

**CRS FOCUS GROUP IN
NANOMEDICINE AND NANOSCALE DELIVERY**

2ND EDITION

MEMBER FEATURE ARTICLES



NANOMEDICINE AND
NANOSCALE DELIVERY





ANDREIA ALMEIDA

i3S – Institute for Research and Innovation in Health Sciences, University of Porto



@almeidaandreia



andreiamsalmeida



INTRODUCE YOURSELF

I am a PhD student at Institute for Research and Innovation in Health Sciences (i3S) finishing my last year and, hopefully, defending my thesis this year!

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

I am a Master of Science in Biomedical Engineering by the Faculty of Engineering, University of Porto (FEUP, Portugal), where I successfully concluded my studies in 2016. My experience has been enlarged since the beginning of the master's program, where I worked in the development of a chitosan-polycaprolactone copolymer to produce polymeric micelles to encapsulate anticancer bioactive molecules for mucosal delivery. I had the opportunity to work with therapeutic polymers for drug delivery and controlled delivery of drugs across biological barriers; new materials for nanoparticles production for drug delivery systems; physical and chemical characterization of pharmaceutical dosage forms; cell culture experience in in vitro models of drug bioavailability, cytotoxicity techniques, and permeability studies. Then, I started my PhD in Biomedical Sciences in collaboration with Vall d'Hebron Research Institute (ES) and, also conducted three short-term scientific missions at Technion - Israel Institute of Technology (IL), University of Seville (ES) and, MJRPharmaJet Industry (DE).

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

The main focus of my PhD project is to design a new chitosan amphiphilic derivative with the ability to form micelles by self-assembly. These polymeric micelles can efficiently encapsulate hydrophobic molecules, as many anticancer drugs, to improve their solubility and oral bioavailability. I have extensively improved my expertise on physico-chemical characterization of polymers, as well as in in vitro cell culture studies as cell viability and intestinal permeability of molecules. Later, I have been working with colorectal cancer animal models, either by cell xenografts or by chemical induction, to study the therapeutic efficacy and safety of my nanosystem.

CURRENT RESEARCH INTERESTS

My current research interests are the design of polymeric micelles, in vitro and in vivo colorectal cancer models for drug delivery, as 3D spheroids or, chemically induced animal models.

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

Since I started in the nanomedicine field during my master's, I got passionate about the beautiful systems we can construct and have a good final outcome at the end. Thus, I continue my career by starting a PhD in this field.

SELECT YOUR BEST PAPER IN NANOMEDICINE

Almeida A., Araújo M., Novoa-Carballal R., Andrade F., Gonçalves H., Reis R.L., Lúcio M., Schwartz S., Sarmento B., Novel amphiphilic chitosan micelles as carriers for hydrophobic anticancer drugs. Materials Science and Engineering C 112;, 2020.

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

I think the nanomedicine field has facing several challenges during the last few years but has been well succeeded. Only a small minority of the systems go to clinical phases or to the market, but this is increasingly the case and I hope that this will be the trend in the future.

CHRISTOPHER M. JEWELL

Minta Martin Professor of Engineering, University of Maryland
Research Biologist, United States Department of Veterans Affairs

 @jewellbioe

 christopher-m-jewell-6702813

 <http://jewell.umd.edu/>



INTRODUCE YOURSELF

I'm a professor, engineer, & mentor at the Univ. of Maryland and U.S. Dept. of Veterans Affairs. I started my lab in 2012 and am committed to a fun, inclusive, and diverse research and training environment. Some things I love about our profession is the constantly evolving team of individuals and scientists, the fun things they say, the excitement of new data, group activities, and the infinite possibility that exists right after writing a grant! In my free time I run, hike, race cars, travel, and canoe.

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

My B.S. degrees are in Chemical Engineering and Molecular Biology (go Lehigh!). I also interned at Merck, Akzo Nobel (The Netherlands), and Proctor & Gamble, which gave me some early insight into industry. After undergrad, I completed my PhD at the University of Wisconsin – Madison with Dave Lynn in Chemical Engineering, then joined the Boston Consulting Group (BCG) Healthcare Practice in New York. At BCG I worked as a consultant in R&D strategy design and Innovation for Pharma and Biotech. One of my clients was in the immunology space, which led me to postdoctoral training in Immune Engineering with Darrell Irvine at MIT and Dan Barouch at Harvard.

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

My lab focuses on immune engineering. We are interested in nanotechnology because of the unique capabilities these technologies offer to i) study and ii) control the immune system. For example, the ability to display antigens or other signals at specific densities, or to tightly juxtapose combinations of immune signals, enables precise perturbation of immune processes and design of strong and specific responses in settings of both immunity (e.g., cancer, vaccination) and tolerance (e.g., autoimmunity).

CURRENT RESEARCH INTERESTS

Our lab has three main thrusts, all driven by integrated teams. One area focuses on understanding how nanomaterials interact with immune cells and tissues through their intrinsic immunogenic profiles. Another area uses self-assembly technologies to build nanomaterials completely from immune signals. This allows simple, rational design without need for carrier components, while maintaining attractive features of conventional nanomaterials. Lastly, our applied work focuses on therapeutic vaccines aimed at cancer and autoimmune diseases such as multiple sclerosis and type 1 diabetes.

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

When I started my lab, immune engineering was just starting to blossom; having training in both immunology and nanotechnology allowed me to quickly establish a niche with lots of tough, exciting questions that require an interdisciplinary tool-kit to study. And of course, great colleagues and strong scientists/engineers! (and fun conferences, socials, and focus groups!)

SELECT YOUR BEST PAPER IN NANOMEDICINE

R. S. Oakes, L. H. Tostanoski, S. M. Kapnick, E. Froimchuk, S. K. Black, X. Zeng, C. M. Jewell. "Exploiting Rational Assembly to Map Distinct Roles of Regulatory Cues During Autoimmune Therapy" ACS Nano 2021. (in press)

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

I think there are tremendous opportunities for translational science that considers clinical needs and constraints early in the course of a nanomedicine project. There are many very interesting, but also complicated materials presented in the literature as therapeutics; however, a large fraction of these aren't informed by real clinical needs, regulatory hurdles, and manufacturing. As these disciplines become more integrated, that will really drive success of translating nanomedicines to the clinic.



BRUNO F.B. SILVA

Staff scientist, INL – International Iberian Nanotechnology Laboratory

@BFB_Silva

bruno-silva-oa8567b/

<https://inl.int/inl-people/bruno-silva/>



INTRODUCE YOURSELF

I am a staff scientist at INL. I am a physical chemist by training, with a focus on colloids and soft matter. I did my undergraduate and PhD studies in Chemistry at the University of Porto. During the PhD I also spent a year at Lund University in Sweden. For my postdoc I received a Marie Curie fellowship to work with Cyrus Safinya at the University of California in Santa Barbara. Since 2015 I have been back in Portugal where I lead a research team in soft matter and nanotechnology for therapeutic applications.

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

During my PhD I studied the self-assembly and phase behaviour of mixtures of cationic and anionic surfactants. For my postdoc I jumped into mixtures of cationic liposomes and DNA (lipoplexes), which are also oppositely charged, but therapeutically more relevant. Electrostatic interactions, enthalpy, entropy and phase diagrams have been constant themes. For characterization I used small-angle X-ray and Neutron scattering (SAXS and SANS), which provide structural information over several length scales without needing to freeze samples. I also developed microfluidics combined with in-situ SAXS.

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

Our research revolves around lipid- and polymer-based nanoassemblies for delivery of nucleic acids. We try to understand at the fundamental level how to better control the structures of these carriers and how such structures influence therapeutic efficacy. We also build customized microfluidic devices to better control the size and structure of DNA nanocarriers, and develop new analytic methodologies that help us characterize and understand our formulations and processes. As an example, we are excited with new results in fluorescence cross-correlation spectroscopy (FCCS) that allows us to quantify the extent of association between DNA and liposomes, and answer tricky questions such as how many DNA plasmids are loaded per lipid nanoparticle. Understanding therapeutically-relevant phenomena in terms of more fundamental interactions is something that we always strive to do.

CURRENT RESEARCH INTERESTS

Lipid-nucleic acid and hybrid lipid-polymer-nucleic acid NPs (i.e. lipoplexes and lipopolyplexes); cubosomes; microfluidics; small-angle scattering for structure characterization; and fluorescence cross-correlation spectroscopy (FCCS) for quantitative colocalization in multi-component formulations.

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

The inherent interdisciplinarity of nanomedicine means that we get to work with people from different scientific backgrounds, which is excellent to keep learning from each other. This makes me a better scientist, but also gives the opportunity to establish new collaborations to address challenging topics.

SELECT YOUR BEST PAPER IN NANOMEDICINE

Gómez-Varela, A.I et al. Fluorescence Cross-Correlation Spectroscopy as a valuable tool to characterize cationic liposome-DNA nanoparticle assembly. *J. Biophotonics* 2020, doi:10.1002/jbio.202000200.

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

At the level of applications the field is booming, boosted by the creativity of a fantastic group of scientists. However, as many challenges require more complex formulations, with multiple components, the characterization becomes challenging, and more advanced methods are needed to accompany this. In my opinion this is one area that we need to start paying more attention, and something where we are trying to make a small contribution with FCCS for quantitative co-localization.

PROFESSOR YAHYA E. CHOOONARA

Wits Advanced Drug Delivery Platform Research Unit,
Department of Pharmacy and Pharmacology, Faculty of Health Sciences
University of the Witwatersrand, Johannesburg, 7 York Road, Parktown, 2193,
South Africa

 @WitsADDP

 yahyachoonara

 <https://www.wits.ac.za/waddp>



INTRODUCE YOURSELF

I am Chair and Head of Pharmacy and Pharmacology at the University of the Witwatersrand (WITS), Johannesburg, South Africa. As a Full Professor of Pharmaceutics I am also Director and Principal Researcher of the Wits Advanced Drug Delivery Platform (WADDP) Research Unit at WITS.

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

My research constitutes 5 thematic areas producing targeted medicines and tissue engineering interventions for infectious, hereditary and lifestyle illnesses: 1) advanced polymeric drug delivery systems, 2) prototyping bioactive-eluting inserts/implants (intra-ocular, -vaginal, -nasal, -cranial and spinal cord devices), 3) synthesizing stimuli-responsive biomaterials for drug delivery and tissue engineering (infectious diseases, neuro-trauma, CNS and ocular disorders, neurological/bone/ovarian cancers and wound healing), 3) applying molecular pharmaceutics to elucidate controlled release mechanisms of novel/complex therapeutic systems and 5) advancing nanomedicines constituting various nanomaterials (nano-gels, -liposomes, -wires, -fibers, -dots) for targeted chemotherapy, biomimetic tissue engineering and improving drug bioavailability (21 granted patents; >280 articles).

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

I develop nanostructures to advance drug delivery and tissue engineering platforms as therapeutic interventions mainly in the Neurosciences (spinal cord, brain and eye). In particular, using Neuro-Nano-Pharmaceutics I am able to manipulate complex biological systems to safely transport bioactives across biological barriers (i.e. Blood-Brain, -Retinal or GIT barriers), target cancer cells/tumours, repair spinal cord/brain tissue after neuro-trauma, improve drug bioavailability and enhance wound healing. My research is interdisciplinary and involves neurologists, neurosurgeons, ophthalmologist, chemists, oncologists and pharmaceutical scientists in conceptualizing various advancements in the field.

CURRENT RESEARCH INTERESTS

Novel therapeutics for Neuro-Trauma (injectable neuro-mimetic nanosplices for brain and spinal cord repair/regeneration), Glioblastoma (injectable neuro-mimetic nanogels for targeted chemotherapy), Parkinson's disease (mucro-retentive targeting nanodots for nose-to-brain delivery), Osteosarcoma (nano-enabled 3D-bioprinted osteoglu for bone regeneration), Platelet-Inspired systems (delivery of drug/clotting factors) and Infectious Diseases (bio-inspired anti-TB and -malaria nanotherapeutics).

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

Nanomedicine research on designing nano-enabled neuro-mimetic therapeutic inserts for our eyes, brain, spinal cord and bones to effectively treat debilitating illnesses has activated my thinking to the futuristic design of pharmaceuticals that are truly 'alive'.

SELECT YOUR BEST PAPER IN NANOMEDICINE

Advances in the treatment of neurodegenerative disorders employing nanotechnology, G Modi, V Pillay, YE Choonara, Ann. N.Y. Acad. Sci. 1184 (2010) 154–172.

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

Current progress in Nanomedicine is poised to make significant life changing breakthroughs for individuals suffering from debilitating CNS illnesses and neuro-trauma. Hence, the quote 'Mind-over-Matter' will soon be transformed clinically to the manic phrase of 'Matter-over-Mind'.



VALENTINA FRANCIA

Department of Clinical Chemistry and Haematology, University Medical Center Utrecht, the Netherlands

Department of Biochemistry & Molecular Biology, University of British Columbia, Canada



@ValeFrancia01



valentinafrancia

INTRODUCE YOURSELF

I am a molecular biologist, working in nanomedicine and gene therapy as a joint postdoctoral fellow between the University of British Columbia (Canada) in the nanomedicines lab of Prof. Cullis and the University Medical Center Utrecht (Netherlands) under the supervision of Prof. Schiffelers. I am Board Member and Social Media Coordinator of the CRS Canada Chapter and also Board Member, Social Media Coordinator, and Chapter Liaison of the BeNeLux & France Local Chapter. I have an interest in open science, EU policies, and scientific outreach.

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

I studied Molecular Biology at the University of Milan (Italy) from which I graduated with a thesis on the cellular mechanisms of resistance to cancer drugs. During my PhD studies at the University of Groningen (Netherlands), under the supervision of Dr. Salvati, I investigated the cellular interactions and endocytosis mechanisms of inorganic nanomaterials. Since 2019 I am working on the biological interactions of gene therapeutics based on the lipid nanoparticle technology developed in Cullis lab.

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

My research is part of the Horizon 2020 consortium "EXPERT" aimed at developing off-the-shelf mRNA nanomedicines (www.expert-project.eu). In this context, my role is to understand the biological interactions of intravenously-injected gene therapeutics. In particular, I am studying how the biomolecular corona affects the stability, organ specificity, and targeting abilities of clinically-relevant lipid nanoparticles for gene delivery. The study of these interactions can help to improve the reproducibility of nanomedicines studies, their in vivo translation, and, overall, their clinical success.

CURRENT RESEARCH INTERESTS

Currently, I am developing a separation method to study the corona of magnetic lipid nanoparticles. I am testing how these magnetic properties can help to isolate lipid nanoparticles from blood after administration and, at the same time, how they can allow us to study nanoparticle biodistribution, silencing efficacy, and interactions with the immune system.

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

As a molecular biologist, nanomedicine was almost unknown to me when I started my PhD. Working in this field opened many doors and collaborations for me, allowing me to work for and with many great scientists and mentors on state-of-the-art technologies. But most of all, nanomedicine made me discover the importance of interdisciplinary and collaboration among different fields.

SELECT YOUR BEST PAPER IN NANOMEDICINE

The Biomolecular Corona of Lipid Nanoparticles for Gene Therapy. *Bioconjugate Chem.* 2020, **31**, 9, 2046–2059,
<https://doi.org/10.1021/acs.bioconjchem.0c00366>

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

This is an exciting time for the field, since the approval of the first nanoparticle-based gene therapeutics (Onpattro) and the SARS-CoV-2 vaccines. These events increased the trust in nanomedicine and I am confident that they will pave the road for many great discoveries in the immediate future.

LEILA ARABI

Department of Pharmaceutical Nanotechnology,
School of Pharmacy, Mashhad University of Medical Sciences, Iran

 @LeilaPharmD_PhD

 leila-arabi-86047749/

 webpage



INTRODUCE YOURSELF

Leila Arabi received her Pharm.D. and Ph.D. degree (summa cum laude) from School of Pharmacy, Mashhad University of Medical Sciences (MUMS), Iran in 2009 and 2015. She had the one-year Ph.D. internship during 2012-2013 at University Hospital Basel, Switzerland. Following her visit to several labs and meetings with academics in the US and Europe, she relocated back to Iran. She is now an Assistant Professor of Pharmaceutical Nanotechnology, School of Pharmacy, Mashhad University of Medical Sciences. She is currently the Communication Chair of Immuno-Delivery Focus group and the Ambassador in Young Scientist Committee of CRS. She also serves as the Assistant Editor of Iranian Journal of Basic Medical Sciences (IJBMS).

LET US KNOW ABOUT YOUR RESEARCH BACKGROUND

As an Assistant Professor with a demonstrated history of working in the Pharmacy & health care, her goal of her research is to link the fields of Pharmaceutical Nanotechnology to cancer Biology and immunology to improve therapeutic efficacy of conventional cancer therapies in patients.

DESCRIBE YOUR RESEARCH IN NANOMEDICINE

Her research is focused on developing nanoscale drug delivery systems with particular emphasis on lipid-based nanoparticle formulation, liposomes for targeted cancer/immune cell drug delivery. She also focuses on combination therapy, tumour penetration, Theranostics, cancer stem cells, Cancer Immunotherapy, and Gene Therapy.

CURRENT RESEARCH INTERESTS

Targeted Cancer Drug Delivery, Tumor Penetration and biodistribution, Tumor Microenvironment, Combination Therapy, Cancer Immunotherapy, Vaccine delivery systems, Biopharmaceutics and Pharmacokinetics, Immunoengineering

HOW DID THE NANOMEDICINE FIELD CONTRIBUTE TO YOUR PROFESSIONAL CAREER?

She is the assistant professor with passion for teaching and research in drug delivery system development to enhance the effectiveness and reduce the toxicity of the chemotherapeutic agents

SELECT YOUR BEST PAPER IN NANOMEDICINE

- Targeting CD44 expressing cancer cells with anti-CD44 monoclonal antibody improves cellular uptake and antitumor efficacy of liposomal doxorubicin - Journal of controlled release 2015
- Doxorubicin-loaded composite nanogels for cancer treatment - Journal of Controlled Release 2020

YOUR OPINION/VIEW ON THE CURRENT PROGRESS OF THE FIELD

With more than 50 Nano-formulations in the market for the treatment of a wide range of indications, there is "hope" for nanomedicines to address real medical problems and unmet needs. The situation of the COVID-19 pandemic and the emergency need for vaccine flourished the field of nanotechnology and lipid-based nanoparticles brought the solution! It was a big step in "Transcending nanomedicine to the next level".