NANO STEM

H2020-MSCA-ITN-2017 G.A. 764958

3rd NANOSTEM

Summer School

An interactive online training event

ZOOM

Monday 5th July – Thursday 8th July 2021

Please note all times are given in CEST

Day 1: Monday 5th July 2021 (Time in CEST)

9:00 – 9:15	Welcome remarks by Prof Marie-Pierre Dehouck (UA)
9:15 – 10:45	Workshop "*How to ace your CV*" by Prof Marina Resmini (QMUL) and Dr Nazende Guenday-Tuereli (MyB)
10:45 – 11:00	**Break**
11:00 – 12:00	Career Option ITN Alumni: Dr Michela Comune, (Project Manager & Product Owner at Inpeco) and Dr Benjamin Fell (Senior Analyst at Costello Medical)
12:00 – 13:30	**Lunch Break**
13:30 – 14:30	"*The art of public speaking and how to ace your interview*" by Prof Marina Resmini
14:30 – 14:45	**Break**
14:45 – 15:45	Career Option: Dr Katrina Krämer (Chemistry World science correspondent at RSC) and Dr Marjolein Heymans (Consultant at Avertim)
15:45 – 16:00	**Break**
16:00 – 17:00	Career Option ITN Alumni: Dr Ania Servant-Jolly (Operations Manager at the Pankhurst Institute) Dr Kiran Chereddy (Program Management and Group Lead of Cell Therapy Operations at Lonza Biologics)

Day2: Tuesday 6th July 2021 (Time in CEST)

9:30 – 10:30	Theoretical Lecture: "*Novel mechanisms of neurogenesis and neural repair*" by Dr Magdalena Goetz (HMGU)
10:30 – 11:00	**Break**
11:00 – 12:00	Theoretical Lecture "*Clinical research on regeneration in the CNS"* by Dr Christopher Grigsby (KI)
12:00- 13:30	**Lunch Break**
13:30- 14:30	Theoretical Lecture: "*Pharmaceutical Quality Management System*" by Dr Benjamin Kirsch (MyB)
14:30 – 14:45	**Break**

14:45 – 15:45 Theoretical Lecture: "*Product development and commercialisation*" by Dr Nazende Günday Türeli (MyB)

15:45 – 17:00 Networking Session

Day 3: Wednesday 7th July 2021(Time in CEST)

9:00 – 10:00 Theoretical Lecture: "*How to use BBB models*" by Dr Caroline Mysiorek and Prof Marie-Pierre Dehouck (UA)

10:00 – 10:30 Break

10:30 – 11:30 Theoretical Lecture "*Integrity control of brain-like endothelial cells and permeability calculations*" by Dr Caroline Mysiorek and Prof Marie-Pierre Dehouck (UA)

11:30 – 13:00 Lunch Break

13:00 – 14:00 **Online Demonstration**: subculture of pericytes and subculture of human endothelial cells/co-culture (UA)

14:00 – 14:30 Break

14:30 – 15:00 **Group activity:** integrity control of the blood-brain barrier *in vitro*, experimental plan (UA)

15:00 – 16:00 **Online demonstration**: Integrity control experiment and analysis of the data (UA)

16:00 – 16:30 Final discussion with data interpretation

Day 4: Thursday 8th July 2021 (Time in CEST)

09:00 – 10:00 "*In vitro blood-brain barrier models: history and evolution"* by Prof Maria Deli (BRC)

10:00 – 10:20 Break

10:20 – 11:50 Workshop "Managing Stress as a Researcher" – Dr Sandra Jumbe (QMUL)

11:50 – 12:00 Final remarks

Organisers

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Abbreviation	Organisation
QMUL	Queen Mary University of London, United Kingdom
CNC	Center for Neurosciences and Cell Biology, University of Coimbra, Portugal
UA	Universite D'artois, France
KI	Karolinska Institutet, Sweden
CHUC	Centro Hospitalar E Universitario De Coimbra, Portugal
HMGU	Helmholtz Zentrum Muenchen, Germany
MyB	MyBiotech GmbH, Germany
UIBK	Universität Innsbruck, Austria
UoB	University of Birmingham, United Kingdom
BRC	Biological Research Centre, Hungary

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ABSTRACTS AND BIOS

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Marina Resmini, Prof.

Professor of Materials Chemistry, Queen Mary University of London

Biography

Marina Resmini was born in Milan, Italy, where she grew up and studied Chemistry at the University of Milan. Following her PhD (1994) she moved first to the University of Amsterdam and then to London, following the award of a prestigious Marie Curie Fellowship. She developed her academic career at Queen Mary University of London, where she is now Professor of Materials Chemistry. Her research interests are focused in the area of functional nano materials with applications at the interface between physical and bio/medical sciences, particularly as enzyme-mimics, sensors and drug delivery systems.
She has a strong interest in inclusion and diversity, in particular supporting young female researchers at the very early stages of their careers; she is now Chair of the RSC Inclusion and Diversity Committee.

Nazende Günday Türeli, PhD.

Head of R&D pharma at MyBiotech GmbH.

Biography

Dr. Nazende Günday Türeli is Head of R&D pharma at MyBiotech GmbH. She is an acknowledged scientific manager with over 15 years of R&D experience at leading positions of international pharmaceutical companies and contract research organizations. Her experience covers a wide range of areas including Quality-by-Design (QbD) approaches on pharmaceutical nano(bio)technology, quality management systems and project management. She has extensive GMP operations knowledge, as well as solid know-how on innovative nano drug delivery systems. She holds a Doctorate in Biopharmaceutics and Pharmaceutical Technology from the University of Saarland, Germany. She is the winner of the 2014 Global CPhI Pharma Awards for Best Innovation in Formulation category. Nazende is currently the industry representative of the Controlled Release Society (CRS) Focus Group Nanomedicine and Nanoscale Delivery (NND).

To date she successfully coordinated and participated as principal investigator in >20 national and international projects receiving funding from H2020, MSCA-ITN, FP7, COST Actions, ESA, EuroNanoMed, Eurostars, Bmbf, ZIM etc., yielding more than 8M € funding for her research projects over the last 5 years.

Abstract

How to ace your CV

Applying for a new job can be a difficult and lengthy process, where rejections are quite common. Preparing a strong CV is the first step and a very important one. There are some many things to consider and different styles to choose from, that sometimes it can be quite daunting! We are here to help: during this session we will take you through all the key steps involved in preparing an outstanding CV. We will discuss the different styles required for an academic CV, to pursue a postdoc, or a CV to apply to industry. We will be talking about CV style, contents, use of key words and how to prepare your cover letter.

Michela Comune, PhD

Project Manager & Product Owner at Inpeco

Dr. Michela Comune was born in Cagliari, the capital of the island of Sardinia (Italy), known as the pearl of the Mediterranean Sea. She lived and studied in Cagliari until December 2007 when she achieved her Bachelor's Degree in Biomedical Engineering from University of Cagliari. After receiving this first important goal, she moved to Pisa (Tuscany, Italy), where she obtained her Master's Degree in Biomedical Engineering (curriculum: Biomedical Technologies) from University of Pisa by discussing the thesis titled "Development and Characterization of Polymeric Therapeutical Nanofilms for the Gastrointestinal Tract" in June 2011. She carried out her thesis at the Center for Micro-Biorobotics of IIT (Italian Institute of Technology) and Scuola Superiore Sant'Anna both located in Pontedera (Pisa).
In December 2011, she was awarded with the prestigious ESR European Marie Curie fellowship to work as researcher for the ITN European project "NanoDrug" at the Biomaterials and Stem Cell-Based Therapeutics research group, directed by Dr. Lino Ferreira, at the Center of neuroscience and cell biology of Coimbra (Portugal). She was a researcher there from 2011 until 2016 working in the field of nanomaterials and drug delivery for biomedical applications. During this time, she was visiting researcher at Sanofi Aventis in Toulouse, France, and at the Louvain Drug Research Institute, UCL, Brussels, Belgium. She received her PhD in Biosciences (curriculum: Biotechnology) from University of Coimbra on September 2016 discussing the thesis "Wound healing and pro-angiogenic properties of LL37-conjugated nanoparticles" approved with Praise and Distinction by unanimity.
In 2017, Michela moved to Tel Aviv (Israel) where she was awarded of a postdoctoral fellowship to join the Bioinspired material and nanotechnology group led by Dr. Lihi Adler-Abramovich at the Goldschleger School of Dental Medicine, Sackler Faculty of medicine of Tel Aviv University. She carried out research activity for 1 year focused on the development and characterization of innovative materials based on low-molecular-weight self-assembled peptides for industrial and medical applications. During her academic career, Michela got 7 years' experience in biomedical laboratory research and development, she participated in numerous international conferences,

she authored 9 peer-reviewed international publications and she has 1 international patented invention.
In October 2018, Michela moved from academia to industry, joining Inpeco, global leader in clinical laboratory and in total laboratory automation, as Process Engineer. She is currently working as a Project manager in the field of healthcare IT products and lab automation. She is managing various projects for the validation and trial of innovative products and for the traceability and automation of the whole anatomical pathology process. She is leading several activities to support the participation of Inpeco in national, international and EU funded research and cooperation projects.

During the NANOSTEM 3rd Summer School, Michela will go over her career focusing on the most significant experiences of the past 10 years, spanning from academic research to industrial product development and business development. She will make room for suggestions, advices and considerations gained not only from good times but especially from difficulties and challenges she faced during these years.

Benjamin Fell, PhD

Senior Analyst at Costello Medical

Ben started his scientific career by completing an undergraduate and Master's degree in Molecular Biotechnology at the University of Lübeck (Germany). He subsequently joined the Marie Curie ITN NANODRUG in 2012 to work on the development of *in vitro* skin models for the assessment of novel nanomaterial-based drug delivery systems (Queen Mary University of London). After obtaining his PhD in 2016, Ben decided to leave academia and scientific research altogether – following the exploration of different alternative career options, he entered the world of medical communications and joined Costello Medical Consulting where he has been successfully working since early 2017.

Costello Medical (http://www.costellomedical.com) is an international medical communications agency that provides scientific support to the pharmaceutical and healthcare industry for the *analysis, interpretation and communication of clinical and health economic data*. As part of his role as Senior Analyst in Costello Medical's Rare Diseases division, Ben particularly focuses on health economics and outcomes research (HEOR) in order to support the successful market access of (ultra-)orphan drugs.

During his presentation, Ben is going to cover the following topics:

- An overview of what medical communications is exactly, and how it can support the development and, more importantly, subsequent patient access for a pharmaceutical product

- The different disciplines and general career options within medical communications, including (but certainly not limited to!): Health Economics and Health Technology Assessment, Evidence Development and Statistics, Medical Affairs and Medical Writing
- Key reasons and benefits of working in medical communications, important transferable skills to successfully enter this field, and some tips and tricks for anyone interested in making this transition

Marina Resmini, Prof

Professor of Materials Chemistry, Queen Mary University of London

Abstract

The art of public speaking and how to ace your interview

Public speaking can be challenging, and it is the second most significant fear, after flying. However, it does not need to be like that!
During the sessions we will discuss the psychology of public speaking, the underlying preparation that you need to do, the importance of understanding and knowing your audience and the most important tips that will allow you a wonderful performance.
We will also cover other aspects of oral communications, such as interviews, and understand how these differ and what each of you can do to ensure the best outcome.

Katrina Krämer, PhD

Chemistry World science correspondent at RSC

Katrina studied chemistry in Germany and Spain before moving to London to do a PhD. While she had always wanted to become a researcher, she realised that there are so many other things someone can do with a chemistry degree. Katrina really enjoyed writing and science communication, so she joined the Royal Society of Chemistry's graduate trainee scheme after finishing her studies. A year later, she got a job in the RSC's Chemistry World team – first as editorial assistant and now as science correspondent. Her favourite piece of advice comes from science journalist Ed Yong: 'Be cautious about all the advice you receive, including this, recognising that everyone is speaking to you from some combination of luck and privilege.'

During her session "*How to become a science journalist in just five easy steps",* Katrina will present a (sometimes interactive) overview of how different media outlets portray science, what a science journalist does all day and what you can get out of doing a PhD even if you don't want to be a researcher.

Marjolein Heymans, PhD

Consultant at Avertim

My name is Marjolein Heymans. I will not talk of myself in third person, because let's be honest, we are not that important!
I was born and raised in Belgium where I also started my academic career by studying a Bachelor and Master's in Biological Sciences at the KU Leuven. I performed my master's thesis at the Belgian Study Center for Nuclear Energy (SCK) on the topic of radiation effects on the prenatal brain. A study in which I spent a lot of time with my new mice friends and for which I was awarded the price for best master thesis. However, by that time I was not interested to prolong my academic career, and I did not continue my study with a PhD. This was because, besides my interest in molecular biology, I was (and am) very interested in environmental issues. Therefore, I started a master-after-master's in environmental Sanitation and Management at the UGhent (Belgium).

Although I kept the two career directions open, after my studies, in 2016 I ended up as an early-stage researcher (PhD) in a Marie Curie ITN called BtRAIN. My new home was Lens, my new university, the University of Artois (France) and my new friends were all talking French (it took me a while to understand any of it). The BtRAIN program focused on CNS barriers and consisted of 12 collegial students located across Europe, focusing on harvesting data on CNS barriers. My study focused on *in vitro* models of the blood-brain barrier and was directed by Maxime Culot, my PI. In my PhD, I learned very quickly that teamwork and collaborations are key to get the bigger picture. I also learned that being in a great work environment is not often taken for granted. And I was super lucky to end up in the Blood-Brain Barrier Lab (LBHE) directed by Fabien Gosselet.

After spending 3 years as a PhD student in the BtRAIN consortium, I defended my PhD (in 2019), and shortly after, I shifted academia for industry. I was very interested to see how my acquired skills from academia could be used in an industrial environment. I started as a life science consultant and had my first project at Pfizer, Puurs (Belgium) in 2019. My first project consisted of anything else but research and focused on implementing a Data Integrity project for complex equipment in the Microbiology lab. In 2020, I shifted to become an internal Pfizer employee as a project engineer continuing to coordinate the DI program in the Microbiology lab, as well as, focusing on method validation for the COVID-Vx vaccine.

Up to now, I did get a taste of two completely different worlds, and I am very curious what the future will bring!

Ania Servant-Jolly, PhD

Operations Manager at the Christabel Pankhurst Institute for Health Technology R&I

Ania successfully completed her PhD in Queen Mary University of London under the supervision of Professor Marina Resmini as a part of the Marie Curie ITN network NASCENT funded by the EU Commission. She went on working as a post-doctoral research associate in the Nanomedicine lab in UCL School of Pharmacy with Prof. Kostas Kostarelos for almost four years where she secured an EPSRC research fellowship for early career researchers developing carbon-based nanomaterials (including carbon nanotubes, graphene and other 2D materials) for advanced drug delivery systems. An opportunity came up to work at the National Graphene Institute (NGI) in Manchester and on securing that role, Ania moved into project management and business development, facilitating interactions with industry to commercialise graphene-based research. Following at the NGI, Ania joined the Faculty of Medical and Human Sciences (now Faculty of Biology, Medicine and Health) in June 2015 as a lead Strategic Funding Manager where she has successfully delivered large research programmes and managed project portfolios at national and international levels across a range of sectors, including manufacturing, pharmaceuticals, chemical, engineering in academic, commercial and clinical environments. Ania is currently acting Operations Manager for the newly created University of Manchester Christabel Pankhurst Institute for Health Technology Research and Innovation.

Kiran Chereddy, PhD

Program Management and Group Lead of Cell Therapy Operations at Lonza Biologics

Kiran Kumar Chereddy, is currently the Group Lead for Program Management – Cell Therapy GMP operations since November 2020 at Lonza Group, a Swiss multinational, chemicals and biotechnology company. In this role, Kiran Chereddy ensures the successful execution of end-to-end cell and gene therapy clinical and commercial manufacturing programs. Previously, he was working as Senior Program Manager in the same group. Before this, Kiran Chereddy was a Project Manager for CAR-T Cell and Gene Therapy at Novartis, USA (10/2018-01/2020) and prior that as a Global PMO manager at Novartis AG, Switzerland. Kiran Chereddy started his industrial career with a graduate program, Sandoz Talent Excellence Program (STEP) at Novartis, Germany. He received his Doctor of Philosophy degree (PhD), with concentration in Pharmaceutical Sciences, from Universite catholique de Louvain within NANODRUG Marie Curie ITN.

Kiran has been working on key selling factors of PhD graduates. During his talk, Kiran would like to share thoughts on presentation of personality and attitude in formal settings. These traits are very much valued during interviews and can be critical selection criteria once the technical knowledge is established by the PhD candidate. Kiran would like to share personal experiences (mistakes and failures) and a few best practices. The expectation is to get the PhD graduates ready for job market and to be agile to embrace the market changes and expectations.

Magdalena Götz, Prof.

Chair of Physiological Genomics, Biomedical Center, Ludwig-Maximilians-Universität München (LMU)

Biography

Magdalena Götz studied Biology at the university of Tübingen and did her Diploma and PhD work in the lab of Jürgen Bolz at the FMI in Tübingen on the mechanisms of how input connections to the cerebral cortex form during development as well as how specific neuronal subtypes are specified. She received the Otto-Hahn Award of the Max Planck Society for this work. She then moved to the National Institute for Medical Research in London to use retroviral vectors for clonal analysis in the lab of Jack Price and identified mechanisms delineating neighboring forebrain regions. She then started her own lab at the Max-Planck Institute for Neurobiology where she made the breakthrough discovery that radial glial cells are neural stem cells. This inspired her to attempt turning also adult mature glial cells into neurons already in 2002 in vitro and in 2005 in vivo. In order to determine which glial cells best to convert to neurons after traumatic brain injury she systematically examined the roles of distinct glial subtypes after traumatic brain injury when she was appointed Director of the Institute of Stem Cell Research at the Helmholtz Center Munich in 2004 and Chair of Physiological Genomics, now at the Biomedical Center of the Ludwig-Maximilians University in Martinsried Munich. This led to the discovery of a novel role of reactive astrocytes and the in vivo direct neuronal reprogramming reaching a very high efficiency and maturity. Magdalena Götz became a member of EMBO in 2006, of The Leopoldina Academy in 2008 and the Bavarian Academy of Sciences in 2017. She received the Familie Hansen Price and the Gottfried-Wilhelm Leibniz Price of the DFG in 2007, followed by many other awards such as the Ernst Schering Price in 2015, the Roger de Spoelberch Prize in 2017, the Schellenberg Prize in 2018 and the Mendel Medal in 2019.

Abstract

Novel mechanisms of neurogenesis and neural repair

We study the mechanisms of neurogenesis in order to implement them for neuronal repair. I will present recent work on a novel centrosomal protein, Akna, regulated with

great precision in subsets of neural stem cells. This led us to unravel an unprecedented centrosome heterogeneity in human neural stem cells revealing and verifying novel disease candidates. I will proceed to present recent data on a master regulator of nuclear compartmentalization by liquid phase transition with key roles in promoting neural stem cell self-renewal and neurogenesis. Interestingly, Trnp1 is also critical for direct neuronal reprogramming which leads to discuss recent progress in direct neuronal reprogramming as a means to replace lost neurons after brain injury. The presentation will be concluded by discussing the integration of replaced neurons into the circuitry of the murine cerebral cortex and present unpublished data about the mechanisms regulating this integration. Taken together, our knowledge about basic mechanisms of neurogenesis allowed making great strides towards neuronal repair.

Christopher Grisby, PhD.

Research fellow at Karolinska Institutet

Biography

Dr. Christopher Grigsby is a StratNeuro research fellow in the Department of Medical Biochemistry and Biophysics at Karolinska Institutet in Stockholm, Sweden. He received his B.S. in Bioengineering from UC Berkeley and his Ph.D. in Biomedical Engineering from Duke University. His research is focused on regenerative medicine, through the design and application of novel biomaterials and nanoparticle systems for cell reprogramming and genome engineering.

Abstract

Clinical research on regeneration in the CNS

In the talk *Clinical research on regeneration in the CNS*, we will discuss several recent advances toward clinical treatments for inherited, traumatic, and degenerative conditions of the central nervous system. Diseases of the nervous system are leading causes of disability, which will cause increasing burden to patients, society, and the economy as population ageing advances. The CNS presents a set of unique challenges to the development of novel regenerative therapies, but promising approaches are emerging with increasing frequency. Stem cell-derived cell replacement therapies are being developed for Parkinson's disease, epilepsy, and spinal cord injury. Meanwhile, recent reports also demonstrate the potential to directly reprogram resident cells in situ using CRISPR-Cas and nucleic acid therapeutics. We will also consider some ways in which biomaterials and nanotechnology can be incorporated to promote tissue regeneration and functional recovery

Benjamin Kirsch, PhD

Head of Quality Assurance MyBiotech GmbH

Biography

Dr. Benjamin Kirsch studied pharmacy at the University of Saarland where he received his diploma in the field of biological assay development. His research focused on *Pseudomonas aeruginosa* related infections, and he received his PhD degree at the Helmholtz Institute for Pharmaceutical Research Saarland in 2017 where he worked on the same field. Following three years of work experience at pharmacy, he changed his career path to pharma industry. Since 2020 he is working in the field of quality control and quality assurance.

Abstract

Pharmaceutical Quality Management System

Good manufacturing practice (GMP) defines a set of regulations for the pharmaceutical industry that is EU- and U.S.-wide accepted to ensure that quality is guaranteed and sustained throughout the whole supply chain. GMP regulates not only the manufacturing but also all the areas and departments, facilities and processes, including equipment and cleaning validations, training, hygiene, purchase, supply, warehouse, regulatory affairs, IT and personnel, as well as contracted manufacturers and suppliers. It is designed to minimize the risks involved in any step of pharmaceutical production which cannot be identified through testing the final product.

GMP is based on a very simple but essential rule: all processes that have an impact on quality must be planned, controlled, and monitored. Quality assurance (QA) in a united form of cGMP guidelines and regulations, quality control (QC) and product quality review (PQR) builds the pharmaceutical quality management (PQM) system in a pharmaceutical company. cGMP serves as an integrated part of QA to warrant that the product quality is consistent and is ensured by producing and controlling with quality standards of the intended product specifications and regulatory requirements. It is embedded in PQM system to ensures quality by verification of facilities, utilities and departments, equipments and processes. 'Quality' is expected to be produced as an output of core rules and regulations under standardized conditions. Controls over the process in pharmaceutical companies serve as tools for quality.
This lecture provides a short insight into pharmaceutical quality management systems with a special focus on harmonization of GMP in QA

Nazende Günday Türeli, PhD.

Head of R&D pharma at MyBiotech GmbH.

Abstract

Product development and commercialisation

Bringing new products to the market requires multidisciplinary collaborations and a well-defined structure for product development and commercialization. This supply chain consists of different stages from idea till manufacturing, distribution and marketing. Its effective implementation defines the success of market penetration.

Multiple functional groups are involved in a product development process. These groups involve research and development, technology transfer and scale-up, manufacturing, marketing and sales. Most companies separate product development and marketing processes due to the fact that each of these groups require different backgrounds, skills and know-how. Additionally, their work culture differs strongly. However, successful market penetration requires a collaboration of these different groups and knowledge transfer among them.

In the medicine today, nano-pharmaceuticals and nano-sized tools are used for the diagnosis, prevention and the treatment of diseases. The emerging field of nanomedicine combines Research & Development & Innovation (R&D&I) areas such as drug delivery, in vivo imaging, in vitro diagnostics, biomaterials and active implants. Nano-pharmaceuticals have the potential to drive the scientific and technological uplift offering great clinical and socio-economic benefits to the society in general, industry and key stakeholders, and patients. Many nano-pharmaceuticals are already in clinical use, and many more are being investigated or in clinical trials. However, there is a constant decline in clinically approved and commercialized nano-pharmaceuticals, even though they clearly get better and better as we improve our understanding on the complexity of human diseases and interaction of nano-pharmaceuticals with their biological surroundings (at level of molecules, cells, organs etc.). Due to the lack of resources to implement GMP manufacturing at-site, the scale-up and production, commercialization of innovative nano-pharmaceuticals is still challenging to main EU nanomedicine market players. To allow successful implementation of the nano-pharmaceuticals in the medicine field, there is an urgent need to establish science- and regulatory-based product development and commercialization supply chain.

This lecture aims to provide workflow for the seamless, timely and cost-friendly transfer of nano-pharmaceuticals from lab bench to clinical trials and to market via necessary consolidated network of facilities, technologies, services and expertise for all the technology transfer aspects from characterization, testing, verification up to scale-up, GMP compliant manufacturing and regulatory guidance.

Marie-Pierre Dehouck, Professor

Professor in physiology at University of Artois

Biography

Professor Marie-Pierre Dehouck is graduated as a physiologist and holds a PhD degree in Physiology from the University of Lille I and a Doctorate degree in Physiology from the Université d' Artois.

During her PhD studies, she set up an in vitro blood brain barrier (BBB) model, consisting in a coculture of bovine brain capillary endothelial cells and rat glial cells. This model represents a valuable tool; its characteristics are very close to the in vivo blood brain barrier and enables transport studies of endogenous molecules or drugs to the brain. This model is extendly used by pharmaceutical industry since the end of her PhD in 1990.

In 1999, she became Professor in Physiology at the Université d'Artois. Her research group investigates the thematic "modelling the BBB" which aims are development, characterization, standardization of physiological and pathological in vitro BBB models. Marie-Pierre Dehouck got involved in the FP7 European project EUSTROKE aiming to the modelling of the neurovascular unit. As part of this project, a three cell culture was developed including endothelial cells, glial cells and pericytes and enables studies of interactions between actors of the neurovascular unit.

Recently, thanks to a collaboration with Professor Lino Ferreira (Coimbra University, Portugal), her group has successfully developed a human in vitro BBB model using human stem cell isolated from umbilical cord blood which has been patented.

Caroline Mysiorek, Ph.D.

Associate Professor at Artois University

Biography

Caroline Mysiorek is associate professor in Artois University, at the Faculty of Sciences in Lens, France where she received her PhD in 2009. During her thesis, she was focused on the blood-brain barrier (BBB) and more precisely the in vitro characterization of the dysfunction of the BBB and its protection following ischemic stroke. Then, she went in Pr. Lydia Sorokin's lab (Muenster, Germany), for a post-doctoral position, to study the involvement of the extra-cellular matrix in the post-ischemic inflammatory processes among the neurovascular unit in the frame of the European Stroke Research Network (EUSTROKE, FP7). Recruited in 2010 at Artois University as associate professor, she continued her research on deciphering the cellular and molecular mechanisms responsible of the loss of integrity of the BBB following stroke before launching in 2013, a new thematic of research focusing on the role of the BBB in brain tumours in 2013. She obtained her habilitation in 2019.

Abstracts

How to use Blood-brain barrier models

The reminders about the blood-brain barrier (BBB) (localization, extent, physical and metabolism properties, environment) will naturally lead to present the interest and the design of in vitro BBBB models developed in the laboratory.
Since 30 years the laboratory leads it research using various *in vitro* models of BBB (human models, murine (rat and mice) and bovine models). Solocultures, cocultures and three cell cultures realized using endothelial cells, glial cells and pericytes alone or in combination, will be presented as well as the need to characterise the model according to its adaptation.
BBB models are used to evaluate the toxicity of the compounds towards the BBB in single dose, repeated doses, drug interactions. Our research activities also focus on a better understanding of the cellular and molecular mechanisms involved in the processes of compounds delivery to the brain and the accessibility of the compounds to the brain prenchyma. In vitro BBB models are also a tool for understanding the role and interactions of the various actors (endothelial cells, pericytes, glial cells) of the neurovascular unit (NVU), in physiological and pathological conditions. As examples: Oxygen, glucose deprivation (OGD) conditions *in vitro* mimics the *in vivo* stroke pathology; a blood-brain tumor barrier (BTB) model has been developed for studying the impact of pediatric glioma cells on the brain endothelial cells and chemoresistance.

Integrity control of brain-like endothelial cells and permeability calculations

Two ways to measure the integrity of endothelial cell monolayers are used in the blood-brain barrier (BBB) field: Measurement of TEER (Trans-Endothelial Electrical Resistance) or measurement of the diffusion of an integrity marker through endothelial cell monolayers. In our laboratory we have opted since almost 30 years for this second method. Our choice will be quickly explained.
The integrity marker is a small and hydrophilic molecule that diffuse slowly through the brain-like endothelial cells (BLECs). Indeed, owing to the presence of the tight junctions, the integrity marker cannot cross easily between BLECs. As there is no transporter or receptor for this molecule, it cannot go through the BLECs. Fluorescent molecules such as Lucifer yellow or Sodium-fluorescein are preferred as integrity markers over radioactive molecules.
BLECS can be cultured in different configurations (solo-, co-, tri-culture). In our laboratory, the ‘gold standard’ used to assess if the 6 days culture has gone well (temperature, CO^2 rate, composition of the medium, eventual contaminations...) is the co-culture of endothelial cells and pericytes and then measurement of integrity marker diffusion before the experiment. However, the integrity markers can be used during or at the end of the experiment to assess a permeability modulation during the experiment time. The course of this integrity control experiment will be explained precisely.

Different calculation methods can be carried out from this experiment : diffusion rate (in percentage), apparent permeability (Papp) or endothelial permeabilty coefficient (Pe) which both correspond to a speed of crossing. Our 'gold standard' in terms of integrity control, is the endothelial permeability coefficient (Pe) that is independent of the concentration of the molecule for integrity markers case and that allows to take into account the permeability of the endothelial cells monolayer alone. These calculations, advantages and disadvantages for each of them will be explained.

Online demonstrations and group activities

The demonstrations will take place at the Faculté des Sciences Jean Perrin (Université d'Artois) in the Laboratoire de la Barrière Hémato-Encéphalique**.**
These practical trainings will be some applications of theorical lectures done in this 3rd summer school session: How to use BBB models and Integrity control of brain-like endothelial cells and permeability calculations.
As a demonstration, in the laboratory, the ESRs will follow the steps to set up the BBB coculture human model. They will observe how to carry out a subculture of pericytes, a subculture of endothelial cells and the assembly of these cells to set up the coculture system.
The ESRs will follow BBB integrity control experiment on different systems of BBB models, soloculture, coculture, tri-cell culture. Calculations (Permeability coefficient, Papp, percentage of crossing) will be performed and compared and discussed in the different configurations of the models.

Maria A. Deli, MD, PhD

Head of the Biological Barriers Research Group at BRC

Biography

Prof. Deli is the head of the Biological Barriers Research Group at BRC and honorary professor at the University of Szeged, Hungary. She has been actively working in the field of biological barriers for over 30 years. She pioneered novel complex co-culture models for the investigation of cellular interactions at the blood-brain barrier and to test protective molecules and drug permeability. With the Biomolecular Electronics Research Group of BRC her team developed microelectronic/microfluidic devices for culture models of biological barriers (doi.org/10.1016/j.snb.2015.07.110, doi.org/10.1039/D0LC00558D, doi.org/10.1177/0271678X21992638). Supervised 9 BSc, 11 MSc and 10 PhD dissertations. Publications: 170, citations: > 8700, H-index: 46. Principal investigator/consortium partner in over 20 national and international grants. She holds two patents on blood-barrier model (WO/2007/072953, 2007) and chip device (P14 00517, 2018)

Instruments/Techniques**:** permeability measurement of pharmacons and natural products across human cell based biological barrier models; zeta potential measurements of nanoparticles and living cells (Malvern Zetasizer Nano); human cell based co-culture models of biological barriers under fluid flow in chip devices; cellular cytotoxicity measurements (MTT, LDH, live/dead); label-free impedance based kinetics of cellular interactions (RTCA, Agilent); immunocytochemistry; cellular uptake experiments; confocal and spinning disk microscopy on stained fixed and living cells; glycocalyx investigations. Prof Deli research interests are: culture models of the blood-brain, respiratory, intestinal and cornea barriers; barrier models in microfluidic devices; organ-on-chip models; protection of biological barriers; effect of natural products on biological barriers; targeted nanoparticles for drug delivery across biological barriers; cell interactions with new nanomaterials; cellular glycocalyx interaction with nanoparticles.

Abstract

In vitro blood-brain barrier models: history and evolution

The history of in vitro blood-brain barrier (BBB) models spans almost 50 years. The isolation of brain microvessels, the first in vitro model, was pioneered by Ferenc Joó and his co-workers in 1973. This technique, with modifications, is still used and makes the basis of genomic and proteomic BBB studies. The observation of Joó et al. in 1978 that endothelial cells grow out of brain capillaries in culture conditions was soon followed by a wide variety of culture-based models to study the physiology, pharmacology and pathology of the BBB (reviewed by Deli et al., 2005). In the last four decades, cell culture based BBB models became well characterized and widely used tools in basic research and CNS drug discovery. In the first wave of models, primary or low passage monolayers were developed from brain endothelial cells of bovine, porcine or rodent origin. Soon the dedifferentiation, the loss of BBB properties, were observed, and with the help of culture inserts with porous membranes co-culture models were established in which brain endothelial cells are grown in the presence of additional brain cell types, like glial cells, brain pericytes or neurons to induce BBB properties. In the last 10 years, human stem cell derived co-culture BBB models were established, which may help to bridge the translational gap between animal cell-based models and clinical application. While these culture models mimic several key BBB functions, they are static and miss the physiological influence of fluid flow. Dynamic BBB models using cartridges of hollow fibers proved the importance of shear stress in the regulation of the endothelial barrier. In the last nine years new microfluidic and/or microelectronic chip devices were published to model the BBB. These lab-on-a-chip devices show very different design and possibilities to monitor barrier functions. Our team developed a versatile microelectronic device for the complex investigation of BBB functions. The 2-channel PDMS based system with integrated transparent gold electrodes allows the co-culture of multiple cell types, visualization of cells by microscopy, fluid flow, real-time electrical resistance monitoring; permeability

measurements and immunostaining. Further development of the lab-on-a-chip device made it possible to measure the streaming potential of brain endothelial cell layers revealing their negative surface charge and to study the effect of fluid flow on barrier and glycocalyx-related genes and surface charge in a human BBB model. Lab-on-a-chip devices enable the kinetic investigation of BBB functions and the generation of body-on-a-chip microphysiological systems by the integration of BBB with different organoids.

References / Further reading

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Sandra Jumbe, PhD

Health Services Researcher & RDS London Adviser

Biography

Dr Jumbe is a health psychologist and researcher based in the Institute of Population Health Sciences at Queen Mary University of London. Her expertise is in health research and behaviour change solutions. This essentially focuses on how biological, social, and psychological factors influence health and illness. She has been involved in consultancy work developing tailored stress management interventions within organisations and group settings. She is also founder of Happy Hub, a start-up that

offers stress management technologies that give employees in organisations the ability to manage health and wellbeing on a personal and organisational level.

Abstract

This workshop aims to promote positive wellbeing and teach strategies to help researchers develop ways to improve stress management. Early career researchers often have to balance issues around planning a long-term project, whilst managing academic challenges and personal problems along the way. Greater emphasis is placed on researchers to self-manage, be self-directed learners and to proactively acquire academic skills for the future. All of these increase stress and can impact on the wellbeing of researchers.

This short workshop will enable participants to develop a positive mental attitude by understanding the differences between pressure and stress. The session will give participants tools and tips on how to manage stress during their postgraduate research in order to maximise success.

With interactive activities including videos, brief meditation and discussion tools, the workshop will walk you through everything you need to know, including:

· what is stress
· why manage it
· how to recognise signs of stress
· practical exercises for managing stress
· keeping healthy