the Scientific Coordinator of the recently approved by the European Commission "The Discoveries Centre for Regenerative and Precision Medicine" (expected direct investment in the next 7 years: 100 millions of euros). He directs the correspondent European Economic Interest Group (EEIG), being the main office registered in Portugal.

As a result of his academic activities Rui L. Reis has been awarded several prizes. Some of the most relevant ones were: i) the Stimulus to Excellence Award 2004 by the Portuguese Minister for Science and Technology for being one of the scientists with higher number of publications and citations in the Portuguese scientific arena (around 70 awardees - only 2 below 40 years old); ii) an Honoris Causa degree in Medicine awarded in 2010 by the historical and highly respected University of Granada in Spain for his world-leading activities in the field of regenerative medicine; (iii) the nomination as a Commander (Comendador, a kind of knighthood) of the Military Order of Santiago de Espada by the Portuguese President of the Republic, June, 2014; (iv) nomination as a foreigner member of the National Academy of Engineering (NAE) of the USA. Feb., 2016 – only 230 foreigner members, being Rui Reis the only Portuguese ever.

His work has been cited around 19450 times (more than 21 citations per article), and he has an h-factor of 68. He was selected as one of 100 most influential Portuguese citizens (in all areas of activity) by the respected Portuguese newspaper EXPRESSO in 2013.

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[KN2]

# Nano-tools and bioinspired tissue engineering approaches for the regeneration of different tissues

Rui L. Reis

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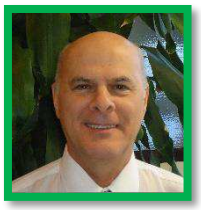
This talk will describe several nano-tools and biomimetic approaches for the regeneration of different tissues. The selection of a proper material to be used as a scaffold or as a hydrogel, in many cases in combination with nanoparticles, to support, hold or encapsulate cells, as well as to control their differentiation, is both a critical and difficult choice. It will ultimately determine the success or failure of any tissue engineering and regenerative medicine (TERM) strategy.

We believe that the use of natural origin polymers is the best option for many different approaches that allow for the regeneration of different tissues. In addition to the selection of appropriate material systems it is of outmost importance the development of processing methodologies that allow for the production of adequate nano delivery systems and scaffolds/matrices.

Furthermore an adequate cell source should be selected. In many cases efficient cell isolation, expansion and differentiation methodologies should be developed and optimized. We have been using different human cell sources namely: mesenchymal stem cells from bone marrow and adipose tissue, cells from amniotic fluids and membranes and cells obtained from umbilical cords.

The potential of each type of cells, to be used to develop novel useful regeneration therapies will be discussed. Their uses and their interactions with different nano systems and natural origin degradable scaffolds and smart hydrogels will be described. Examples of the engineering of different tissues will be presented.



**René Roy**

René Roy holds a Canadian Research Chair in Therapeutic Chemistry in the Department of Chemistry of the Université du Québec à Montréal (Qc, Canada). He has published over 310 publications and has contributed to the development of two commercial carbohydrate-based vaccines against meningitis. His actual interests are in multivalent carbohydrate-protein interactions, medicinal chemistry, and in nanomaterials**.**

[KN3]

# Glycodendrimers or Janus Glycodendrimersomes: that is the question?

René Roy

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The modular synthesis of several libraries of self-assembling amphiphilic Janus dendrimers with sugar head groups will be presented in light of the stability, size, and bioactivity of the resulting liposomes formed [1]. These unprecedented sugar-containing dendrimers were denoted as amphiphilic Janus glycodendrimers. Their self-assembly by simple injection of organic solution into water or buffer and by hydration was analyzed by a combination of methods including dynamic light scattering, confocal microscopy, cryogenic transmission electron microscopy (TEM), Fourier transform analysis, and micropipet-aspiration experiments to assess mechanical properties. These libraries revealed a diversity of hard and soft assemblies, including unilamellar spherical, polygonal, and tubular vesicles. These assemblies are stable over time in water and in buffer, exhibit narrow molecular-weight distribution, and display dimensions that are programmable by the concentration of the solution from which they were injected. This study highlighted the molecular principles leading to single-type soft glycodendrimersomes assembled from amphiphilic Janus glycodendrimers. The multivalency of glycodendrimersomes with different sizes and their ligand bioactivity were demonstrated by selective agglutination with a diversity of sugar-binding protein receptors including leguminous, bacterial, and mammalian lectins. This novel approach will be compared to the complex syntheses of glycodendrimers using glyconanosynthons strategy [2].

In addition, an accelerated modular synthesis with three different topologies formed from either two or one carbohydrate head groups or a mixed hybrid thereof with a hydrophilic arm was also achieved to evaluate the effects of the relative sugar densities upon protein binding [3]. The hybrid structures were the most efficient in lectin bindings. These results demonstrated the candidacy of glycodendrimersomes as new mimics of biological membranes with programmable glycan ligand presentations [4] as supramolecular lectin blockers, vaccines, and targeted delivery devices.



## References

[1] Percec, V.; Leowanawat, P.; Sun, H.-J.; Kulikov, O.; Nusbaum, C.D.; Tran, T.M.; Bertin, A.; Wilson, D.A.; et al. *J. Am. Chem. Soc.*, **2013**, *135*, 9055.
[2] Roy, R.; Shiao, T.C. *Chem Soc. Rev.*, **2015**, *44*, 3924.
[3] Zhang, S.; Moussodia, R.-O.; Sun, H.-J.; Leowanawat, P.; Muncan, A.; Nusbaum, C.D.; Chelling, K.M.; Heiney, P.A.; et al. *Angew. Chem Int. Ed.*, **2014**, *53*, 10899.
[4] Zhang, S.; Moussodia, R.-O.; Murzeau, C.; Sun, H.-J.; Klein, M.L.; Vértesy, S.; André, S.; Roy, R.; et al. *Angew. Chem. Int. ed.*, **2015**, *54*, 4036.

**Jean-Pierre Majoral**

Jean-Pierre Majoral is Emeritus Director of Research at the CNRS in Toulouse. His research interest is focused on the design and the properties of macromolecules such as phosphorus dendrimers and hyperbranched polymers. Main efforts are directed to the use of dendrimers in medicinal chemistry and material sciences. Emphasis is also laid on immobilization of molecular and macromolecular organo- and metal catalysts and their use for fine chemical synthesis. He received a dozen of various prestigious awards from Germany, Poland, Spain, UK and France. He is a member of several Academies of Sciences worldwide and an author of 600 publications and 45 patents.

[KN4]

# Design and applications of phosphorus dendrimers in nanomedicine

Jean-Pierre Majoral

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Beside polymeric, solid-lipid, ceramic, magnetic and metal based nanoparticles, and polymeric micelles, dendrimer nanostructures represent outstanding nano-carriers in medicine, Dendrimers are highly branched, uniformly distributed structures, having defined molecular weight, shape, size, host-guest entrapment properties, and diameters in the 2 to 10 nm range size. In addition, 3D multi-functional groups on the dendrimer outer shell – generally doubling with each additional generation – allow to covalently linking different moieties such as drugs to the surface of dendrimers (conjugate approach). The well-defined molecular weight and monodispersity of dendrimers induce reproducible pharmacokinetics unlike polymers. Indeed, dendrimers belong to the nanoworld, but they are constituted of soft matter in marked contrast with classical hard nanoparticles.

Among the different types of dendrimers reported up to now phosphorus dendrimers that are dendrimers having one phosphorus atom at each branching point plays more and more an important role because of their intrinsic properties: easy regioselective functionalization of the core, within the structure and at the surface with the grafting of 2, 3, and even 4 different terminal groups on the outer shell, possibility to play with the hydrophilicity/hydrophobicity of the surface and of the core, the interior being hydrophobic, high thermal stability etc. Such properties allowed the use of these dendrimers in different fields ranging from biology, material science to catalysis. Regarding biology and medicinal chemistry water soluble phosphorus dendrimers display interesting behaviors. Ammonium-ended phosphorus dendrimers are efficient transfection agents, have a high antiprion activity, interact with amyloid monomers and consequently fibril formation is prevented, or affect Alzheimer's ($A\beta_{1\text{-}28}$) peptide and MAP-Tau protein aggregation. Polycationic phosphorus dendrimers having an optimized two-photon absorption chromophore as core allowed the imaging of the vascular network in the dorsal part of the rat olfactory bulb or was used for intra-cardiac injection in a living Xenopus tadpole allowing imaging of the blood vessels of the tail: no toxicity was detected for all these experiments.

On the other hand polyanionic phosphorus dendrimers display also fascinating properties, as well as neutral phosphorus dendrimers active *per se*.

After a brief illustration of the diversity of synthesis of phosphorus dendrimers, the lecture will be focused on different applications of cationic, anionic or neutral phosphorus dendrimers in nanomedicine: anti-inflammatory properties, anti-aging, imaging, diagnosis etc., thus illustrating their fascinating properties.

**Wolf-Dieter Mueller**

Wolf-Dieter Mueller is a Full Professor of Charité Universitätsmedizin Berlin, Institute for Dental, Oral, and Maxillary Medicine. He is the head of the Dental and Biomaterial research group in Berlin, Germany.

[KN5]

# E-spinning nano fibres of PBCA for biomedical application – state of the art and first results

Yaquelin Ramos Carriles[1], Ruben Alvarez Brito [2] & Wolf-Dieter Mueller[2,*]

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Nano-fibres are very interesting products in the biomedical field, due to their very high porosity and surface area. These characteristics allow them to be used as drug delivery systems, for the promotion of wound healing as well as for tissue engineering of different tissues such as blood vessels, bones and muscles. There are only some applications of e-spinning technique to produce nano-fibres based on PBCA. PBCA are biodegradable polymers with a high degradation rate. The application fields are wound healing and drug delivery systems. The aim of our work is in a first step to produce nano fibres on PBCA and to test their biocompatibility in contact with fibroblasts in-vitro. A laboratory set-up for e-spinning was developed and with two in molecular weight different PBCA solutions nano fibres were produced. With help of scanning electron microscopy their structures was assessed. The biocompatibility was tested direct in contact with fibroblasts. After 1, 3, 7, 14 days the cells were stained (life – dead staining) for observation with help of CLSM. In summary a set-up could be manufactured for producing nano-fibres of PBCA on different carriers with an average diameter of 500 nm with round or flat shape. The in-vitro tests reveal a high biocompatible behaviour with a surprisingly good cell growth onto the fibre meshes.

**Bingbo Zhang**

Bingbo Zhang joined Tongji University upon graduation from Tianjin University in 2009 with a Ph.D. degree. Currently, he is a Principal Investigator of Institute of Photomedicine at Tongji University School of Medicine, Shanghai, China. His research interests focus on protein and peptide-based biomimetic nanoparticles for cancer nanotheranostics. He has published over 40 peer-reviewed papers in international journals.

[KN6]

# Functional proteins promote nanotheranostics

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The poor delivery efficiency of nanoparticles to malignant tissues seriously hinders the development of nanomedicine [1]. Studies show that protein corona on the injected nanoparticles can significantly change the identity of nanoparticles [2]. As such, physiological response (kinetics, toxicity and distribution) will be triggered. Currently, protein-and peptide-based biomimetic nanoparticles have been demonstrated to be an efficient and promising strategy for improved diagnosis and therapy in biomedical field [3]. This strategy is found to be bio-inspired, straightforward and environmentally benign. And it can endow nanoparticles with good stability, excellent biocompatibility, high water solubility, and rich surface functional groups for further conjugation. We did pioneering work on reducing nonspecific binding and phase transfer of quantum dots by using the unique domain and amino acid sequence of albumin bovine serum (BSA) protein under ultrasound condition [4]. Furthermore, BSA protein was used for biomimetic mineralization of nanoparticles for biomedical imaging and therapy [5-7]. Particularly, other functional proteins were explored for bioinspired synthesis of nanoparticles, and the inherent mechanism was preliminarily studied *via* short peptides. These protein or peptide-mediated nanoparticles are coated by proteins or peptides, which drastically eliminate protein coronas. It can be therefore believed that this advanced strategy can promote the advancement of nanotheranostics.

**Acknowledgments**: This work was supported by the National Natural Science Foundation of China (81371618, 81271629), Shanghai Innovation Program (14ZZ039), Program for Outstanding Young Teachers in Tongji University, and the Fundamental Research Funds for the Central Universities.



## References

[1] Wilhelm, S.; Tavares, A.J.; Dai, Q.; Ohta, S.; Audet J.; Dvorak, H.F.; Chan, W.C.W. *Nat. Rev. Mater.*, **2016**, *1*, 16014.
[2] Walkey, C.D.; Chan, W.C.W. *Chem. Soc. Rev.*, **2012**, *41*, 2780.
[3] Luk, B.T.; Zhang, L. *J. Control. Release*, **2015**, *220*, 600.
[4] Zhang, B.; Wang, X.; Liu, F.; Cheng, Y.; Shi, D. *Langmuir*, **2012**, *28*, 16605.
[5] Zhang, B.; Jin, H.; Li, Y.; Chen, B.; Liu, S.; Shi, D. *J. Mater. Chem.*, **2012**, *22*, 14494.
[6] Zhang, J.; Hao, G.; Yao, C.; Yu, J.; Wang, J.; Weitao, Y.; Hu, C.; Zhang, B. *ACS Appl. Mater. Interfaces*, **2016**, *8*, 16612.
[7] Zhang, A.; Tu, Y.; Qin, S.; Li, Y.; Zhou, J.; Chen, N.; Lu, Q.; Zhang, B. *J. Colloid Interface Sci.*, **2012**, *372*, 239.

**M. Angeles Muñoz-Fernández**

M. Angeles Muñoz-Fernández is the head of Laboratorio InmunoBiologia Molecular and of BioBanco of Hospital General Universitario Gregorio Marañón, Madrid, Spain. To date, she is the author of 356 publications in international refereed journals (h-index= 31), 4 books, 34 book chapters and 15 patents in the field of dendrimers for nanomedicine. She is the author of more than 626 communications in National and International Congresses and Principal investigator of 51 research projects. She was also involved in the creation of 2 startups (GenoMadrid SL, DendriCo SL) and 2 spin-offs (Ambiox Biotech SL and SimCosmetics Biotech SL).

[KN7]

# Proof-of-concept of new carbosilane dendrimers with dual-prevention against HIV-1/HSV-2 co-infection s topical microbicided

Mª Angeles Muñoz-Fernández[1,2,*], R. Ceña-Díez[1], P. García-Broncano[3], F.J. de la Mata[4], R. Gómez[4] & J.L. Jiménez[2]

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A safe and effective prophylactic vaccine for HSV-2/HIV-1 remains elusive. The vulnerability of women to the HSV-2/HIV-1 co-infection due to cultural/social aspects does not provide women power to negotiate the use of a condom, discuss fidelity with their partners or leave risky relationships. The development of new prevention strategies aimed at halting the spread of HSV-2/HIV-1 in regions such as sub-Saharan Africa are clearly needed. One of these strategies includes the development of safe, effective, and low-priced topical microbicides that should prevent the HSV-2/HIV-1 entry and maintain the integrity of the vaginal epithelial barrier. The field of nanotechnology, specifically dendrimers, plays an important role in addressing this challenge. The generations of polyanionic carbosilane dendrimers with silicon atom core, (G1-S4 generation zero, 4 sulphate end-groups) and G2-S16 (1st-generation, 16 sulfonate end-groups) have showed a potent and broad-spectrum anti-HIV-1/HSV-2 activity *in vitro* and *in vivo*. Thus, when applied intravaginally to h-BLT mice 3% G2-S16 gel protected against the R5-HIV-$1_{JR-CSF}$ vaginal transmission in 84%. Topical 3% G2-S16 and 3% G1-S4 proved capable to prevent the HSV-2 infection vaginally at 100% and 90% in female BALB/c mice, respectively. No irritation or inflammation processes were detected in female mice after seven consecutive doses vaginally. G2-S16 and G1-S4 prevented the rectal HSV-2 transmission over 90% in BALB/c mice. Our results suggest that G1-S4 and G2-S16 exert anti-HSV-2/HIV-1 activity at early stages of the viral replication inactivating the virus, blocking the adsorption, and the HSV-2/HIV-1 entry. We showed that dendrimers are active against semen-exposed HIV-1 particles, which their infectivity has been enhanced by the presence of amyloid fibrils of semen.

Our study represents the first demonstration indicating that HIV-1 vaginally infects humanized BLT mice and that transmission of the virus can be efficiently blocked by vaginally applied G2-S16. Our results indicate that polyanionic carbosilane dendrimers have an excellent potential to prevent the vaginal transmission of HSV-2/HIV-1. These results provide strong experimental evidence in the development of dendrimers based topical microbicides to prevent vaginal the HSV-2/HIV-1 transmission in humans.



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**Ana Paula Pêgo**

Ana Pêgo got her Ph.D. in Polymer Chemistry and Biomaterials from the University of Twente, the Netherlands, in 2002. In 2003 she became a researcher at INEB where she is a Principal Investigator since 2012. She is the Coordinator of the nBTT - nanoBiomaterials for Targeted Therapies Group and leader of the nanoBiomaterials for Neurosciences team. By using nanomedicine strategies, her team aims at providing *in situ* and in a targeted manner the required signals to promote nervous tissue regeneration. The research on new biomaterials for application in neurosciences includes the development of new polymers for the design of alternative vectors to viruses for efficient nucleic acid delivery and preparation of nerve grafts for spinal cord injury treatment. Societal and ethical issues that concern Regenerative Medicine and NanoMedicine are also a topic in which Ana Pêgo is involved. She has been appointed the Scientific Director of the Bioimaging Centre for Biomaterials and Regenerative Therapies of INEB, and she is, an Invited Associate Professor at the Instituto de Ciências Biomédicas Abel Salazar (ICBAS) and at the Faculty of Engineering of the University of Porto. To date, she is the author of 58 publications in international refereed journals (h-index= 21; total number of citations = 1582 – source: SCOPUS, November 2016), 3 book chapters and 2 patents. She is also the author of more than 100 communications in international scientific events.

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[KN8]

# BDNF gene therapy vectorized by neuron-targeted nanoparticles is neuroprotective in the context of nerve injury

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The application of biomaterials in neurosciences has given so far a substantial contribute to the development of implantable and interfaceable devices dedicated to the restoration of a number of neural functions. But the use of biomaterials in the context of nervous system regenerative medicine is still in its infancy. We have been dedicated to using nano-enabled solutions to the design of new therapeutic approaches towards the enhancement of the process of nerve regeneration.

In this presentation we put forward a novel non-viral biomaterial-based nanoparticle for neuron-targeted retrograde gene delivery based on a thiol trimethylated chitosan (TMCSH). The nanoparticles were grafted with the non-toxic carboxylic fragment of the tetanus neurotoxin (HC) to allow neuron targeting, which has been confirmed by molecular recognition force spectroscopy [1]. Using a microfluidic platform we have shown the capacity of these nanoparticles to be retrogradely transported to the cell body of dorsal root ganglia neurons after a peripheral administration. Finally, the performance of this targeted nanoformulation to deliver therapeutic genes to peripheral neurons and rescue them from degeneration was explored *in vivo,* in a peripheral nerve crush injury animal model, using as therapeutic transgene a plasmid DNA encoding for the brain-derived neurotrophic factor (BDNF). Using this animal model, in which nerve degeneration and regeneration occurs in a well-established cascade of events, we were able to establish the effect of the proposed nanoparticles in protecting peripheral nerves from degeneration, enhancing the speed of nerve regeneration and functional recovery.



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## References

[1] Oliveira, H.; Rangl, M.; Ebner, A.; Mayer, B.; Hinterdorfer, P.; Pêgo, A.P. *Small*, **2011**, *7*, 1236.

**Serge Mignani**

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[KN9]

# Nanotechnologies in general and phosphorus dendrimers in particular to treat cancers. Current situation and next steps

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The main objective of nanomedicine research is the development of nanoparticles as drug delivery systems or drugs per se to fight diseases, such as cancers, which are a leading cause of death within developed nations.

Nanotechnology, in particular the nanocarrier approach to drug delivery, has attracted much attention in the development of targeted anticancer therapies aimed at avoiding, for instance, the systemic toxicities of classical small molecule cytotoxic drugs. The nanotherapeutic technologies currently used and proposed for anticancer drug delivery therapies are as follows: polymer-drug conjugates, polymer micelles, liposomes, dendrons, dendrimers, mesoporous silica, albumin nanoparticles, metallic nanoparticles, chitosan nanoparticles etc.

Results from pre-clinical and clinical trials using nanoparticles are encouraging, suggesting that nanoparticles provide opportunities to design and tune particular properties of drugs. Such interventions are not possible with other types of therapeutics and have thus fueled much enthusiasm with regards the wealth of opportunities afforded by this emerging field of nanoscience in oncology.

The focus of this presentation will be analyzing the current challenges and remaining issues facing this infinite armada in systematic cancer nanotherapy. The future of cancer nanomedicine will be presented and analyzed with regards nanoparticles such as original phosphorus metallodendrimers (Fe, Cu and Au) and corresponding free dendrimers developed in collaboration with the Professor J-P. Majoral (LCC, Toulouse, France). Potent anti-proliferative phosphorus (metallo)dendrimers (both solid and liquid tumors), interesting metal type tumor inhibition selectivity, good antiproliferative selectivity versus normal cell lines, and strong combination effects with several known anti-cancer agents will be presented and discussed as well original established mechanism of action.

# INVITED ORAL COMMUNICATIONS

[IOC1]

# Nanotechnology in the combat of infectious diseases: the case of Dengue and Zika

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Dengue and Zika are the fastest growing reemerging diseases to date, with more than half of the human population presently at risk [1]. Although numerous strategies have been developed over the years to hinder the spread of these two vector-borne diseases, no effective antiviral drug or vaccine that targets either the Dengue virus (DENV) or the Zika virus (ZIKV) exist. In each case, viral, vector and host factors may be considered as potential targets for therapeutic intervention in the transmission of disease.

In this work, an overview of the impact of infectious diseases on Global Health will be presented. Progress in the development of therapeutic agents targeted specifically at Dengue and Zika will be highlighted. The role of nanotechnology in the fight against these two diseases will then be discussed, with focus being placed namely on the use of nanoparticles (e. g., dendrimers [2]) as therapeutic agents (e.g., viral inhibitors, vaccines).

**Acknowledgments**: This work is supported by the Fundação para a Ciência e a Tecnologia (FCT) through the CQM Strategic Project PEst-UID/QUI/00674/2013 (CQM is a FCT National Research Unit). CSA acknowledges the Associação Regional para o Desenvolvimento da Investigação Tecnologia e Inovação (ARDITI) for a Post-doc Grant (002458/2015/132). The Bilateral Agreement between Portugal/India (FCT/DST 2013/2015-Ref 441.00) and RED CYTED 214RT0482 (Project VIHVACD) are also acknowledged.



## References

[1] World Health Organization. *WHO*, **2014**, 1.
[2] He, X.; Alves, C.S.; Oliveira, N.; Rodrigues, J.; Zhu, J.; Bányai, I.; Tomás, H.; Shi, X. *Colloids Surf., B*, **2015**, *125*, 82.

[IOC2]

# Recent advances on brain drug delivery for the treatment of neurodegenerative diseases

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Neurodegenerative diseases represent a major and growing public health burden. Currently, there are no treatments available and medications only treat symptoms, but do not retard neurodegeneration process. Phytochemicals from medicinal plants and fruits may provide protection against neurological disorders, such as Alzheimer's and Parkinson's diseases. However, these polyphenol compounds present poor bioavailability which compromises their arrival and delivery into the brain. Hence, we have been interested in developing smart nanoparticles for enhancing the bioavailability of phytochemicals and their delivery into the brain through the blood-brain barrier in a better and more effective way. This is of the utmost importance since these compounds present a large spectrum of neurological effects that can be enhanced if the delivery into the brain can be achieved.

We have been employed solid lipid nanoparticles composed of biodegradable and biocompatible lipid excipients well tolerated by the organism to load and protect polyphenols from undesired metabolism, and to facilitate blood-brain barrier crossing. Additionally, functionalization of the lipid nanoparticles with apolipoprotein E and transferrin enables their binding to receptors on brain endothelial cells, inducing the crossing of the whole nanosystem across the blood-brain barrier [1].

Transmission electron microscopy images revealed spherical and uniform nanoparticles with smooth surfaces, dynamic light scattering gave sizes under 200 nm, zeta potential around -30 mV and very high rates of polyphenols encapsulation up to 80%. hCMEC/D3 cell monolayes have been used as a model of the blood-brain barrier and results reveal a significant increase of polyphenols permeability when encapsulated in functionalized nanoparticles compared with the non-functionalized ones [2].

In summary, this work brings a novel strategy for phytochemicals specialized delivery into the brain, improving their current application as potent neuroprotective compounds.



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## References

[1] Neves, A.R.; Queiroz, J.F.; Weksler, B.; Romero, I.A.; Couraud, P-O.; Reis, S. *Nanotechnology*, **2015**, *26*, 495103.
[2] Neves, A.R.; Queiroz, J.F.; Reis, S. *J. Nanobiotechnol.* **2016**, *14*. DOI: 10.1186/s12951-016-0177-x.

[IOC3]

# Biodegradable PEG-GATGE dendritic block copolymers: synthesis and potential as siRNA vectors

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The unique structural characteristics of the dendritic nanostructures, namely globular, well-defined and very branched structure, multivalency, low polydispersity and controllable nanosize, make them into promising carriers for different bioactive molecules. Particularly relevant is their capacity to complex and protect nucleic acids (NA) in compact nanostructures (coined "dendriplexes") with application as non-viral vectors in gene therapy [1]. Despite the progress in the design of dendritic structures with enhanced features for biomedical applications, one of the main drawbacks of the most currently used dendritic formulations is their non-degradability under physiological conditions that can result in cytotoxicity/complications induced by the accumulation of non-degradable synthetic materials inside cells or in tissues [2]. Moreover, in the gene therapy field, vector stability can further hinder the intracellular release of the NA from the dendriplex, consequently leading to low transfection efficiencies [3]. Therefore, biodegradable cationic dendritic structures have been eagerly awaited. However, the development of these dendritic nanocarriers is challenging because of the undesired and/or premature degradation observed during their synthesis and/or application. This explains the still reduced number of biodegradable dendritic structures reported for specific functions in biomedicine [4].

In the present work, we describe the synthesis and characterization of a novel family of biodegradable, biocompatible, water-soluble and non-toxic PEG-GATGE dendritic block copolymers. They can be easily and efficiently functionalized with different functional groups, thus they are able to act as suitable vectors for several biomedical applications. Here, their successful functionalization with different unprotected amine groups allowed the efficient complexation and protection of siRNA and, therefore, to explore their biofunctionality as vectors of this NA. It was found that the hydrophobia of the GATGE building unit confers to these biodegradable systems a great ability to complex, protect and mediate the internalization of siRNA. Moreover, the degradable character was crucial for a better siRNA release from the dendriplexes, contributing to a significant improvement of the transfection efficiency compared to their hydrolytically stable dendritic copolymer counterparts.

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## References

[1] a) Dufès, C.; Uchegbu, I.F.; Schätzlein, A.G. *Adv. Drug Delivery Rev.*, **2005**, *57*, 2177. b) Biswas, S.; Torchilin, V.P. *Pharmaceuticals*, **2013**, *6*, 161.
[2] Jones, C.F.; Campbell, R.A.; Brooks, A.E.; Assemi, S.; Tadjiki, S.; Thiagarajan, G.; Mulcock, C.; Weyrich, A.S.; et al. *ACS Nano*, **2012**, *6*, 9900.
[3] He, C.L.; Zhuang, X.L.; Tang, Z.H.; Tian, H.Y.; Chen, X.S. *Adv. Healthc. Mater.*, **2012**, *1*, 48.
[4] Leiro, V.; Garcia, J.P.; Tomás, H.; Pêgo, A.P. *Bioconjug. Chem.*, **2015**, *26*, 1182.

[IOC4]

# Separation and purification of immunoglobulin Y (IgY) from chicken egg yolk using carbon nanotubes

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Due to the current rise of drug-resistant microorganisms, passive immunization employing antibodies has become a hot topic of research [1]. In this context, an emerging alternative consists in the investigation of antibodies existent in egg yolk (immunoglobulin Y, IgY), which play a similar biological role as traditional mammal antibodies (IgG). The use of IgY offers many advantages over mammalian antibodies, such as the large amounts that accumulate in the egg yolk (50-100 mg IgY per egg) and the reduction of painful manipulations, e.g. the stressful bleeding of animals to obtain the serum [2]. In fact, chicken IgY samples can be easily obtained by a non-invasive method based on the simple eggs collection. Several methodologies to purify IgY from the complex lipophilic egg yolk matrix have been proposed, namely ultrafiltration and precipitation with polymers or salts [3]. Nevertheless, these approaches have shown to be time-consuming and not able to provide high purification factors [3]. In this context, the extraction/purification of IgY from the water soluble proteins fraction (WSPF) of egg yolk was investigated using multi-walled carbon nanotubes (MWCNTs). The surface of MWCNTs was chemically modified through liquid phase oxidation and selective removal of oxygen-containing surface groups at different temperatures. The MWCNTs were characterized by transmission electron microscopy (TEM) and Attenuated total reflection - Fourier transform infrared (ATR – FTIR) before and after IgY purification process. At the optimised conditions, recovery yields up to 80% and purification levels up to 60% were obtained.



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## References

[1] Kovacs-Nolan, J.; Mine, Y. *Annu. Rev. Food Sci. Technol.*, **2012**, *3*, 163.
[2] Schade, R.; Staak, C.; Hendriksen, C; Erhard, M.H.; Hugl, H.; Koch, G.; Larsson, A.; Pollmann, W.; et al. *ATLA*, **1996**, *24*, 925.
[3] Meulenaer, B.; Huyghebaert, A. *Food Agric. Immun.*, **2001**, *13*, 275.

[IOC5]

# Dielectric, piezoelectric and pyroelectric properties of self-assembled diphenylalanine microtubes

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Recently, short aromatic peptides have attracted significant interest because they can spontaneously form fascinating discrete and well-ordered structures at the nanoscale: nanotubes, nanospheres, nanofibrils, and hydrogels [1]. Peptide nanotubes (PNTs) based on diphenylalanine ($NH_2$-Phe-Phe-COOH, FF) possess unique biological and physical properties such as inherent biocompatibility, high aspect ratio and remarkably rigid structure [1]. Strong piezoelectricity found recently in FF adds a new important functionality useful for the development of sensors, actuators and micromechanical systems [2]. Piezoefect was found to be surprisingly stable being strongly dependent on the chemical modifications and synthesis conditions [3]. Thus, biocompatible, lightweight and highly mechanically stable FF PNTs are an attractive material for the fabrication of future generation of resonance biosensors [4].

In this work, we report the results of our recent studies on the growth and characterization of FF PNTs by piezoelectric, dielectric, and pyroelectric methods [5-7]. A method of growth of large (mm size!) microtubes consisting of multiple PNTs was developed [5] and thus the tubes could be transferred and mounted on structured substrates. Piezoelectric properties were then evaluated either by the resonance method or by quantitative Piezoresponse Force Microscopy (PFM). We show that the entire piezoelectric matrix of diphenylalanine peptide microtubes could be measured if the proper arrangement of the tubes is constructed [6]. Piezoelectric coefficients were high comparable to those of ZnO. Low temperature phase transitions were rigorously studied by dielectric spectroscopy. Several anomalies were found in the temperature range 100-350 K accompanied by the strong dielectric relaxation. Unusual behavior of the dielectric relaxation times observed in this work was attested to the relaxation of water molecules in PNT nanochannels and their interaction with hexagonal rings via C=O groups. Pyroelectric effect in FF single PNT was also evaluated giving rise to a facile conversion of heat into electrical current [7]. The mechanism of strong piezoelectricity, pyroelectricity and dielectric relaxation in PNTs will be discussed.



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## References

[1] Adler-Abramovich, L.; Gazit, E. *Chem. Soc. Rev.*, **2014**, *43*, 6881.
[2] Kholkin, A.L.; Amdursky, N.; Bdikin, I.; Rosenman, G.; Gazit, E. *ACS Nano*, **2010**, *4*, 610.
[3] Heredia, A.; Bdikin, I.; Kopyl, S.; Mishina, E.; Semin, S.; Sigov, A.; German, K.; Bystrov, V.; et al. *J. Phys. D: Appl. Phys.*, **2010**, *43*, 462001.
[4] Bosne, E.D.; Heredia, A.; Kopyl, S.; Karpinsky, D.V.; Pinto, A.G.; Kholkin, A.L. *Appl. Phys. Lett.*, **2013**, *102*, 073504.
[5] Nuraeva, A.; Vasilev, S.; Vasileva, D.; Zelenovskiy, P.; Chezganov, D.; Esin, A.; Kopyl, S.; Romanyuk, K.; et al. *Cryst. Growth Des.*, **2016**, *16*, 1472.
[6] Vasilev, S.; Zelenovskiy, P.; Vasileva, D.; Nuraeva, A.; Shur, V.Y.; Kholkin, A.L. *J. Phys. Chem. Solids*, **2016**, *93*, 68.
[7] Bosne, E.D.; Heredia, A.; Kopyl, S.; Karpinsky, D.V.; Pinto, A.G.; Kholkin, A.L. *Appl. Phys. Lett.*, **2013**, *102*, 073504. (http://www.newswise.com/articles/pyroelectric-peptide-microtubes-turn-heat-to-electric-currents)

[IOC6]

# Anti-inflammatory effects of phosphodendrimers

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New phosphorus dendrimers have been tested for its anti-inflammatory activity to be considered as the base for the development of novel treatments for multiple sclerosis. The new molecules did not produce any toxicity on mouse cortical neurons and astrocytes even at concentrations of 10 µM indicating that no toxicity might be expected in healthy central nervous system when used as a potential treatment for multiple sclerosis. Moreover, the dendrimers did not show any toxicity on macrophages isolated from mice peritoneum or lymphocytes isolated from mice thymus. To test the anti-inflammatory properties of the dendrimers we used the LPS-stimulation of macrophages paradigm. Macrophages were isolated from the peritoneum of thyoglycolate-treated mice and stimulated with bacterial LPS (100 ng/mL). This stimulation induced a time-dependent increase in nitric oxide (NO) production due to the induction of the expression of the enzyme nitric oxide synthase (iNOS). Both iNOS induction and NO production were blocked in a dose-dependent way by the phosphodendrimers. LPS induces iNOS by promoting the translocation of the transcription factor NFkB from the macrophage cytosol to the nucleus where it promotes the expression of the iNOS gene. The phosphodendrimers markedly block LPS-induced NFkB translocation from cytosol to the nucleus in mice macrophages providing a mechanism of action for its anti-inflammatory activity. Moreover, the phosphodendrimers inhibit LPS-induced macrophage secretion of the pro-inflammatory cytokines Tumor Necrosis Factor α (TNFα) and IL-1 while preserving secretion of the anti-inflammatory cytokines IL-4 and IL-10. Taking together, these results support a potential anti-inflammatory therapeutic use of phosphorous dendrimers.



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[IOC7]

# Design of new nano-carriers based on bioinformatics analysis of protein-DNA interactions. Molecular dynamics and experimental validation

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Biomimetics, or the use of principles of Nature for developing new materials, could help Nanomedicine to solve new paradigms. One of the current challenges in Nanomedicine is the rational design of new efficient and safer gene carriers. Poly(amidoamine) (PAMAM) dendrimers are a well-known class of nanoparticle, extensively used as non-viral nucleic acid carriers, due to their positively charged end-groups. In spite of that, several factors have to be improved for their successful application in in vitro and in vivo systems, associated to the affinity for nucleic acids and at the same time, avoid cytotoxicity induction. An efficient means for rational design of dendrimers as a carrier of a particular agent involves interaction among atomic-scale studies, chemical synthesis, and biological characterization. In the search of new functional groups that could be used as new dendrimer-reactive groups, we followed a biomimetic approach, to determine the amino acids with higher prevalence in the Protein-DNA contact zone, and later, introduce them or a mixture of them as terminal groups of dendrimers, generating a new class of nanoparticle. Molecular dynamics studies of two systems: PAMAM-Arg and PAMAM- Lys were also performed in order to describe the formation of complexes with DNA. Results confirmed that the introduction of amino acids as terminal groups of a dendrimer might result in promising new gene carriers. Finally, we developed new dendrimer-based nanoparticles and we carried out nucleic acid transfection experiments showing successful results in the increase of the efficiency over commercial reagents.

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[IOC8]

# Graphene-based devices for bio-sensing platforms

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Biosensing systems became ubiquitous in recent years in the medical and biomedical fields, spanning a large range of health applications, from prognosis and/or diagnosis of diseases, to personalized medicine. The possibility of increased integration and miniaturization for mass production at economic cost of biosensor devices, with enhanced performance (specificity, sensitivity and fast response) will pave the way for yet another boost in biosensor use in clinical practice and in point-of-care/point-of-use diagnosis and therapy.

The graphene 2D carbon lattice and its electronic structure provide a surface of extreme sensitivity to electric fields and charges, thus suggesting its use for molecular detection based on electronic transducing. However, graphene high sensitivity and chemical stability comes at the cost of a poor analyte selectivity. Therefore, the fabrication of biosensors based on graphene interfaces requires surface functionalization, with the graphene being the transducing element, in case of field-effect transistors (bio-FETs), or part of the transducing element, in case of electrochemical biosensing. Here we immobilized probe molecules on CVD graphene surfaces for specific biorecognition of two important types of analytes – antigens (proteins) and DNA – in clean-room fabricated devices at the wafer scale (Figure 1).

The immuno-FET is developed by immobilization of antibodies specific to the hemorrhagic transformation of ischemic stroke. The device was able to detect the specific biomarker (MMP-9) in concentrations down to 0.1 ng/mL, for which a shift in Dirac point of up to 130 ± 10 mV in the transfer curve was measured. Compared with existing MMP-9 immunoassays our immuno-FET has similar or higher sensitivity and, because it is based on a much simpler protocol than conventional methods, has a much shorter time to diagnostic.

The nucleic acid sensor is developed by immobilization of single-stranded DNA (25 nucleotides long) on the pyrene derivative-functionalized graphene transistor channel. Hybridization with complementary DNA was detected down to 1 aM, with a saturation attained at 100 fM. Electrochemical biosensing based on microelectrode arrays (Figure 2) covered with graphene functionalized with the same DNA sequence was successful in detection in the range 5 pM to 50 nM, with the ability to detect single nucleotide polymorphism.

This results open the possibility for fabrication of sensors with high sensitivity and low cost to be used in health, environment and food industries.



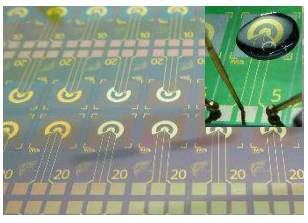

**Figure 1.** Graphene transistor chips fabricated at the wafer scale (partial view). Inset shows DUT.

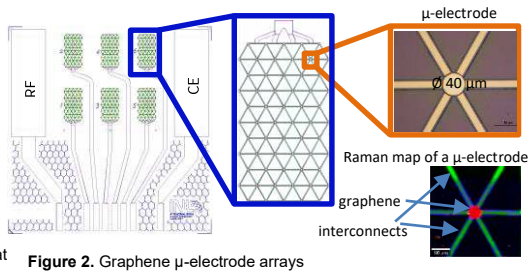


**Figure 2.** Graphene µ-electrode arrays

[IOC9]

# PEGylated polyethylenimine-entrapped gold nanoparticles for lung cancer CT diagnosis

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Gold nanoparticles (Au NPs), with high X-ray attenuation coefficient, has good potential in CT imaging application for tumor diagnosis. Here, we report the design and synthesis of polyethylene glycol (PEG)-modified branched polyethyleneimine (PEI) with different number of AuNPs inside, following acetylating the remaining surface amines of PEI for blood pool, lymph node, and lung cancer CT imaging. The molar ratio of PEI with Au NPs were set to 1:50, 1:100, 1:200, 1:300 and 1:400, respectively. The formed unacetylated PEGylated PEI-entrapped AuNPs (Au PENPs) and acetylated Au PENPs were characterized via different methods. Results show that $(Au^0)_{50}$-PEI.$NH_2$-*m*PEG has the highist X-ray attenuation coefficient with the slop of 6862.0 of fitted curve compared with other Au PENPs. Thinking of cytobiocompatibility and materials amount that used in *vivo* study, we choose $(Au^0)_{100}$-PEI.NHAc-*m*PEG with the slop of 6522.4 of fitted curve for the further study. The $(Au^0)_{100}$-PEI.NHAc-*m*PEG are cytocompatible in a given concentration range and can be used as a contrast agent for effective CT imaging of the blood pool and major organs of rats, lymph node of rabbits, and the xenografted lung cancer model of nude mice with different Au concentration. Importantly, the PEGylated Au PENPs could be excreted out of the body with time. In summary, the results from this study indicate that the formed $(Au^0)_{100}$-PEI.NHAc-*m*PEG could be a potential CT contrast agents for application in diagnosis of lung cancer.

[IOC10]

# Magnetic nanomaterials for brain cancer treatment

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Despite substantial advances in diagnosis and therapy, improvements in the survival rates of patients with malignant brain tumors have only shown modest progress within the last decade. Magnetic nanomaterials that can be precisely controlled under a magnetic field and transform the field into other forms of energy open the way for innovative cancer treatment. Magnetic field-driven mechanical destruction can be an effective approach for brain cancer treatment. In this work, the use of magnetic nanomaterials under a rotating magnetic field with ultra-low frequency induces cancer cell death. The internalized materials cause cell membrane damage and initiate programmed cell death via mechanical force *in vitro* and *in vivo* [1]. Furthermore, the combination of magnetic nanomaterials and an FDA approved neural stem cell line with their inherent tumor-tropic migratory capability, offer a novel controlled delivery system which may facilitate efficient delivery of therapeutic agents to malignant gliomas via magnetic field triggered carrier destruction [2]. Overall, the magnetic nanomaterials can be served as novel therapeutic platforms and may be translational for brain tumor treatment.



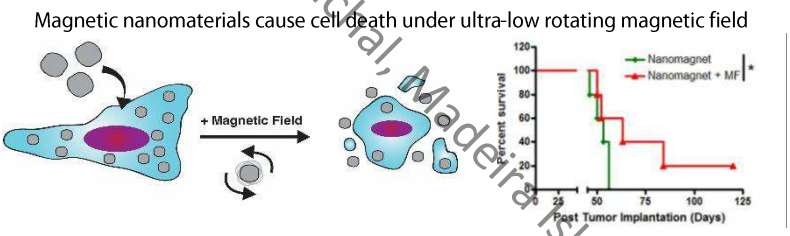


Figure 1: Schematic of magnetic nanomaterials cause cell death in vitro (left) and the in vivo therapeutic effect (right).

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## References

[1] Cheng, Y.; Muroski, M.E.; Petit, D.C.; Mansell, R.; Vemulkar, T.; Morshed, R.A.; Han, Y.; Balyasnikova, I.V.; et al. *J. Control. Release*, **2016**, *223*, 75.
[2] Muroski, M.E.; Morshed, R.A.; Cheng, Y.; Vemulkar, T.; Mansell, R.; Han, Y.; Zhang, L.; Aboody, K.S.; et al. *PLoS One*, **2016**, *11*, e0145129.

# ORAL COMMUNICATIONS

[OC1]

# Anti-*Helicobacter pylori* activity of docosahexaenoic acid loaded nanostructured lipid carriers

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*Helicobacter pylori* (*Hp*) colonize the human stomach of more than 50% of the World's population [1]. The exacerbated bacterial resistance and non-compliance to therapy of *Hp* treatment are the major reasons for the failure of antibiotic therapy usually applied [2]. Novel alternatives have been investigated such as lipophilic compounds as docosahexaenoic acid (DHA). Although, the effective effect of free DHA *in vitro* and *in vivo* against *Hp* [3], some drawbacks are needed to overcome. The aim of this work is to encapsulate DHA on biodegradable and biocompatible lipid-based drug delivery systems (Nanostructured Lipid Carriers - NLC) to improve their *Hp* activity. NLCs were selected due to theirs potential to encapsulate poorly water-soluble drugs [4].

NLCs were synthesized by hot homogenization and ultrasonication using a mixture of solid lipid/liquid lipid/stabilizer [5]. Efficiency studies were performed by *Hp* J99 growth with NLCs during 24h and colony forming units (CFU) counting. *Hp* morphology was evaluated by SEM and TEM. Cytotoxicity of NLCs towards a gastric carcinoma cell line (MKN45) was performed using LDH and MTT assays.

DHA-loaded NLC with 302±14 nm of diameter and negative charge (around -28mV) was successfully developed with a DHA entrapment efficiency of 66%. This DHA-loaded NLC has a bactericidal activity against *Hp* J99, in a dose-dependent manner. DHA incorporation into NLCs greatly improves its bactericidal activity, since DHA-loaded NLCs, even at very low concentrations (25 µM) are bactericidal against *Hp* in opposite to free DHA that was only bactericidal at concentrations around 500µM. The interaction of DHA-loaded NLC with *Hp* leads to the disruption of bacterial membrane and leakage of cytoplasmic content. Furthermore, at bactericidal concentrations, these NLCs are not cytotoxic to human gastric adenocarcinoma cells. Our findings suggest that DHA-loaded NLC may be used as an antibacterial nanotherapeutic or an adjunct agent in *Hp* infection treatment.

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## References:

[1] Wroblewski, L.; Peek, R.M. Jr; Wilson, K.T. *Clin. Microbiol. Rev.*, **2010**, *23*, 713.
[2] Vakil, N. Am. *J.* Gastroenterol., **2006**, *101*, 497.
[3] Correia, M.; Michel, V.; Matos, A.; Carvalho, P.; Oliveira, M.J.; Ferreira, R.M.; Dillies, M-A.; Huerre, M.; et al. *PloS One*, **2012**, *7*, e35072.
[4] Beloqui, A.; Solinís, M.A.; Rodríguez-Gascón, A.; Almeida, A.J.; Préat, V. *Nanomedicine*, **2016**, *12*, 143.
[5] Neves, A.R.; Lúcio, M.; Martis, S.; Lima, J.L.C.; Reis, S. *Int. J. Nanomedicine*, **2013**, *8*, 177.

[OC2]

# DNA/PAMAM dendrimer gel-like films as potential drug delivery platforms

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DNA and poly(amidoamine) (PAMAM) dendrimers have been used together in several scientific fields for a broad range of applications, mostly due to DNA's well known molecular recognition properties and negative charge. Due to their physical and chemical structure, as well as positive charge, PAMAM dendrimers allow the interaction with other molecules, either by covalent bonding or self-assembly [1]. Because of their opposite charges, self-assembly is achievable between DNA and PAMAM dendrimers. Indeed, complexation between them established by electrostatic interactionshas been used as a model of DNA-histone interactions in nucleosomes [2]. Here, we report a gel-like hybrid film based on salmon's double stranded DNA and PAMAM dendrimers only formed under specific experimental conditions (temperature program, pH, ionic strength, amine/phosphate (N/P) ratio and DNA size). Several PAMAM dendrimer generations (3, 4, 5) were used and were successfull in film preparation. The films have been characterized in terms of composition (the presence of DNA and PAMAM dendrimers was confirmed), zeta-potential (positive), scanning electron microscopy (interconnected granular structures were revealed), and circular dichroism signal (an intense peak at ≈ 300nm reflected a strong chirality response - a case of gelation-induced supramolecular chirality) [3]. The amount of DNA included in the film was generation-dependent and stability studies revealed a negligible DNA release over time, which was dependent on PAMAM generation and serum content. Otherc ationic polymers (chitosan lactate, poly(allylamine) hydrochloride and poly(ethylenimine) (PEI) were also tested for film formation, being PEI the only successful polymer for this purpose, probably due to its branched structure similar to PAMAM. Drug loading and release studies were performed with the prepared hybrid films using doxorubicin (DOX). The loading capacity was independent of the polymer used in film preparation (loading efficiency ≈ 85%). DOX release was sustained in water, PBS or serum containing medium, while a burst release was observed in serum-free cell culture medium. The results show that these films may have a great potential as drug delivery platforms.



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## References

[1] Patel, H.N.; Patel, P.M. *Int. J. Pharm. Bio. Sci.*, **2013**, *4*, 454.
[2] Huang, Y.C.; Su, C.J.; Chen, C.Y.; Chen, H.L.; Jeng, U.S.; Berezhnoy, N.V.; Nordenskiöld, L.; Ivanov, V.A. *Macromolecules*, **2016**, *49*, 4277.
[3] Duan, P.; Cao, H.; Zhang, L.; Liu, M. *Soft Matter*, **2014**, *10*, 5428.

[OC3]

# Ruthenium poly(alkylidenamine)-based dendrimers: Synthesis, and characterization studies

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Nanomedicine has evolved on finding new materials and drugs with increased solubility and prolonged circulation for the diagnosis and therapy of cancer, as well as for infectious diseases [1,2]. Dendrimers present promising properties for biomedical applications due to their excellent biocompatibility and good physiological stability [3].

The therapeutic properties of metals or metal complexes combined with the advantages of dendrimers (*e.g.*, improving their solubility) provide an entirely different approach to the discovery of new nanomaterials for diagnosis and therapy. The ruthenium-based compounds offer several advantages when compared with the traditional metallodrugs, such as the well-known antineoplastic chemotherapy drug *cisplatin* [4]. The main reason behind this is the fact that ruthenium compounds exhibit a diverse mode of action, tend to present less side effects than platinum compounds, and are able to mimic the behavior of iron, by binding proteins in the plasma [4].

Based on our previous experience in the field [5,6], and with the aim of developing new metallodendrimers with improved cytotoxicity and activity against HIV infection, we have drawn up, in a first step, a family of poly(alkylidenamine)-based dendrimers (generation 0 and 1) with different terminal groups including nitriles, amines, sulfonate and carboxylate. All these compounds were prepared and characterized by NMR, MS and IR techniques. In a second step, the nitrile terminal groups on the surface of the dendrimers (G0) were used to grow the dendrimer generation (G0→G1), also acting as a bridging group for the surface complexation (G1) of metal complexes such as $[Ru(\eta^5\text{-}C_5H_5)(PPh_3)_2]^+$.



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## References

[1] Hsu, H.; Bugno, J.; Lee, S.-r.; Hong, S. *WIREs Nanomed Nanobiotechnol*, **2016**. doi: 10.1002/wnan.1409.
[2] Sánchez-Rodríguez, J.; Vacas-Córdoba, E.; Gómez, R.; De La Mata, F.J.; Muñoz-Fernández, M.A. *Antiviral Res.*, **2015**, *113*, 33.
[3] Mignani, S.; Majoral, J.P. *New J. Chem.*, **2013**, *37*, 3337.
[4] Govender, P.; Riedel, T.; Dyson, P.J.; Smith, G.S. *J. Organomet. Chem.*, **2015**, *799*, 38.
[5] Jardim, M.G.; Rissanen, K.; Rodrigues, J. *Eur. J. Inorg. Chem.*, **2010**, *11*, 1729
[6] Rodrigues, J.; Jardim, M.G.; Figueira, J.; Gouveia, M.; Tomás, H.; Rissanen, K. *New J. Chem.*, **2011**, *35*, 1938.

[OC4]

# Gd-chelated poly(propylene imine) dendrimers with densely organized maltose shells for enhanced MR imaging applications

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We report the design of the fourth generation poly(propylene imine) (PPI) glycodendrimers for magnetic resonance (MR) imaging applications. The glycodendrimers were designed to have a densely organized maltose shell (MAL DS) and several tetraazacyclododecane tetraacetic acid (DOTA) ligands that were attached to the periphery of PPI dendrimers for Gd(III) chelation. We show that the formed MAL DS-modified PPI dendrimers possess good cytocompatibility and hemocompatibility in the studied concentration range. With the longitudinal relaxivity ($r_1$) of PPI-MAL DS-DOTA(Gd) (10.2 $mM^{-1}s^{-1}$), which is 3.0 times higher than that of DOTA(Gd) (3.4 $mM^{-1}s^{-1}$), the developed PPI-MAL DS-DOTA(Gd) nanocomplexes can be used as an efficient contrast agent for MR imaging of cancer cells *in vitro*, and animal aorta, renal artery, kidney, and bladder *in vivo*. Furthermore, tissue distribution studies show that the glycodendrimer/Gd complexes are able to be metabolizedand cleared out of the body at 48 h postinjection. The developed PPI-MAL DS-DOTA(Gd) may be further functionalized for MR imaging of different biological systems.

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[OC5]

# The fascinating blue fluorescence of PAMAM dendrimers

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Polyamidoamine (PAMAM) dendrimers are very well known as potential nanocarriers for drug/gene delivery and bioimaging [1]. Nevertheless, they present several limitations such as toxicity and weak fluorescence. Several approaches could be used to overlap these limitations, e.g. by decreasing/masking the number of amine groups on the surface and by labelling the dendrimer surface with fluorescent molecules. Beyond these strategies, no other approaches have been profoundly explored towards the improvement of their cytocompatibility and fluorescence properties [2].

With the aim of understanding the mechanism of fluorescence in oxidized PAMAM dendrimers and explore their properties for biological and imaging applications, different generations of pristine amine-terminated PAMAM dendrimers (G3, G4, and G5) were treated with ammonium persulfate (APS). These APS-treated dendrimers (APSG3, APSG4, and APS-G5) were studied according to their stability in solution, pH effect, *in vitro* cytotoxicity and photoluminescence.

The results show that the dendrimers treated with APS have an intense fluorescence/absorption compared to the pure PAMAM dendrimers. Solutions of these dendrimers display a blue luminescence when irradiated at 366nm which is pH and generation dependent. In the UV-vis spectra, the maximum absorbance increases with the generation, and the fluorescence intensity decreases. Regarding to cell viability tests, the APS treated PAMAM dendrimers are less cytotoxic than pure PAMAM dendrimers, probably because of the modification of the surface groups. Photoluminescence studies on solid state reveal that APS treated dendrimers present similar emission spectra independently of the generation, but also that the emission at 480 nm is more intense than in the dendrimer precursors. Furthermore, in solution, the emission of APSG3, APSG4, and APSG5 samples is orders of magnitude stronger than that of the non-APS treated dendrimers.

Our results indicate that it is possible to enhance the fluorescence of PAMAM dendrimers without using fluorescent probes and simultaneously reduce their toxicity. The current work is being validated, and other studies are being performed for drug delivery and imaging



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## References

[1] Gonçalves, M.; Maciel, D.; Capêlo, D.; Xiao, S.; Sun, W.; Rodrigues, J.; Shi, X.; Tomás, H.; et al. *Biomacromolecules*, **2014**, *15*, 492.
[2] Kesharwani, P.; Jain, K.; Jain, N.K. *Prog. Polym. Sci.*, **2014**, *39*, 268.

[OC6]

# In vitro effects of PAMAM dendrimers on cells using $^{1}$H NMR metabolomics

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Cancer is one of the leading causes of death worldwide, affecting the lives of millions of people, having huge psychological, economic and social impact in our society. As such, there is a need to develop new and innovative technologies for its early detection and treatment. Nanotechnology can provide innovative approaches for cancer therapy and imaging. In this context, dendrimers are being studied as drug/gene deliver vehicles, as well as carriers for molecules/chemical groups and/or inorganic particles used as contrast agents in medical imaging. Indeed, dendrimers can target solid tumor sites through the enhanced permeability and retention effect and also by active targeting after adequate chemical functionalization [1]. However, the cellular effects of dendrimers should be carefully analysed and understood before their *in vivo* application, which include their metabolic consequences, a subject scarcely explored in the literature.

The aim of this project is the assessment of the *in vitro* cellular effects of polyamidoamine (PAMAM) dendrimers in order to understand their mechanism of action and guarantee that their use in the biomedical field is non-dangerous. As such, the metabolic changes induced by PAMAM dendrimers on cells cultured *in vitro* were monitored by $^{1}$H NMR metabolomics comparing the results between treated and untreated cells (the NIH 3T3 cell lines were used). Analyses were performed on complete spectral data, as well as quantified metabolic data in intracellular and extracellular media, leading to the determination of the most significantly affected metabolites. Our preliminary results show changes in the metabolic profiles in extracellular medium as well as in the intracellular one, due to PAMAM dendrimer exposition. Aditionally, the analysis of the metabolic profiles demonstrated the power of NMR metabolomics as a tool for molecular profiling of nanomaterials' effects onn cells.



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## References

[1] Leiro, V.; Garcia, J.P.; Tomás, H.; Pêgo, A.P. *Bioconj. Chem.*, **2015**, *26*, 1182.
[2] Lefort, N.; Brown, A.; Lloy, V.; Ouellette, R.; Touaibia, M.; Culf, A.S.; Cuperlovic-Culfa. M.J. *Pharmaceut. Biomed. Analysis*, **2014**, *93*, 77.

[OC7]

# Laponite®/alginate based materials: evaluation of two different strategies for doxorubicin delivery

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During the last decades, a complex variety of materials, both natural and synthetic, have been studied as delivery systems for drugs and/or genes. For this purpose, materials must fulfill several features, such as low toxicity, biodegradability, high drug loading efficiency, water solubility and easy administration. Alginate (AG), which is a natural anionic polysaccharide with favorable properties for medical application (namely, relatively low cost, low toxicity, and mild gelation processes), alone or combined with other materials, has been applied in this scope [1]. Nevertheless, drug loading efficiencies and sustained release capacities still need to be improved in these systems, as well as their stimuli-responsiveness properties [2]. Laponite® (LP), a type of synthetic clay which presents a nanodisk structure (25 nm in diameter and 0.92 nm in thickness), has an unusual chemical arrangement, presenting a negative charge at its surface and a positive one at its edges. This particular characteristic, together with its biocompatibility, bioactivity, and degradability, makes LP a good candidate for application in drug delivery [3]. Over the last 30 years, doxorubicin (Dox) has been extensively used to treat several types of cancer, although it induces toxicity to major organs [4]. Here we present two different strategies based on AG and LP for the effectively delivery of Dox but aimed at minimizing its side effects. The first one consisted in a degradable macroscopic AG/LP/Dox hybrid hydrogel crosslinked with calcium ions for the local delivery of Dox [5]. The degradation of this hydrogel gave rise to nanohybrid particles that were able to penetrate in cancer cells and serve as shuttles for the drug. The second one involved the direct preparation of nanohybrids (aimed at being administrated by intravenous injection) by, first, adsorbing Dox on LP nanodisks through electrostatic interactions, and then coating the system with AG to avoid the burst release of the drug [6]. Both approaches were easy to implement, conducted to sustained drug delivery systems, and resulted in a high accumulation of Dox inside CAL-72 cells that led to significant cell death.



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## References

[1] Li, Y.; Rodrigues, J.; Tomás, H., *Chem. Soc. Rev.*, **2012**, *41*, 2193.
[2] Lee, K.Y.; Mooney, D.J. *Prog. Polym. Sci.*, **2012**, *37*, 106.
[3] Bonn, D.; Kellay, H.; Tanaka, H.; Wegdam, G.; Meunier, J. *Langmuir*, **1999**, *15*, 7534.
[4] Tacar, O.; Sriamornsak, P.; Dass, C.J. *Pharm. Pharmacol.*, **2013**, *65*, 157.
[5] Gonçalves, M.; Figueira, P.; Maciel, D.; Rodrigues, J.; Shi, X.; Tomás, H.; Li, Y. *Macromol. Biosci*, **2014**, *14*, 110.
[6] Gonçalves, M.; Figueira, P.; Maciel, D.; Rodrigues, J.; Qu, X.; Liu, C.; Tomás, H.; Li, Y. *Acta Biomater.*, **2014**, *10*, 300.

# POSTER COMMUNICATIONS

[PC1]

# Nano based ceramic devices for dental application a new approach

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Ceramics are widely used in dentistry. The oxide ceramics based on alumina and/ or zirconias are real substitutes for metal frame structures. Based on their high stiffness, high E-modulus and in case of tetragonal phase stabilized zirconia the high fracture toughness the possibility appears with the same dimensions as for metal frames ceramic based structure in dental laboratories to produce and to apply in the mouth of the patient. But there are some other problems concerning the bonding stability between core and cover ceramic and between core ceramic and cement. Using nano particle sized zirconia and alumina powder and powder from feldspar it seems to be possible to overcome this lack. BY application of the EPD technique it is possible to produce well reproducible structured 3D forms, like dental crowns, with a layered structure. This system allows adhering feldspar ceramic to bond onto the surface without chipping under load and to roughening the inner surface for improving the bonding strength to the cement. Based on this technique the bond strength between core ceramic and cover ceramic can increase by 40% which reduce the chipping rate and improve the life time of such dental construction. Interesting is that such layered systems working with a high effectiveness obviously some critical parameter as the CTE are not identically. Besides the interface between the layers are impressed as very tough and well connected obviously the particle size of the powders are not the same and the residual grain size is even not equal. Summarized, the application of ceramic layered structures are possible and shows interesting structure features which support the application in dentistry.

[PC2]

# PAMAM dendrimers as a platform for the preparation of low-generation of ruthenium metallodendrimers

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Dendrimers with different terminal groups as well conjugated with a variety of ligands at their periphery could have therapeutic, biomedical and diagnostic applications [1].

The goal of this work was, to synthetize and characterize, new PAMAM dendrimers based: G0/G1-CN, G0/G1-CNRu($\eta^5$-$C_5H_5$)($PPh_3$)$_2$, G0/G1-$CO_2{}^tBu$ and G0/G1-OH. The polynitrile dendrimer – G0-$(CN)_4$ – synthetized from the G0-PAMAM, was used as the precursor for the synthesis of the nitrile ruthenium based metallodendrimer G0-(CNRu($\eta^5$-$C_5H_5$)($PPh_3$)$_2$)$_4$. Ruthenium complexes proved to be a promising alternative to the clinically used platinum antitumor metallodrug [1, 2]. The preparation of these dendrimers was accomplished by adapting the reported methodology developed by us[3] and their characterization was performed by $^1H$ and $^{31}P$-NMR and FTIR structural techniques. The synthesis and characterization of similar compounds – G1-$(CN)_8$ and G1-(CNRu($\eta^5$-$C_5H_5$)($PPh_3$)$_2$)$_8$ – with the double of nitrile and ruthenium moieties as terminal groups, is on ongoing.

The hydroxyl compounds G0-$(OH)_8$ and G1-$(OH)_{16}$, were synthetized from the G0-$(CO_2{}^tBu)_8$ and G1-$(CO_2{}^tBu)_{16}$, respectively. The applied synthetic strategy was adapted from the reported methodology of N. Jayaraman et al. [4,5] and the techniques used for the characterization of each dendrimer were the $^1H$ and $^{13}C$-NMR, FTIR, MS and elementary analysis. These hydroxyl moieties can be the precursors for the preparation of novel low generation acetylide ruthenium based metallodendrimers having in view the comparison of the anticancer activity of these compounds with the already prepared nitrile ruthenium based metallodendrimers G0/G1-(CNRu($\eta^5$-$C_5H_5$)($PPh_3$)$_2$).



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## References

[1] Rodrigues, J.; Jardim, M.G.; Figueira, J.; Gouveia, M.; Tomás, H.; Rissanen, K. *New J.* Chem, **2011**, *35*, 1938.
[2] Aderibigbe, B.A. *J. Inorg. Organomet. Polym.* **2015**, *25*, 339.
[3] Jardim, M.G.; Rissanen, K.; Rodrigues, J. *Eur. J. Inorg. Chem,* **2010**, *11*, 1729.
[4] Krishna, T.R.; Jayaraman, N. *J. Org. Chem.*, **2003**, *68*, 9694.
[5] Jayamurugan, G.; Jayaraman, N. *Tetrahedron*, **2006**, *62*, 9582.

[PC3]

# Functionalized magnetic nanoparticles for the purification of immunoglobulin Y (IgY)

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Due to the actual emergence of antibiotic-resistant pathogens, the application of antigen-specific antibodies in passive immunotherapy represents an imperative reality in the near future. In addition to the more investigated mammal antibodies, antibodies from egg yolk (IgY) can be obtained in higher titres and by non-invasive methodologies [1]. Up to date, several methods, such as precipitation, dialysis, ultrafiltration and chromatography are available for IgY purification [2]. Nevertheless, the production cost of IgY still remains higher than other drug therapies due to the lack of cost-effective purification techniques. The development of a cost-effective and scalable new strategy for the purification of IgY is thus in high demand and will have a high impact in economics and human health. In this work, a new platform for the purification of IgY using amino functionalized magnetic nanoparticles (AFMN) was investigated. Magnetic nanoparticles ($Fe_3O_4$) were synthesized, coated with silica and functionalized with amino groups [3], and also characterized in terms of their morphological, chemical and structural features. The immunoglobulin extraction assays with magnetic particles were carried out envisaging the development of a new method of purification, and where extraction yields up to 93% and purification levels up to 94% have been obtained.

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## References

[1] Kovacs-Nolan, J.; Mine, Y. *Annu. Rev. Food Sci. Technol.*, **2012**, *3*, 163.
[2] Li, B.; Zou, X.; Zhao, Y.; Sun, L.; Li, S. *Mater Sci Eng C Mater Biol Appl.* **2013**, *33*, 2595.
[3] Girginova, P.I.; Daniel-da-Silva, A.L.; Lopes, C.B.; Figueira, P.; Otero, M.; Amaral, V.S.; Pereira, E.; Trindade, T. *J. Colloid Interface Sci.*, **2010**, *345*, 234.

[PC4]

# Capture of circulating tumor cells using gelatin/laponite® nanofibers

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Circulating Tumor Cells (CTCs) detection in blood is nowadays considered a biomarker of cancer and metastasis, thus being very important for the understanding, diagnostic, monitoring and treatment of cancer (namely for the development of personalized therapies). However, among other limitations, the current technologies to isolate and characterize CTCs suffer from low yield and selectivity [1]. The main goal of this work is to develop a new system for the capture and subsequent proliferation (for later molecular characterization) of CTCs based on a nanocomposite cell trap consisting of gelatin nanofibers reinforced with the synthetic nanoclay - Laponite®. On the one hand, nanofibers have a structure that resembles the natural extracellular matrix [2] with a large surface area/volume ratio, as well as high porosity, and so can be a good substrate for cell adhesion. On the other hand, gelatin is a natural, biocompatible and biodegradable polymer that has origin in collagen and thus may also provide chemical interaction between nanofibers and cells. Furthermore, Laponite® may improve the overall efficiency of the system by affecting the morphology and the mechanical properties of the nanofibers. Indeed, it is reported that nanoroughened surfaces may increase the capture of CTCs in substrates without antibodies usually used for their recognition [3].

Gelatin nanofibers with and without 5% (w/w) of Laponite® were then prepared using the electrospinning technique [4] and characterized by contact angle measurement, FTIR spectroscopy, SEM and EDX spectroscopy. Different experimental conditions were used, namely gelatin concentration, and electrospinning deposition time. Mats containing fibers with a nanoscale diameter were always successfully obtained. Preliminary results using NIH 3T3 cells and assessed through a metabolic activity assay revealed that the initial cell attachment was similar for all fiber substrates, but also that cell growth was higher for fibers prepared with 300 mg/mL gelatin solutions, independently of Laponite®'s presence. However, mats prepared with a gelatin concentration of 400 mg/mL were more homogeneous in terms of morphology.



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## References

[1] Yoon, H.J.; Kozminsky, M.; Nagrath, S. *ACS Nano*, **2014**, *8*, 1995.
[2] He, C.; Nie, W.; Feng, W.J. *Mater. Chem. B*, **2014**, *2*, 7828.
[3] Chen, W.; Weng, S.; Zhang, F.; Allen, S.; Li, X.; Bao, L.; Lam, R.H.W.; Macoska, J.A.; et al. *ACS Nano*, **2013**, *7*, 566.
[4] Bhardwaj, N.; Kundu, S.C. *Biotechnol. Adv.*, **2010**, *28*, 325.

[PC5]

# Hyaluronic acid-modified dendrimer entrapped gold nanoparticles for cancer cell targeting and detection

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Nanoparticles (NPs) have become increasingly important in a wide range of biomedical applications (e.g., drug delivery, disease diagnosis) as they display properties including reduced cytotoxicity and side effects [1]. Poly(amidoamine) (PAMAM) dendrimers are considered as perfect templates because of their nanoscale size, controlled shape, well-defined composition, symmetric dimension and monodisperse distribution [2]. These unique features have allowed for their use as templates or stabilizers to prepare inorganic NPs [3]. Moreover, modification of the terminal groups of PAMAM dendrimers with targeting molecules, imaging agents or drugs has allowed for alternative approaches to those conventionally used in medicine in the diagnosis and treatment of cancer [3].

With the aim of developing probes for targeted computed tomography (CT) of CD44 receptor-overexpressing cancer cells, hyaluronic acid (HA)-modified dendrimer entrapped gold nanoparticles (AuNPs) were prepared in this work. AuNPs, which have been used as contrast agents for X-ray CT imaging due to their strong X-ray attenuation characteristics [4], were entrapped in amine-terminated generation 5 PAMAM dendrimers ($G5.NH_2$). The formed dendrimer-entrapped AuNPs (Au DENPs) were then functionalized with HA, a high molecular weight glycosaminoglycan frequently used as a drug carrier and a ligand on NPs to target CD44 receptor-overexpressing cells [5]. The formed HA-modified Au DENPs were characterized using $^1$H NMR spectroscopy, dynamic light scattering, zeta potential measurements and UV-Vis spectroscopy. Preliminary studies were also performed to test the cytotoxicity of the prepared NPs on HEK293T and MCF7 cells.



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## References

[1] De Jong, W.H.; Borm, P.J.A. *Int. J. Nanomedicine*, **2008**, *3*, 133.
[2] Shan, Y.; Luo, T.; Peng, C.; Sheng, R.; Cao, A.; Cao, X.; Shen, M.; Guo, R.; et al. *Biomaterials*, **2012**, *33*, 3025.
[3] Guo, R.; Wang, H.; Peng, C.; Shen, M.; Pan, M.; Cao, X.; Zhang, G.; Shi, X. *J. Phys. Chem. C*, **2010**, *114*, 50.
[4] Xu, C.; Tung, G.A.; Sun, S. *Chem. Mater.*, **2008**, *20*, 4167.
[5] Platt, V.M.; Szoka, F.C. *Mol. Pharm.*, **2008**, *5*, 474.

[PC6]

# DNA delivery and intracellular imaging nano platform based on fluorescent carbon dots and PAMAM dendrimers

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Carbon dots are small carbon nanoparticles that were first discovered by Xu *et al.*[1] in 2004 and described as carbon quantum dots in 2006 by Sun *et al.*[2] Carbon nanodots (CNDs) and carbon quantum dots (CQDs) have a quasi-spherical shape with a size range between 1-10 nm. CNDs and CQDs are organized in distinct structures; CNDs have an amorphous carbon structure while CQDs present a crystalline structure with $sp^2$ hybridization, both have surface functional groups such as: carboxyl (COOH), hydroxyl (OH) and amino groups ($NH_2$).[3] They present very interesting properties, *e.g.* good photostability, low cytotoxicity, surface functionalization, water solubility and high quantum yields when compared to other fluorescent molecules.[4] The combination of fluorescent carbon dots with PAMAM-$NH_2$ dendrimers is not so extensively studied, therefore the conjugation between them presents interesting properties for biomedical applications. In this work, preliminary results on the preparation of CNDs synthesized by using starting materials that are rich in carbon, oxygen, hydrogen and nitrogen content, such as: citric acid, ascorbic acid, oxaloacetic acid, 1,3,5-tricyanobenzene and 1,6-hexanediamine and characterized by DLS, UV-vis, Fluorescence spectroscopy, and FTIR will be presented.

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## References

[1] Xu, X.; Ray, R.; Gu, Y.; Ploehn, H.J.; Gearheart, L.; Raker, K.; Scrivens, W.A.; *J. Am. Chem. Soc.* **2004**, *126*, 12736
[2] Sun, Y-P.; Zhou, B.; Lin, Y.; Wang, W.; Fernando, K.A.S.; Panthank, P.; Jaouad, M.; Harruf, B.A.; Wang, X.; Wang, H.; Luo, P.G.; Yang, H.; Kose, M.E.; Chen, B.; Veca, L.M.; Xie, S-Y.; *J. Am. Chem. Soc.* **2006**, *128*, 7756
[3] Cayuela, A.; Soriano, M.L.; Carrillo-Carrión, C.; Valcárcel, M.; *Chem. Commun.*, **2016**, 52, 1311
[4] Kozak, Q.; Sudolska, M.; Dramarik, G.; Ciglu, P.; Otyeka, M.; Zboril, R.; *Chem. Mat.*, **2016**, *28*, 4085

[PC7]

# Development and characterization of electrochemical biosensors based on PAMAM dendrimers

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This project aims the development of an electrochemical biosensor based on PAMAM dendrimers for the detection of analytes of biological nature. Dendrimers are macromolecules known for their controllable size, molecular uniformity, surface functionality and high stability [1-3]. Additionally, dendrimers are an ideal matrix for the immobilization of biomolecules [1], not affecting its activity towards analytes. The resource to self-assembled monolayers is one of the used approaches for the attachment of dendrimers to the electrode's surface [1]. To enhance the sensor's sensibility, conductive moieties such as gold nanoparticles could be used as well. These metal nanoparticles are particularly reported as innocuous towards most biomolecules and effective as conductivity enhancers [4-5].

In this work, it is presented the step-by-step modification of gold and glassy carbon electrodes in order to fabricate an electrochemical biosensor based on PAMAM dendrimers. After each modification step, the characterization of the modified electrode will be accomplished with a resource to electrochemical techniques, and to microscopic techniques. In this effort, it will be experimented the self-assembly of adequate molecules which could actuate as a linker between the electrode surface and the PAMAM dendrimers. It will also be analyzed the effect of deposition of gold nanoparticles on the biosensor performance.

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## References

[1] Satija, J.; Sai, V. V. R.; Mukherji, S. J. Mater. Chem., 2011, 21, 14367.
[2] Hasanzadeh, M.; Shadjou, N.; Eskandani, M.; Soleymani, J.; Jafari, F.; Guardia, M. de la. Trends Anal. Chem., 2014, 53, 137.
[3] Zhu, C.; Yang, G.; Li, H.; Du, D.; Lin, Y. Anal. Chem., 2015, 87, 230.
[4] Cao, X.; Ye, Y.; Liu, S. Anal. Biochem., 2011, 417, 1.
[5] Li, N. B.; Kwak, J. Electroanalysis, 2007, 23, 2428.

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