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Abstract book

(Abstracts are classified in the order of the oral presentations)
(Titles and Numbers of the posters are presented at the end)

Low Conversion Chemistry for Stoichiometric Bioconjugation.

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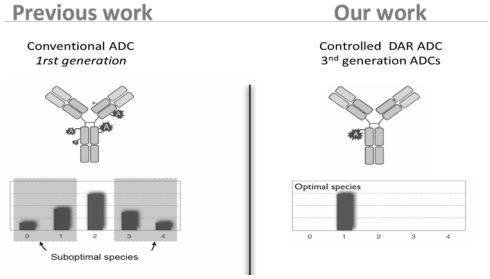
The development of ADC into clinic has shed light on the negative consequences of heterogeneous bioconjugation. Moving away from classical lysine-based coupling leading to ADCs with average DAR of 4 and high number of DAR species, the pharma companies evolved toward site-specific conjugation with precise, although lower, DAR and only few species. These new generation of conjugates establish the superiority of tailored conjugation but on the other hand require the use of engineered antibody and/or complex enzymatic process not always straightforward to transfer into GMP processes.
Reflecting on this issue we have designed a new conjugation methodology involving native protein and leading to conjugates with a unique DAR this without unconjugated or over conjugated protein. Our general bio-conjugation method applies with virtually no limitations on proteins and payloads (drugs, protein, molecular probe). It furthermore enables preparation of conjugate bearing one, two or more payloads, with precise control of the degree of conjugation for each of them.



Among others we produced ADC bearing two drugs with DAR 2 for the first one and DAR 1 for the second one. Most interestingly simple mono conjugated DAR 1 opened interesting prospects as a building block to engineer precise protein-oligonucleotide, protein-protein, protein-nanoparticle constructs.

Biography

Alain WAGNER has completed his PhD in 1991 from Strasbourg University and has been a postdoctoral fellow at Affymax Research Institute with Peter Schultz from 1991 to 1994 He then joined Centre National de la Recherche Scientifique (CNRS). He is Head of the Biofunctional Chemistry team. Alain has published more than 150 papers in peered reviewed reputed journals, is inventor of more than 20 patents and co-funder of 5 start-ups.

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Bioorthogonal Reactions of Heterodienes: Application in Bioimaging and Beyond

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Bioorthogonal reactions became an invaluable tool in modern chemical biology. These reactions proceed selectively under strict biological conditions and enable modification and study of biomolecules in their native environment. Heterodienes represent unique class of bioorthogonal reagents having excellent reactivity and versatility for use on biological systems. We have discovered that cycloadditions of various heterodienes can lead to formation of a new type of fluorescent products directly in the reaction with various dienophiles. The developed fluorogenic reactions can be successfully applied for bioimaging. In addition, this type of chemistry enables selective bioorthogonal deprotection and subsequent release of caged small molecules inside live cells. This offers unique opportunity to control biochemical processes by purely chemical tools.

Biography

Milan VRABEL has completed his PhD in 2008 from The University of Chemical Technology, and has been a postdoctoral fellow in the Ludwig-Maximilians University Munich before being hired by the Institute of Organic Chemistry and Biochemistry (IOCB), Prague in 2014. He is the head of a junior group pursuing research in the development, improvement and use of bioorthogonal reactions. The interdisciplinary nature of the research enabled publishing in respected, peer-reviewed, international journals. In 2016, Milan was awarded an ERC Starting Grant which aims to develop new chemical tools for studying fundamental questions in glycobiology and related disciplines. He actively serves as a reviewer for various scientific journals and since 2017 is a remote evaluator for the EU Research an Innovation programme Horizon 2020.

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Carbon dots for biomedical applications

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Carbon dots (CDs) represent a new class of stable and highly biocompatible fluorescent nanomaterials with promising applications in many fields such as cell labeling, optical imaging, LED diodes, or optoelectronic technologies.[1] Compared with organic fluorophores, carbon dots show almost a hundred times brighter fluorescence and stability against photobleaching. Unlike toxic quantum dots (QDs), CDs reveal extraordinarily higher biocompatibility. CDs can be used as an efficient fluorescent probe for stem cell labeling and tracking, as we showed recently, where homing of CDs-labeled stem cells into a mouse tumor has been demonstrated *in vivo* for the first time.[2] Another example of CDs' unique optical behavior shows that that they can be used as a highly sensible and reliable intracellular nanothermometer for cancer cells.[3] All these advantages as well as the fact that emission wavelengths can be tuned via a surface shell or suitable doping in the graphitic core open the door for real biological and technological applications. Therefore, cytotoxicity of CDs should be thoroughly explored. In my talk, I will present recent results of our research into CDs along with their bioapplications and latest findings related to cytotoxicity of two types of CDs that have an opposite surface charge, including gene expression profiling together with most significant deregulated pathways in human lung cancer and healthy cells.

Biography

Katerina POLÁKOVÁ obtained her Ph.D. degree from Palacký University in Olomouc in 2009. She started her research into iron oxide nanoparticles—their synthesis and application as MRI contrast agents. Currently, she is head of a bio-laboratory at Regional Centre of Advanced Technologies and Materials (www.rcptm.com). The Bio-Med group mainly focuses on studying cytotoxicity of carbon-based nanoparticles, and together with synthetic chemists at RCPTM they are developing magnetic and carbon-based nanomaterials for diagnostic and therapeutic applications.

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Chiral fluorescent probes for chemical biology and catalysis

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Inevitable consequence of aerobic life is oxidative damage to an organism caused by reactive oxygen species (ROS). The sources of ROS can be either endogenous or exogenous. These reactive molecules play an important role in cell signaling. However, the ROS level can be elevated and disturb normal redox balance, which causes oxidative stress that challenges the integrity of an organism and is believed to be a major cause of aging and aging-related diseases. We have recently developed new chiral fluorescent probes that can trace the activity of an important subclass of enzymes responsible for oxidative stress management. Importantly, chirality of the probes is essential for the targeting the particular class of enzymes. By using the probes, we have discovered new determinants in oxidative stress response in bacteria that might be relevant for anti-bacterial strategies exploiting oxidative damage. On the other hand, the chiral probes enabled us to discover highly stereoselective enzymes that we employed for the asymmetric production of high value chiral synthons and pharmaceuticals. Moreover, we utilized the probes for the development of high-throughput assay for directed evolution of enzymes with tailor made catalytic properties.

Biography

Jiří MÍŠEK has completed his PhD in organic chemistry in 2008 from Charles University and the Institute of Organic Chemistry and Biochemistry in Prague under the supervision of Dr. Ivo Starý. Then he was awarded Roche Research Foundation fellowship that he spent as postdoctoral fellow in the lab of Prof. Stefan Matile at University of Geneva. He pursued projects in bioorganic chemistry. In 2011 he moved to University of California in Irvine, where he carried out research into artificial riboswitches with Prof. Andrej Luptak. In 2015 he established his own research lab at Charles University in Prague. His research interest spans from chemical biology to biocatalysis.

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Optimized miniplasmid vectors for non-viral gene therapy.

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Nonviral gene therapy requires a high yield and a low cost production of eukaryotic expression vectors that meet defined criteria such as biosafety and quality of pharmaceutical grade. To fulfil these objectives, we designed a novel antibiotic-free selection system. The proposed strategy relies on the suppression of a chromosomal amber mutation by a plasmid-borne function. We first introduced a nonsense mutation into the essential Escherichia coli thyA gene, resulting in thymidine auxotrophy. The bacterial strain was optimised for the production of pFARs that are small and novel plasmids devoid of antibiotic resistance markers and encoding an amber suppressor t-RNA. In transplanted tumours, muscle, liver or skin, transgene expression levels were superior with the pFAR derivative, as compared with a plasmid carrying a kanamycin resistance gene. Thus, we designed a novel strategy for the efficient production of biosafe plasmids and demonstrated their potentiality for nonviral gene delivery and high-level transgene expression in several tissues.

Age-related macular degeneration (AMD) is the most common cause of severe vision loss in the elderly. Neovascular AMD (nAMD) is characterized by choroidal blood vessels growing into the subretinal space, which results from overexpression of the vascular endothelial growth factor and decreased expression of the pigment epithelium-derived factor (PEDF). We have developed an approach, which involves the transplantation of genetically modified pigment epithelial (PE) cells that stably overexpress PEDF. Using electroporation, the PEDF transgene is delivered in plasmids free of antibiotic resistance markers (pFAR) by the enhanced Sleeping Beauty (SB100X) transposon system.

Keywords: gene therapy; plasmid; clinical trial; transposon; age-related macular degeneration.

Biography

Pr Daniel Scherman Member of European Academy of Sciences EURASC - Head of Medicine and Life Sciences Division.

Pr Daniel Scherman is Exceptional Class Director of the CNRS National Scientific Research Center - France. He was born in 1953. Competence fields. Drug delivery and targeting, Gene therapy, Non viral Gene delivery, In vivo imaging. Scientific Publications: 340 publications in reviewed journals; 50 reviews or books chapters in the fields of molecular pharmacology, neurology, cell biology, drug delivery, gene delivery and gene targeting, 35 patent applications. Main present and recent functions: 2002 - 2018: creator and director of the Chemical and Genetic Pharmacology and Bioimaging Unit Partners : INSERM, CNRS, Pharmacy University, Ecole Nationale Supérieure de Chimie de Paris (staff 50). 2009-ongoing: President of the Committee of "Non Viral Gene Therapy" of the European Society of Cell and Gene Therapy (ESGCT). Member of the Non Viral Gene Therapy Committee of the American Society of Gene Therapy (ASGT) (two 3 years terms). 2014-2018: President of the Pharmacology and Bioimaging Section of the French National Center for Scientific Research (CNRS).

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Hydrophilic and amphiphilic copolymers useable as efficient nanotherapeutics or diagnostics

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Nanotechnology-based therapeutics, with many so called "nanomedicines", such as water-soluble polymers, polymeric micelles, liposomes, polymersomes and nanoparticles, are being explored intensively to improve disease treatment. Nanomedicine has been increasingly utilized to treat neoplastic and inflammatory diseases. Among studied nanomedicines the significant position belongs to water-soluble synthetic copolymers based on N-2-hydroxypropylmethacrylamide (HPMA) because of their excellent biocompatibility and non-immunogenicity. Moreover, combination of their therapeutic potential with simultaneous non-invasive diagnostics can yield to highly efficient theranostics, which enable to concurrently observe the disease progression and system pharmacokinetics. Obtained results showed a high potential and capability of nano-sized copolymer-drug conjugates for specific delivery of drugs and their combinations to aggressive solid tumors and thus for their efficient treatment. Main emphasis will be given to description of potential of water-soluble polymers in the field of nanomedicine. Polymer-based systems, micellar and star polymer-drug conjugates, will be presented and their potential for enhanced passive tumor accumulation and release of drug in the acidic milieu of a tumor will be shown. Moreover, in vivo noninvasive multispectral optical imaging and positron emission tomography of fluorescently or radio labeled polymer carriers will be discussed.

Biography

Tomáš ETRYCH has completed his PhD in Polymer chemistry from Charles University in Prague, now he is a Research Professor of Polymer chemistry and head of Department of Biomedical Polymers of Institute of Macromolecular Chemistry of the CAS. He has published more than 140 papers in reputed international journals, which were cited more than 4000 times and is an author of 9 patents. His research focus is based on preparation and characterization of water-soluble and micellar drug delivery systems and/or diagnostic probes for effective treatment and diagnostics of cancer and inflammatory diseases.

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Tuning self-assembling polyplexes with an endosomal pH-sensitive disassembling ability favors intracytosolic delivery of oligonucleotides and proteins

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Synthetic nucleic acids and their formulations are emerging as therapeutic treatments for gene-related neuropathy or muscular diseases. However, the passage of nucleic acids across the plasma membrane remains an important issue. Expanding the therapeutic scope of antibodies to intracellular pathology-mediating targets will also depend on our ability to develop antibody derivatives and specialized delivery systems.
Effectiveness of a macromolecular delivery system relies in part on our abilities to build assemblies that respond to biological stimuli for payload release at the right time and location. We will report the synthesis, physical properties and delivery abilities of various PEIs that were conceived to self-assemble in biological fluids but disassemble exclusively inside endosomes to release the payload in a spatiotemporal manner. Specifically, various aromatic domains were grafted to the "proton-sponge" polyethylenimine (PEI) to diminish its water solubility in a pH-dependent manner. The chemical modification did not impact the PEI buffering abilities and modified PEIs having a pH-disassembly switch near pH 6.0 that is encountered inside PEI-buffered endosomes, were observed to be reliable and efficient carriers for intracytosolic delivery of nucleic acids and proteins. The selected polymers were also able to assist oligonucleotide delivery in *in vivo* models of tumor and muscular dystrophy.

Biography
Dr. ZUBER received his Ph.D. in Organic and Supramolecular Chemistry on Dec 1995 from the University of Strasbourg, working with J.P Behr and S.M. Hecht. After a postdoctoral work at the Oregon Health Sciences University in Portland, OR, USA, he was hired in 1999 by the CNRS to develop synthetic virus-like systems and methods for delivering nucleic acids and proteins inside living cells. He is currently co-leading the Team « Chemo Biology Intervention » that prepare high affinity ligands and conjugates for detecting or modulating activities of selected intracellular targets.

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Design of novel human neutral sphingomyelinase 2 inhibitors as potential therapeutics

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Human neutral sphingomyelinase 2 (nSMase2) is an enzyme responsible for the cleavage of sphingomyelin to phosphorylcholine and ceramide. This process is essential for formation and release of exosomes, extracellular vehicles (EVs) that are crucially involved in intracellular communication. EVs are able to carry various cargos, which differ in composition depending on stimuli that are responsible for their release. Under pathological circumstances, EVs transfer pathological load. Chronic increase of brain nSMase2 activity and related exosome release has been implicated in various pathological processes including the progression of Alzheimer's disease (AD). Therefore, nSMase2 can be considered as a viable therapeutic target.
Our team has recently identified the first nSMase2 inhibitor which possesses both favorable pharmacodynamics and pharmacokinetic (PK) parameters, a compound with a code name PDDC. This compound exerts good oral bioavailability, brain penetration and significant inhibition of exosome release from the brain *in vivo*.
In my talk I will present our journey towards this derivative starting from two high-throughput screening hits. Since the crystal structure of the nSMase2 inhibitor was unavailable, we used ligand-based drug design and performed an extensive structure-activity relationship study. We identified numerous interesting compounds with submicromolar activities against nSMase and selected PDDC as our tool compound for further *in vitro* and *in vivo* studies.

Biography

Radim is now a group leader at the IOCB Prague. He is also a lecturer of Chemical Biology and Basic Principles of Drug Discovery at Palacký University, Olomouc. He got his Mgr. (equivalent of MSc.) in pharmacy from the Faculty of Pharmacy in Hradec Králové, Charles University - his master thesis was done at University of Crete, Heraklion, Greece (Prof. Manolis Stratakis). He obtained his Ph.D. in organic chemistry from the Faculty of Science, Charles University, Prague (Dr. Hubert Hřebabecký, Prof. Antonín Holý group at IOCB Prague) and spent his postdoctoral stay in Laboratory of Medicinal Chemistry, University of Ghent, Belgium (Prof. Serge Van Calenbergh). He is a (co)-author of 55 papers in the field of medicinal/organic chemistry.

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Discovery of first-in-class extracellular FLT3 inhibitors by in silico and experimental high-throughput screening: From hits to a preclinical candidate

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The FLT3 receptor tyrosine kinase has recently been identified as a key target in triggering and maintaining chronic neuropathic pain [1]. A first in silico screening of 5 million commercially available compounds led us to identify the very first extracellular inhibitors of this receptor, which have been optimized by medicinal chemistry to BDT001, the first specific FLT3 negative allosteric modulator (NAM) able to completely reverse neuropathic pain in rodents [1]. To find potential back-ups to BDT001, we undertook the experimental screening of the French Compound Library (45000 compounds) thanks to an in vitro time-resolved FRET assay. The HTS assay yielded 110 hits from 10 different chemical series whose developability has been determined by early absorption-distribution-metabolism-excretion-toxicity (ADMET) studies of representative hits. Three chemical series, with a strong oral bioavailability potential, have been prioritized for medicinal chemistry hit to lead optimization. Like BDT001, these compounds are NAMs of the FLT3 receptor tyrosine kinase and exhibit anti-hyperalgesic properties in mice.
FLT3 NAMs represent a first-in-class series of novel analgesic compounds to treat neuropathic pain with a long-lasting duration of action, a clear superiority to standard of cares (antiepileptics, antidepressants) and a lack of addiction potential as seen with opiates.

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Structure-Activity Relationships of 3,5-Dinitrophenyl-Containing Heterocyclic Compounds as Selective Antitubercular Agents

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Tuberculosis (TB), one of the most widespread and dangerous infectious diseases, is among the world's top 10 causes of death, and it claimed more than 1.6 million lives (3% of all deaths) in 2017. This is comparable with the number of deaths caused by lung cancer, diabetes, Alzheimer disease or road injuries. The main threat to successful recovery from TB is the ability of *Mycobacterium tuberculosis* (*M. tuberculosis*) to mutate and survive under the conditions of anti-TB therapy. The treatment duration of drug-susceptible TB is usually 6 months and a combination of four first-line anti-TB drugs is used. However, the treatment durations of multidrug-resistant (MDR) and extensively drug-resistant (XDR) forms of TB are 18-24 months, combinations of more than four second-line drugs have to be administered and only 55% of patients are successfully treated. That´s why it is necessary to continue to identify and develop new effective anti-TB agents.
In 2014, our research group identified 1- or 2-substituted 5-(3,5-dinitrobenzylsulfanyl) tetrazoles as potent antitubercular compounds with minimum inhibitory concentration (MIC) values of 1 μM against *M. tuberculosis*. Later, we found that isosteres of those compounds, 3,5-dinitrobenzylsulfanyl-substitued 1,3,4-oxadiazoles[1] and their reverse analogues, 3,5-dinitrophenyl-substituted 1,3,4-oxadiazoles,[2] showed outstanding activities against both drug-susceptible and MDR/XDR strains of *M. tuberculosis* with MIC values reaching 0.03 μM (0.011-0.026 μg/mL), which are superior to those of all current first-line anti-TB drugs. Furthermore, compounds of these series had low *in vitro* cytotoxicity and no genotoxicity. Similar results were obtained with series of triazole analogues of these lead compounds. Regarding the mechanism of action of these compounds, we proved that 3,5-dinitrobenzylsulfanyl-substituted heterocycles act as antitubercular agents by a different mechanism than what is seen with 3,5-dinitrophenyl-substituted heterocycles, where the inhibition of DprE1 played the main role. The syntheses and structure-activity relationships with respect to antimycobacterial activity, toxicity and selectivity of action of these compounds will be discussed.

Biography

Jaroslav ROH has completed his PhD in 2010 from Faculty of Pharmacy in Hradec Králové, Charles University (Czech Republic). Then he spent several months at the University of Bath (UK) at the Department of Pharmacy and Pharmacology. He is a vice-dean for scientific activity, doctoral studies and technology transfer and head of the Department of Organic and Bioorganic Chemistry at the Faculty of Pharmacy in Hradec Králové, Charles University. He is an author or co-author of 38 research articles (WoS) and 6 national patents and 2 PCT patent applications.

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Phenotypic screenings for the identification of new drugs and new targets involved in host-mycobacteria interactions

Priscille BRODIN

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The current regimen for the treatment of Tuberculosis includes a combination of antibiotics that had been developed for their strong efficacy against the axenic bacterium. However, the tubercle bacillus is able to invade a variety of host cells and the sequential timing of the early steps of the invasion processes are the key to the pathogenicity of the bacterium. It is thus important to reinvestigate the multitherapy through this angle to come up with radical advances for tuberculosis drug discovery. We developed miniaturized phenotypic assays based on the use of automated confocal fluorescent microscopy, coupled with dedicated quantitative image analysis, to monitor *M. tuberculosis* entry and growth in various host cells as well as phagosomal acidification stabilization. These high throughput visual approaches enabled screening of a large number of drugs, of their combination and of siRNA libraries. Results on novel chemical entities and new cellular targets will be presented here and open novel avenues for dual host- and pathogen-directed therapies.

Biography

Priscille BRODIN has completed her PhD in 2000 from Paris University and has been a postdoctoral fellow in the Institut Pasteur Paris before being hired by the Institut National de la Santé et de la Recherche Médicale (INSERM) in 2005. She is head of the Chemical Genomics and Intracellular Mycobacteria Team at the Center for Infection and Immunity of Lille. In addition to pursuing drug discovery efforts to combat tuberculosis, including the optimization of drug delivery and drug combinations, she focus on characterizing key host signaling pathways used by *M. tuberculosis* for replication. As partner in the EquipEx ImagInEx BioMed project, she developed an automated platform for cell-based assays, now affiliated to Chembiofrance (https://chembiofrance.cn.cnrs.fr/en/ directed by J.L. Galzi) and provide expertise in high-throughput content screening to teams working on HCS projects. For example, one such project involved deciphering a novel pathway mediated by a bacterial lipid to achieve pain control. She was laureate of an ERC Grant (INTRACELLTB) and published > 100 papers.

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MRI-guided Therapies in Interventional Radiology

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Image-guided, minimally invasive procedures have revolutionized the practice of cancer treatment over the past decade, with an increasing number of targeted organs (liver, brain, breast, pancreas, lungs, bone metastasis, prostate…). They have been shown to be associated with significantly reduced hospitalization times, lower complication rates, and lower adjusted expenditures than their equivalent open surgical procedures[1,2]. They offer new therapeutic options and allow to treat patients that would not be able to tolerate large, invasive interventions. These procedures rely on the use of medical imaging (CT-scan, MRI, ultrasound...) for their guidance and monitoring. Among these imaging modalities, Magnetic Resonance Imaging (MRI) is strongly developing because of the absence of radiation for physicians and patients. MR-compatible instrumentation for ablation has also been developed over the past decade with FDA and CE marked clinical devices. New advances in rapid MRI acquisition techniques and reconstruction capabilities, together with real-time image processing allow image several imaging planes per second in any orientation for therapy targeting, real-time monitoring of temperature changes during the ablation, automatic feedback to the ablation device for optimal energy deposition during the procedure and evaluation of the therapeutic outcome.

After a short review on the major clinical indications, this talk will be focused on some of the most significant technological challenges and solutions in interventional MRI. This includes thermal ablation technology, either using percutaneous approach (radiofrequency (RF), laser ablation, cryoablation) or fully non-invasive, extracorporeal approach (High Intensity Focused Ultrasound (HIFU), which is based on the interaction between the acoustic energy and biological tissue). Interventional MRI acquisition protocols and methods will also be reviewed, particularly in the field of real-time monitoring of the therapy.

Biography

Elodie BRETON is an MRI physicist whose early work focused on fast quantitative cardiac MRI at NYU. She started working in 2011 in the field of interventional MRI (musculoskeletal and abdominal) at the ICube laboratory along with Pr. Gangi, head of the Interventional Imaging department in Strasbourg University Hospital. She develops fast MRI techniques for planning, guiding and monitoring image-guided therapies.
Jonathan VAPPOU is a CNRS research scientist in ultrasound and image-guided therapies, holding a PhD thesis in MR Elastography, after which he worked as a postdoc at the Ultrasound Elasticity and Imaging Laboratory at Columbia University, NY, before joining the ICube laboratory. He is developing therapeutic ultrasound activities in this laboratory.

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Small animal imaging centre of the Institute of Molecular and Translational Medicine

Miroslav POPPER

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The Institute of Molecular and Translational Medicine (IMTM), Faculty of Medicine and Dentistry, Palacký University in Olomouc is cutting-edge biomedical research institute in the Czech Republic. The IMTM's mission is basic and translational biomedical research with the goal to understand the underlying causes of cancer and infectious diseases and to develop future human medicines and diagnostics. IMTM contains several research groups and facilities including small animal imaging centre. The Small Animal Imaging Centre (SAIC) of IMTM provides a non-invasive multi-modality imaging and image analysis to observe various disease and biological models in living systems. Our state-of-the-art instrumentation currently comprises extensive suite of imaging modalities e.g. positron emission tomography (PET), single photon emission computed tomography (SPECT), computed tomography (CT), optical imaging (including bioluminescence and fluorescence ranging from green to near infrared) and ultrasound (US). In addition, fully equipped radiochemistry lab and dedicated housing for animals undergoing longitudinal imaging studies is available. SAIC is mainly focused on the development of novel radiopharmaceuticals and molecular imaging agents. This includes the development of novel radiolabelling strategies, *in vitro* and *in vivo* evaluation of novel tracer candidates using broad spectrum of imaging approaches. It also develops novel small animal models of various diseases, particularly for infectious diseases and cancer. The presentation will introduce SAIC and present the main directions of our research.

Biography

Miroslav POPPER has completed his PhD in 2016 at Laboratory of Gnotobiology (University of Veterinary Medicine and Pharmacy in Košice). He is head of the animal facility of the Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry Palacky University Olomouc. He has published 4 scientific articles printed in current contents journals (CC), and 18 articles published at proceedings of the scientific conferences.

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Optical guided theranostic approaches

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Reducing adverse effects on healthy tissues and improving the accumulation of drugs at the correct site is of major importance for the treatment of cancers. To this aim, our team is developing multifunctional theranostic particles targeting tumor cells and/or the tumor microenvironment. Because they are theranostic agents, they serve for diagnosis as well as for therapy. We particularly focus on optical-based systems for their detection and possible on site(s) activation.
Indeed, in recent years, imaging methods using near-infrared light (λ 700-900 nm) have been applied to non-invasive real-time imaging in mice and are now entering clinic phases. We are now entering in a new era of the SWIR imaging (λ 900-1700 nm) due to the development of adapted camera. Optical imaging can also be combined with ultrasonic imaging modalities and provide additional information (photoacoustics).
We have developed several nano-vectors and optical systems for the diagnosis and targeted therapy of cancers as well as for the diagnostics of other diseases. The different nanosystems are based on scaffolds of organic and inorganic molecules and can deliver contrast agents with different drugs or pro-drugs. Using near-infrared imaging, we can track their distribution, monitor their function and therapeutic activity using non-invasive, non-radiative, real-time in vivo imaging and then activate them once at the tumor site using light or X-Rays.

Biography

Jean-Luc COLL, DR INSERM, is in charge of the team "Cancer Targets and Experimental Therapeutics" at IAB in Grenoble. Dr Coll had an initial training in molecular biology (thesis in microbial genetics on *E coli*), and then focused on cancer, first as a postdoc at the Burnham Institute (La Jolla USA) and then in the Cancer Research Center of Lyon (CRCL- Centre Léon Bérard). Since the last 20 years, he has been working at the interfaces between biology, chemistry, physics and medicine with a clinical (veterinary and human) and industrial (2 Start-up) vision. Dr Coll is in particular focused on the use of near-infrared labeled nanoparticles to target tumors, guide surgery and enhance radiotherapy, phototherapy or innovative therapies. In addition to the developments of nanovectors, he is also deeply involved in the generation of innovative adapted medical device

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In vivo Photoacoustic Monitoring of the Biodistribution of Cyanine Dyes Doped HPMA in Healthy and Tumor Mice

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Combined high frequency ultrasound and photoacoustic (PA) *in vivo* imaging is attractive for providing information about anatomical and molecular changes of selected tissues in real time. PA imaging allows for the monitoring of native compounds in tissues e.g. oxy- and deoxy-haemoglobin or artificial exogenous contrast agents e.g. fluorescent dyes. The ratio between oxy- and deoxy-haemoglobin is an important parameter for the evaluation of the tumor hypoxia level [1] and can be measured together with cyanine dyes in a so-called optical window (700-900 nm) where the native tissue has low absorption levels. The second important parameter for tumor characterization is its own vascularization which is closely related to the distribution of metabolites and therapeutics.
Studying cyanine dyes is attractive for their variable absorption especially in the NIR spectral region, enabling them to avoid overlapping with endogenous contrast. Many efforts are devoted to polymer attached dyes for targeted drug delivery based on water soluble polymers. Herein we compare biodistribution of water soluble HPMA polymer labeled with three cyanine dyes, namely: Cy7, Cy7.5 and Indocyanine green (ICG) using optoacoustic imaging technique in healthy and patient-derived xenograft (PDX) NodCg bearing patient malignant lymphoma treated with cytarabine and controlled non-treated PDX lymphoma mice. The work is focused on the tumor vascularization and tumor oxygenation in cancer tissues as well as biodistribution of HPMA-dye in all abovementioned mice. Our study suggests the HPMA-dye (dye= Cy7, Cy7.5, ICG) showed a strong signal after 24 hours in the implanted subcutaneous subcutaneous tumor, liver and spleen.

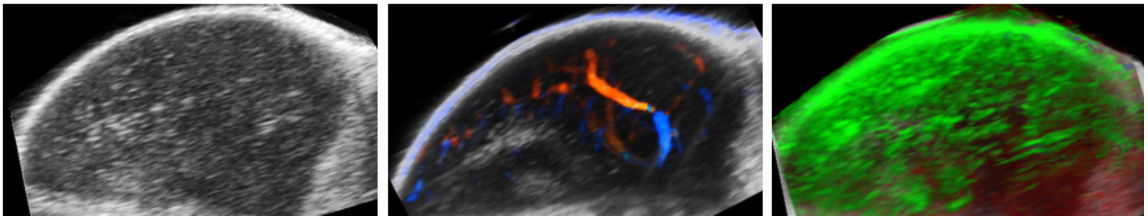

Figure 1. Left to right: Ultrasound *in vivo* imaging, combined ultrasound/Color Doppler imaging and ultrasound/photoacoustic imaging of the Mantle cell lymphoma tumor.

Biography

Peter KEŠA has obtained his PhD from Pavol Jozef Safarik University in Kosice, Slovak Republic. He is interested in preclinical photoacoustic imaging of small animals.

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PET imaging of mantle cell lymphoma

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Xenografts of mantle cell lymphoma, that is a non-Hodgkin lymphoma (NHL) with a bad outlook, were imaged by the FDG positron emission tomography (PET), that represents a widely clinical and preclinical imaging method useful for high energy active tissue identification. Primary cells from patients and standardized cell lines HBL and JEKO were compared. There was also investigated impact of the treatment of animals with an VEGF blocker Bevacizumab (Avastin). Images were evaluated by an eye and by standardized uptake values (SUV). When uptake of standardized cells was high even without quantification, remarkable differences were observed among primary cells. This is an interesting phenomenon for the future utilization in the clinical praxis.

Biography

Adam MODRÝ has completed MSc. degree at UCT Prague in 2011 in the field of synthetic and medicinal chemistry, where he was dealing with the problematic of coupling reactions on the calixarenes structures. During the study he has spent 6 months in KU Leuven (Belgium). After finishing the study, he stayed another 9 months in TU Dortmund (Germany) in the group of molecular imprinting. After coming back to Czechia, he started to work for a 5 years in the commercial sphere at Draslovka Kolín, where he spent a most of time with synthesis and laboratory to plant scale-up of amino acids. From the spring 2018 he is a member of CAPI, where he is responsible for nuclear imaging.

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Mechanism-guided novel therapies for treating inflammatory diseases

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Nowadays, pharmacologic treatments of inflammatory and autoimmune diseases are largely palliative rather than curative. They result in non-specific immunosuppression, which can be associated with disruption of natural and induced immunity with significant, sometimes dramatic, adverse effects. Among the novel strategies that are under development, tools that target specific molecular pathways and cells, and more precisely modulate the immune system to restore normal tolerance mechanisms, are central. In these approaches, peptide therapeutics constitute a class of agents that display many physicochemical advantages. Among them, the phosphopeptide P140 is very promising for treating patients with systemic lupus, and probably more largely patients with chronic inflammatory diseases. P140/Lupuzor is currently evaluated in phase III-clinical studies worldwide. This peptide targets key elements of chaperone-mediated autophagy, which are hyperactivated in lupus. The "correcting" effect of P140 on autophagy results in a weaker signaling of autoreactive T and B cells, leading to a significant improvement of physiopathological conditions. These findings open novel avenues of therapeutic intervention in pathological conditions in which reduction of autophagy activity is desired. After the era of drugs classified as "disease-modifying" therapeutics, a new type of "mechanism-guided" therapies starts to emerge for treating inflammatory diseases.

Biography

Since 2001, Sylviane MULLER is the head and coordinator of the *Drug discovery center for cancer and inflammation Medalis* awarded 'Laboratory of Excellence'. She was the former Director of the CNRS Unit *Immunopathology and therapeutic chemistry* (2001-2017) and of the CNRS Institute of Molecular and Cellular Biology in Strasbourg (2016-2017). She was Distinguished Class Research Director in CNRS (until 2018). She is presently Professor at the Institute of Advanced Studies of the Strasbourg University (chair of Therapeutic immunology) and Emeritus Director at CNRS, and continues to carry out research with her team in the laboratory of "Biotechnology and cell signaling". She earned her doctorate in Sciences at the University of Strasbourg and was a postdoctoral researcher in Freiburg (Germany) at the Max-Planck Institute for Immunobiology. S. Muller holds 30 patents and has published more than 375 publications and review articles/chapters. She co-founded Neosystem (today Polypeptide France) and ImmuPharma. She was awarded the Silver Medal of CNRS (2010), the CNRS Innovation Medal (2015), the Léon Velluz Prize from the French Academy of Sciences (2016). She was a Finalist of the 2017 European Inventor Award (category Research). S. MULLER is Chevalier de l'Ordre de la Légion d'Honneur (2010) and Officier de l'Ordre National du Mérite (2016).

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Anti-cancer immune responses and targeted therapy based on polymer drug delivery systems

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Polymer drug delivery systems represent a modern strategy for tumor treatment, which possess the ability to potentiate the treatment effect of the parent drug without significant systemic toxicity, and ensure a higher rate of the activation of the anti-tumor immune responses during and after the treatment. Conjugation of a low-molecular weight drug to a synthetic polymer carrier enables targeted drug delivery to tumor tissue or cells, while limiting the exposure of normal tissues. Water-soluble *N*-(2-hydroxypropyl)methacrylamide (HPMA) is one of the most promising drug carriers, enabling creation of variable carrier architecture, controlled drug release, and solubilisation of hydrophobic drugs. The conjugates show significantly extended circulation time and preferentially accumulate in solid tumor tissue by Enhanced Permeability and Retention (EPR) effect. In experimental tumor models, the HPMA copolymer conjugates carrying cancerostatic drugs have proven reduced systemic toxicity, high antitumor efficacy, and ability to induce complete tumor regression with subsequent tumor resistance. Indeed, the immune system of the host is co-responsible for the curative effect of the treatment. The resistance is induced during the treatment, where antigens released from the tumors due to the drug administration serve as endogenous vaccine to activate immune anti-tumor mechanisms. Moreover, the treatment with the polymer cytotoxic drugs appears beneficial in combination with checkpoint inhibitors, which significantly improved therapy of many cancers. The HPMA-based drug delivery system is also explored to deliver agents, which could reduce activity of suppressor cells in the tumor microenvironment, in order to achieve synergistic effect of targeted chemotherapy and modulation of the host anti-tumor immune responses.

Biography

RNDr. Milada ŠÍROVÁ, PhD. is a member of Laboratory of Tumor Immunology at the Institute of Microbiology, Czech Academy of Sciences in Prague. For the last two decades, she has specialized in the study of drug delivery, namely relation of the structure and effects of the polymer drug delivery systems designed for targeting drugs to solid tumors and impacts of the therapy on the anti-tumor immune responses. She collaborates with the team of polymer chemists at the Institute of Macromolecular Chemistry in Prague, and is a principal (co)-investigator in a number of joint projects. She published papers concerning genetic regulation of immune responses, immunogenicity of biomaterials for regenerative medicine, and polymer-based drug delivery to tumors.

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A bifunctional biased mu opioid agonist - neuropeptide FF receptor antagonist as analgesic with improved acute and chronic side effects

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Opioid analgesics, such as morphine and fentanyl, continue to be the cornerstones for treating moderate to severe pain. However, upon chronic administration, their efficiency is limited because of prominent side effects such as tolerance and dependence. One hypothesis for the occurrence of these side effects is that the chronic stimulation of the opioid system may trigger its endogenous counterparts, anti-opioid systems, producing hyperalgesia (opioid-induced hyperalgesia, OIH) and analgesic tolerance. Previous data from our lab and others have shown that RF9, an antagonist of neuropeptide FF receptors (NPFF1R and NPFF2R), efficiently blocks opioid-induced hyperalgesia and tolerance when co-administered with fentanyl or morphine in rodents. In this study, we designed multi-target molecules that display mu-opioid receptor (MOR) agonist activity, as well as NPFF receptor antagonist properties. To this purpose a set of unnatural peptide ligands was generated, which combines an already known high affinity mu-opioid receptor agonist together with the carboxyl-terminal RF-amide signature of NPFF. In vitro characterization of these compounds led to identification of KGFF03 and KGFF09 as G protein-biased MOPr agonists with full agonist or antagonist activity at NPFFRs, respectively. In agreement with their biased MOPr agonism, KGFF03/09 showed reduced respiratory depression in mice, as compared to the unbiased parent opioid agonist KGOP01. Chronic subcutaneous administration of KGOP01 and KGFF03 in mice rapidly induced hyperalgesia and analgesic tolerance, effects that were not observed upon chronic treatment with KGFF09. This favorable profile was further confirmed in a model of persistent inflammatory pain. In addition, we showed that KGFF09 induced less physical dependence compared to KGOP01 and KGFF03. Altogether, our data establish that combining within a single molecule G protein-biased MOPr agonism and NPFFR antagonism have beneficial effects on both acute and chronic side effects of conventional opioid analgesics. This strategy can lead to the development of novel and potent antinociceptive drugs with limited side effects upon acute and chronic administration.

Biography

Frédéric SIMONIN is recognized for its expertise in the field of GPCRs and particularly in molecular biology and pharmacology of opioid and related peptide receptors. Since 2005, he has been working on adaptations following chronic stimulation of GPCRs and particularly the development of hyperalgesia following opiates chronic administration or in chronic pain syndromes. He has published the discovery of the first selective and small antagonist for NPFF receptors that prevents the development of morphine analgesic tolerance and hyperalgesia, and is currently working at the characterization of novel antagonists of other RF-amide receptors as well as compounds that neutralize the activity of different chemokines. Frédéric SIMONIN also discovered a novel family of proteins that interact with GPCRs, named GASP, which play a critical role in the development of adverse side effects associated with chronic stimulation of different GPCRs and several diseases. He has a strong expertise in the engineering and phenotyping of genetically modified mice and published several high impact factor papers in this field.

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An innervated, vascularized and immunocompetent human skin model to study cutaneous neuroimmune interactions.

Vincent FLACHER

Laboratoire CNRS UPR3572 Immunology, Immunopathology and Therapeutic Chemistry (I^2CT), Institut de Biologie Moléculaire et Cellulaire, Université de Strasbourg, Strasbourg, France.

Pathogens, sensitizing chemicals and autoimmune diseases trigger T cell-driven inflammation in the skin under control of cutaneous Dendritic Cells (DCs). No in vitro human model recapitulates the features of cutaneous immune responses. Indeed, such models frequently lack an epidermal barrier, necessary to investigate topically applied compounds, and fail to acknowledge the influence of non-immune cells which modulate the activation of DCs and T cells. This represents a major shortcoming and prevents accurate pre-clinical evaluation of anti-inflammatory drugs, vaccine adjuvants or potentially allergenic chemicals (sensitizers). To resolve this, we developed a novel Innervated and Vascularized immunocompetent Tissue-Engineered Skin Tissue-Engineered Skin (IV-iTES) combining all structural and functional elements of the healthy skin.
The IV-iTES model integrates human keratinocytes, fibroblasts, dendritic cells and pseudo-capillaries, as well as a sensory nerve network derived from either murine embryos or human induced pluripotent stem (iPS) cells. Our culture conditions were adjusted to guarantee a stable phenotype for all cell populations, thereby mimicking steady-state human skin. The structure of the resulting co-culture and cell-specific markers were thoroughly characterized. Sensory nerves could be triggered in situ by agonists of their specific receptors and subsequently released neuropeptides substance P and CGRP. When exposed to known sensitizers and control molecules, cytokines were released in the supernatant with a pattern that reflected the properties of the chemicals. Altogether, the IV-iTES should allow in-depth investigations and predictions on cutaneous toxicity, angiogenesis and inflammation.

Biography

Vincent FLACHER obtained a PhD in Immunology in 2005. He worked with Pr. Nikolaus Romani and Pr. Ralph Steinman as a postdoctoral fellow on the therapeutic harnessing of skin dendritic cells at the laboratory for Langerhans cell research in Innsbruck, Austria. In 2012, he joined the team of Dr. Christopher Mueller as a permanent CNRS researcher in the laboratory for Immunology, Immunopathology and Therapeutic Chemistry in Strasbourg, France. There, he is responsible for research programs investigating the crosstalk of dendritic cells and macrophages with their cellular environment in the skin and other organs. In this context, he recently codeveloped with Dr. François Berthod (Québec, Canada) an immunocompetent and innervated model of human skin, which will be applied to fundamental and applied research on interactions between the nervous and the immune systems.

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Nucleolus precursor bodies: Atypical organelles in atypical cells

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The nucleolus is the quintessential example of a membrane-less organelle. Located within the cell nucleus, nucleoli are the site of ribosomal RNA (rRNA) production and ribosome subunit assembly. Nucleoli typically exhibit a tripartite organization. However, under certain conditions, the morphology and protein composition of nucleoli can change and atypical nucleoli can be observed. Mammalian oocytes and early embryos represent one such example. Here, the nucleolar material forms a homogenous dense body called the "nucleolus precursor body" (NPB). Over the past years we have shown that these atypical nucleoli are strictly of maternal origin and essential for early embryonic development. In contrast to their expected role in ribosome biogenesis, they seem to be involved in remodeling the embryonic chromatin. When NPBs are absent, the centric and pericentric heterochromatin collapses, fails to be remodeled and embryos arrest at the two cell stage. However, the exact mechanism by which NPBs participate in this process or whether there is a specific NPB component directly involved in the chromatin remodeling remains to be determined. By using advanced micromanipulations of mouse oocytes and embryos we show that the amount of the NPB material is critical in the context of development. While the excess of this material seems to be well tolerated by embryos with only mild perturbations to their developmental program, even a mild reduction of the NPB mass has detrimental effects on the developmental ability. Moreover, we find that the NPB material is not species-specific and interorder NPB exchange can be performed successfully. In these experiments, the critical factor affecting the developmental outcome is the amount of the NPB material transferred.

Biography

Helena FULKOVA (FULKA) obtained her PhD from the Charles University in 2008 and is currently employed at the Institute of Experimental Medicine, AS CR and the Institute of Animal Science in Prague. Together with colleagues, she has published over 40 scientific papers with more than 700 citations in international journals including Science, Development, Trends in Molecular Medicine or Stem Cells. HF has a long-standing experience working with mammalian oocytes and embryos, advanced in vitro reproductive technologies including micromanipulations, genetic manipulation, and participated in developing some unorthodox approaches such as interspecific nuclear transfer, embryonic stem cell derivation from maturing oocytes or microsurgical removal of nucleoli from oocytes and embryos.

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Modulation of amphiphysin and dynamin rescues severe congenital myopathies

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Centronuclear and myotubular myopathies (CNM) are a group of severe muscle diseases characterized by muscle weakness and organelles mis-positioning in myofibers. The severe X-linked form, also called myotublar myopathy, is caused by loss-of-function mutations in the phosphoinositide phosphatase Myotubularin (MTM1), while two main autosomal forms are due to mutations in Amphiphysin 2 (BIN1) or Dynamin 2 (DNM2). Albeit these proteins are associated to lipid metabolism and membrane remodeling, their links and the underlying CNM pathomechanisms are still unclear. Moreover, there is a strong need for therapeutic solutions for the different CNM forms.

In order to decipher the CNM pathway and test rescuing strategies, we have created and validated corresponding faithful mouse models and modulated these genes in all models. We now report mice models for the MTM1, BIN1 and DNM2 forms, reproducing severe muscle weakness and nuclei centralization that are viable at least until 2 months, so the effect of therapies can be tested and assessed. Modulation of the different CNM genes in the different forms of CNM in mice revealed a strong epistasis. Results highlight that MTM1, BIN1 and DNM2 are part of a common pathway regulating myofiber intracellular organization. These experiments also identified two therapeutic targets, BIN1 and DNM2, which modulation can rescue the lifespan, muscle weakness and histopathology of different CNM forms in mice. For example, reduction or normalization of DNM2 level, either by genetic cross, antisense oligonucleotides, or AAV expressing shRNA, can prevent the development of MTM1, BIN1 and DNM2 related CNM. Moreover, injection of antisense oligonucleotides to severely affected Mtm1KO mice can block the progression of the disease after one week and revert the phenotype within 2 weeks. In addition, overexpression of BIN1, though genetic cross with a mouse overexpressing human BIN1 or through AAV transduction, can also rescue the disease in the MTM1, BIN1 and DNM2 related CNM models.

These results indicate that MTM1, BIN1 and DNM2 regulate muscle development, organization and function through a common pathway, and define BIN1 as a negative regulator of DNM2 in vivo. Our data also define a so-called “cross-therapy” paradigm, where modulation of a CNM gene can rescue the defects linked to other CNM genes.

Work done with Valentina Lionello, Belinda Cowling, Hichem Tasfaout, Anne-Sophie Nicot, Christine Kretz, Suzie Buono, Ivana Prokic, Vasugi Nattarayan, and Xenia Massana Munoz

Biography

Jocelyn LAPORTE completed his PhD in 1997 from Strasbourg University before being hired by the Institut National de la Santé et de la Recherche Médicale (INSERM) in 1998. He is leading a team at the IGBMC (Illkirch) studying the genetic and cellular bases of neuromuscular diseases and validating therapeutic proof-of-concept in laboratory models. His team’s research is translational with impact on routine genetic diagnosis at hospitals and creation of a start-up developing human clinical trials.

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Modulation of cytosolic Proliferating Cell Nuclear Antigen (PCNA) in neutrophils to promote the resolution of inflammation

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Research in to neutrophil biology in the last ten years has uncovered a number of unexpected aspects of this poorly understood innate immune cell. There has been increasing appreciation of the heterogeneity of neutrophils with ongoing categorization of neutrophil subsets, including myeloid-derived suppressor cells and low density granulocytes. Finally studies of neutrophil cell death, both apoptotic and non-apoptotic, has revealed remarkable differences compared to other cell types. The Proliferating cell nuclear antigen (PCNA) has been characterised as a mediator of cell proliferation but has been identified by our group as a novel mediator of neutrophil apoptosis. Normally expressed primarily in the nucleus in the majority of cell-types, PCNA is expressed in the cytoplasm of mature neutrophils where it sequesters pro-caspases, limiting their activation and delaying apoptosis. Peptides derived from the endogenously expressed cyclin-dependent kinase inhibitor, p21, displace the pro-caspases from PCNA and facilitate activation to trigger neutrophil apoptosis. More recently, we have described that PCNA could control NADPH oxidase in neutrophils thereby linking activation and apoptosis in neutrophils. Accordingly, we Have recently shown that the cytosolic PCNA scaffold can be harnessed for anti-inflammatory purposes in a murine model of zymosan-induced peritonitis, chronic Pseudomonas aeruginosa pulmonary infection and colitis. This new data highlight important discoveries in the field of anti-inflammatory therapies and might be translated to clinical applications.

Biography

Véronique WITKO has completed her PhD from Université Pierre et Maris Curie, Paris VI in 1995 and her HDR from the Université Paris Descartes in 2002. VW is Director of Research (DR1) at INSERM (Institut National pour la Santé et la Recherche Médicale) and Group leader at the Cochin Institute, Paris France in the department of Immunology, Inflammation and Infection (3I) of the team entitled : "Neutrophils and vasculitis.

VWS is a councilor at the society for Leukocyte Biology and is a member of the Admnistrative Council of the Societé Française d'Immunologie (SFI); Coordinator of the « Neutrophil club » created in July 2014 at the SFI.

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Polymer-based drug delivery systems for treatment and diagnosis of inflammatory diseases

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Inflammation resolution in chronic inflammatory diseases (CID), e.g. rheumatoid arthritis (RA), still remains problematic and current therapy reduces disease symptoms and leads to severe side effects. The use of water-soluble polymer drug conjugates may significantly improve CID treatment due to their passive targeting into inflammation and controlled drug release. The polymers are accumulated in inflamed tissues due to ELVIS effect (extravasation through leaky vasculature and subsequent inflammatory cell-mediated sequestration). The polymer conjugates with dexamethasone (Dex) based on biocompatible copolymers of *N*-(2-hydroxypropyl) methacrylamide (HPMA) have exhibited superior anti-inflammatory activity in RA rat model with minimized side effects compared to free Dex. To study polymer biodistribution *in vivo*, several fluorescently labeled polymer systems with diverse M_w were synthesized and their fate in mice with acute arthritis was observed. The polymer carriers were accumulated in inflamed joints to a higher extent than in healthy joints and the accumulation occurred 30 min after i.v. polymer injection and remained till the end of the experiment (72 h). The accumulation rate was molecular-weight dependent – the carriers with higher molecular weight exhibited enhanced accumulation rate. Thus, the HPMA-based polymer carriers enable passive targeting to inflamed tissue and their conjugates with antiinflammatory drugs may improve the CID treatment.

Biography

Eva KOZIOLOVÁ has completed her PhD from Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (IMC) in 2016. She was awarded a "Prix de Pharmacie" organized by the French Embassy in Prague in 2016. She passed one-year postdoctoral internship in France at the University of Montpellier and at the University Paris Descartes. She is currently employed at the Department of Biomedicinal Polymers of IMC. Her research is focused on preparation of diverse polymer-based drug delivery systems for effective treatment of cancer and inflammation. She has published 18 papers in reputed international journals and presented her work at numerous international conferences.

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Dynamics of GPCR signaling and application to bioactive molecules discovery

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Excessive signaling by chemokines has been associated with chronic inflammation or cancer, thus attracting substantial attention as promising therapeutic targets. Inspired by chemokine-clearing molecules shaped by pathogens to escape the immune system, we designed a generic screening assay to discover chemokine-neutralizing molecules (neutraligands) and unambiguously distinguish them from molecules that block the receptor (receptor antagonists). This assay, called TRIC-r, combines time-resolved intracellular calcium recordings with pre-incubation of bioactive compounds either with the chemokine or the receptor-expressing cells. We describe the identification of high affinity neutraligands of CXCL12, CCL17 and CCL22, three chemokines involved in Th2-type inflammations. The decoy molecules inhibit in vitro chemokine-induced intracellular calcium responses, CCR4 and CXCR4 endocytosis and human T cell migration. In vivo, they inhibit inflammation in several models of inflammation such as asthma or atopic dermatitis, in particular they block the recruitment of eosinophils, dendritic cells and CD4+T cells. Their mechanism of action and long lasting effects will be described in details from the in vitro up to the in vivo level.

Biography

Jean-Luc GALZI has completed his PhD in 1987 from Strasbourg University and has been a postdoctoral fellow in the Institut Pasteur Paris before being hired by the Centre national de la Recherche Scientifique (CNRS) in 1990. He is the director of the Institute of Research on Biotechnologies at the school of biotechnology of Strasbourg, and is the director of the national Research Infrastructure ChemBioFrance devoted the “discovery of small molecules for health and research applications”. He has published more than 100 papers in reputed pharmacology and more generalist journals and is member of the scientific board from the CNRS and the French Alliance for Health and Life Sciences (Aviesan).

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1. **DOVGAN Igor,** *Biofunctional Chemistry, UMR 7199, Faculty of Pharmacy, LabEx Medalis, 74 Route du Rhin, 67400 Strasbourg-Illkirch, France.*
   Automated one-to-one linkage of proteins and payload.

2. **GROYSBECK Nadja,** *UMR 7242 Biotechnology & Cellular Signaling, CNRS-University of Strasbourg, France.*
   Thiolate-specific conjugation of cetuximab and nanobody to circa 2 nm gold nanoparticles as novel approach for targeting and imaging.

3. **JUNG Marie-Louise,** *Prestwick Chemical, 220, Boulevard Gonthier d'Andernach, 67400 Strasbourg-Illkirch, France.*
   The Prestwick Chemical Library, a valuable tool for screening.

4. **KARABANOVICH Galina,** *Farmaceutic Faculty, Charles University, Hradec Kralove.*
   Novel derivatives of dexrazoxane: synthesis and structure in vitro cardioprotective activity relationships study.

5. **KRATOCHVÍLOVÁ Adéla,** *Institute of Animal Physiology and Genetics, CAS, Laboratory of Odontogenesis and Osteogenesis, Brno, Czech Republic.*
   Inhibition of pro-apoptotic caspases in osteoblasts causes changes in expression of Ocn and Phex genes.

6. **LE GUEVEL Xavier,** *INSERM U1209/UGA/ CNRS UMR5309, Institut for Advanced Biosciences, La Tronche, France.*
   Development of gold nanoclusters for optical imaging in the shortwave infrared window.

7. **LIBÁNSKÁ Alena,** *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Heyrovského nám. 2, 162 06 Prague 6, Czech Republic.*
   Delivery systems for treatment and diagnosis of inflammatory diseases.

8. **MULLER Quentin,** *Laboratoire CNRS UPR3572, Immunology, Immunopathology and Therapeutic Chemistry (I2CT), Institut de Biologie Moléculaire et Cellulaire, Université de Strasbourg, Strasbourg, France.*
   Innervated and Vascularized Immunocompetent Human Tissue Engineering Skin to the Study of Cutaneous Neuroinflammation.

9. **QUILLET Raphaëlle,** *UMR7242-BSC, CNRS, University of Strasbourg, 67400 Illkirch, France.*
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10. **RETNAKUMAR Sruthi Vijaya,** *School of Biotechnology, University of Strasbourg, France.*
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11. **ROQUES Caroline,** *UTCBS Unité des Technologies Chimiques et Biologiques pour la Santé, UMR CNRS 8258 / Inserm U1022, Faculté de Pharmacie de Paris.*
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12. **SILVA-ROJAS Roberto,** *Pathophysiology of Neuromuscular Diseases Team, Translational Medecine and Neurogenetics Department, Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), 67400 Illkirch-Graffenstaden*.
    Reversal of the cellular phenotype of tubular aggregate myopathy (TAM) using a pharmacological approach.

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