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ABSTRACTS

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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). We have synthesized various polymer conjugates with dexamethasone (Dex) based on biocompatible copolymers of *N*-(2-hydroxypropyl) methacrylamide (HPMA) differing in hydrodynamic size or pH-sensitive release rate of Dex. They exhibited superior anti-inflammatory activity compared to free Dex in two murine models of arthritis, i.e. acute single-joint arthritis (adjuvant induced arthritis) and chronic polyarticular arthritis (collagen II-induced arthritis). The polymer conjugates exhibit prolonged blood circulation, enhanced inflammatory site accumulation, site-specific drug release and subsequent elimination of the carrier via urine excretion. The pH-sensitive drug attachment enabled enhanced blood circulation with minimal systemic drug release, as well as rapid drug activation in affected joints. Importantly, unlike free DEX, the polymer nanomedicines were able to diminish joint inflammation and arthritis-induced bone damage - even at a reduced dosing regimen - as evaluated by micro computed tomography (micro-CT).

Keywords: polymer conjugate; drug delivery; inflammation; HPMA; dexamethasone; adjuvant induced arthritis; collagen II-induced arthritis; passive targeting

This work was supported by the by the Czech Science Foundation (grant No. 19-00956Y).

Biography

Eva Randárová 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 26 papers in reputed international journals and presented her work at numerous international conferences.

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LIPOSOMAL CONSTRUCTS TO INDUCE ANTI-TUMORAL IMMUNE RESPONSES

Sylvie Fournel

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Currently, a challenging goal in the area of cancer treatment is the development of innovative targeted antitumoral immunotherapies with a long-term efficiency. In this context, we took advantage of liposomal nanoparticles properties for the conception of a tunable vaccine platform allowing the strategical conception of vaccines containing: i) a CD4 epitope peptide able to stimulate CD4+ T helper cells ii) a tumor CD8 epitope peptide, which induces the differentiation of CD8+ T cells in cytotoxic T cells and iii) Toll or Nod-Like receptor agonist(s), which act as adjuvant for the activation of dendritic cells. After several screening stages, liposomal vaccines were successfully tested in several preclinical murine models. We compared several types of adjuvants, several delivery strategies, etc. In this work, we demonstrated the value of a customizable liposomal platform for the conception of personalized vaccines

Jacoberger-Foissac, C, Saliba, H., Wantz, M., ***Seguin, C.,*** Flacher, V., Frisch, B, Heurtault*, B., **Fournel, S*.** Liposomes as tunable platform to decipher the antitumor immune response triggered. Eur J Pharm Biopharm. **2020**, 152 : 348-357. doi.org/10.1016/j.ejpb.2020.05.026Jacoberger-Foissac, C., Saliba, H., ***Seguin, C.,*** Brion, A., Kakhi, Z., Frisch, B., **Fournel, S.*,** Heurtault, B*. Optimization of peptide-based cancer vaccine compositions, by sequential screening, using versatile liposomal platform. Int. J. Pharm. 2019, 562, 342-350. **.**DOI: 10.1016/j.ijpharm.2019.03.002

Biography

Sylvie Fournel is professor of immunology at the Life Science faculty of Strasbourg university. She received her PhD in 1996 at Lyon University. After a post-doctoral position in Toulouse, she moved to Strasbourg university as associate professor in 1999 and became full professor in 2006. She always worked on immunomodulation (how to modulate immune responses) first in the context of autoimmune diseases and more recently in the context of cancer and biomaterials. Her research team (at the interface between chemistry, pharmaceutics technology and biology), is located at the Faculty of Pharmacy of Strasbourg. Her research interests are the development of innovative therapies against cancers and deleterious inflammation.

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CHITOSAN-BASED HYDROGEL FOR CONTROLLED RELEASE OF TRASTUZUMAB

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Trastuzumab represents a breakthrough in treating HER2+ breast cancer patients, increasing the number of definitively cured patients when given in adjuvant setting for early breast cancer and increasing the length of survival for metastatic breast cancer. Since 2013, subcutaneous trastuzumab (H-SC) was approved by the European Medicines Agency as an alternative to conventional trastuzumab intravenous (H-IV) infusion. The H-SC formulation includes recombinant human hyaluronidase (rHuPH20) as an excipient to allow the administration of the subcutaneous volume required to deliver the dose of trastuzumab. Interestingly, population modeling and simulation showed that a fixed H-SC dose given every 3 weeks is comparable with H-IV administered at the same schedule and based on patient's weight. The randomized phase III HannaH study, comparing H-SC with H-IV in patients with HER2+ early breast cancer, validated that the pharmacokinetic profile and efficacy of H-SC was non-inferior to H-IV with comparable safety profile and comparable survival outcomes. Additionally, the PrefHer and MetaspHer studies reported the overwhelming preferences of patients to be treated with H-SC rather than H-IV. With the recent development of trastuzumab biosimilar, however, most of the institutions switch back to IV formulation due to the lower access cost of the drug. Here, we developed a fully biodegradable and biocompatible hydrogel formulation enabling similar pharmacokinetic profile than H-SC while offering additional advantages such as higher dosage and controlled/sustained release properties opening the door for the first-in-class trastuzumab biosimilar SC formulation.

Biography

Alexandre Detappe completed his PhD in nanomedicine applied to medical physics at the University of Lyon/Harvard Medical School in 2017 under the supervision of Prof. Olivier Tillement and Prof. Ross Berbeco. He then conducted a postdoctoral research at MIT and Dana-Farber Cancer Institute with Prof. Irene Ghobrial and Prof. Peter Ghoroghchian in nanomedicine applied to Multiple Myeloma. Since mid-2019, he is Professor of Medicine at the Institut de Cancérologie Strasbourg Europe (ICANS). Research in the Nanotranslational Laboratory at ICANS focuses on combining polymer engineering, synthetic chemistry, immunonanotherapy, and bioengineering of new nanomaterials for biomedical applications. Main application areas are drug delivery, development of novel imaging biomarkers, and optimization of the biofunctionalization of those nanocarriers to improve their specificity and to activate the immune system. translation to the clinic.

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MODULAR AND ADAPTIVE DENDRIMER NANOSYSTEMS FOR BIOMEDICAL APPLICATIONS

Ling Peng

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The application of nanotechnology is widely expected to bring breakthrough in medicine for disease treatment and diagnosis. Dendrimers are ideal materials for elaborating nanomedicine by virtue of their well-defined structure, multivalent cooperativity and nanosize *per se*. I will present our recent studies on modular and adaptive dendrimer nanosystems, constructed via self-assembling of amphiphilic dendrimers,[1] for the delivery of imaging agents,[2] anticancer drugs[3] and nucleic acid therapeutics[4] in cancer detection and treatment. The self-assembling approach to create supramolecular dendrimer is completely novel in concept yet easy to implement in practice, offering a fresh perspective for exploiting the advantageous features of supramolecular dendrimers in biomedical applications.

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Biography

Dr Ling Peng is a CNRS research director at Centre Interdisciplinaire de Nanoscience de Marseille in France. She is a leading expert in developing functional dendrimer nanosystems for biomedical applications such as delivery of anticancer drugs, nucleic acid therapeutics and imaging agents. Her team has been labelled by La Ligue contre Le Cancer for developing nanomedicine in cancer therapy. Dr Peng is a distinguished member of French Chemical Society, and was awarded by the French Academy of Science with the Prize of Dr & Mrs Henri Labbé.

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LUMINESCENT OCTAHEDRAL CLUSTER COMPLEXES FOR BIOLOGICAL APPLICATIONS

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The octahedral cluster complexes $[\{M_6L^i_8\}L^a_6]^n$ (M = Mo, W, Re; L^i = I, S, *etc*.) have attracted a broad interest for the design of photofunctional materials for medicinal, luminescent, and radioluminescent applications [1]. The cluster core $\{M_6L^i_8\}^{4+}$ endows the complexes with robust photophysical properties and the deliberate choice of inorganic/organic apical ligands L^a allows for tuning their physico-chemical and biological properties. Under light irradiation, the complexes form long-lived triplet states that relax via red luminescence, produce singlet oxygen $O_2(^1\Delta_g)$ in high yields, and remain good $O_2(^1\Delta_g)$ photosensitizers even in their aggregated form in contrast to commonly used organic photosensitizers such as porphyrins. Recently we discovered that the complexes can be also excited *via* X-rays [2]. Thus, promising results have already been obtained in the area of X-ray induced photodynamic therapy and radiocontrasting agents.
I will delineate the properties of these complexes, their cytotoxicity and photodynamic activity, and their antiproliferative effects upon X-ray irradiation. The complexes represent an efficient starting point for the development of pharmaceuticals intended to increase the efficacy of cancer radiotherapy, and for photodynamic therapy or photoinactivation of bacteria.
[1] K. Kirakci, K. Lang *et al*., *Dalton Trans*. **2013**, *42*, 7224.
[2] K. Kirakci, K. Lang *et al*., *Biomater. Sci*. **2021**, *9*, 2893 and references therein

Biography
Kamil Lang received his PhD from the Institute of Inorganic Chemistry of the Czech Academy of Sciences (IIC) in 1992. After postdoctoral stays at the University of Barcelona, Cornell University, and University of California Santa Cruz he joined the IIC, where he currently serves as a director. His research interests are photophysics, photochemistry, supramolecular chemistry, porous materials, luminescent materials, transition metal clusters, host-guest interactions, and reactive oxygen species with focus on singlet oxygen. He is a (co)author of 160 papers in impacted journals.

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ADVANCES IN NEURAL INTERFACE TECHNOLOGY – MINIMALISTIC RECORDING AND STIMULATION

Eric Daniel Głowacki

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A great demand exists for minimally-invasive neuromodulation technologies to enable next-generation bioelectronic medicine. This field involves using artificial electrical impulses to achieve a therapeutic outcome, and is successfully deployed in a growing range of clinical applications. Examples include Parkinson's disease, where implanted deep brain stimulators can essentially eliminate symptoms of this condition; epilepsy, where closed-loop stimulators record pathological activity and deliver therapeutic impulses; and various spinal cord and peripheral nerve conditions. The list of applications expands constantly, as patient outcomes often are superior to what can be achieved with pharmaceutical interventions. In this presentation, I will introduce examples of bioelectronic medicine and the newest technologies that are pushing the current limits. A major focus will be minimalistic neural interface technology for selective stimulation of the nervous system. Creating minimally-invasive neuromodulation implants relies on solving advanced materials science and engineering problems. Wireless power delivery will be discussed as one of the major technical challenges in such implanted devices. I will summarize our research team's efforts in using wireless optoelectronic technology for small and conformable nerve and brain stimulation, as well as recent advances in noninvasive stimulation using high-frequency interfering electrical fields.

Biography

Eric Glowacki studied chemistry at the University of Rochester, USA, completing BSc and MSc degrees in chemistry (2009). He worked on optoelectronic materials. In parallel, he studied history, earning a dual degree in 2009. He completed his PhD in chemistry in 2013 at the Johannes Kepler University in Linz, Austria, specializing in flexible electronic devices. He continued as a postdoc in Linz (2013-2016), with research interest moving into the field of electrophysiology and especially optoelectronic stimulation of excitable cells. Between 2016-2020, he led a research group at Linköping University in Sweden within the Wallenberg Center for Molecular Medicine. In 2020, he was awarded the ERC Starting Grant, with which he moved to CEITEC, Brno University of Technology, establishing a new research group dedicated to bioelectronics. Eric is interested in neural interface technologies and bioelectronic medicine, as well as fundamental research in electrophysiology and reactive oxygen in physiology.

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WATER-SOLUBLE POLYMER THERAPEUTICS AND DIAGNOSTICS

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Conjugates of hydrophilic polymers with cytostatic drugs offer numerous advantages in treatment of malignancies compared with the low-molecular weight cancerostatics. The polymer conjugates generally exhibit higher solubility, prolonged blood circulation and increased accumulation in solid tumors. In this study, water soluble copolymers based on *N*-(2-hydroxypropyl)methacrylamide (HPMA) containing covalently bound anticancer drug cytarabine (araC) were designed, synthesized and evaluated for their anti-lymphoma efficacy *in vivo*. Prepared polymer-drug conjugates varied in the rate of hydrolytic release of the drug from the polymer backbone depending on type of the spacer between the drug and the polymer carrier. All the conjugates with araC were more efficient in elimination of mantle cell lymphomas using patient-derived xenograft murine models in comparison with free araC.
Alternatively, the polymer carrier can be labeled with a fluorescent dye to form a polymer probe designed as a diagnostic tool for a fluorescence-guided endoscopic surgery. Specific accumulation of the polymer conjugate in the tumor mass is accompanied with the fluorescence signal originating from the malignant cells, which enables more precise resection of the tumor without damaging the surrounding heathy tissue.
Both systems exhibited high tumor accumulation based on the EPR effect; consequently, these polymer systems are promising candidates for tumor treatment or diagnostics.
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Biography

Robert Pola has completed his PhD at the Institute of Macromolecular Chemistry, Academy of Sciences of the Czech Republic (IMC) in 2009. He spent half-year postdoctoral internship in Spain at the Research Center Principe Felipe in Valencia. He is currently employed at the Department of Biomedical Polymers of IMC. His research is focused on preparation of polymer-based drug delivery systems targeted with synthetic oligopeptides for either effective treatment of cancer or for imaging of tumors. He has published 42 papers in reputed international journals and presented his work at numerous international conferences.

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INNOVATIVE THERAPIES AGAINST CANCERS OF THE AERODIGESTIVE SYSTEM: TO REACTIVATE OR TO BYPASS *TP53*, THAT IS THE QUESTION…

Christian Gaiddon

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Cancers of the aerodigestive system (gastric, lung and head & neck) remain with a particularly dramatic outcome for patients, illustrated by a 5-years survival bellow 30%. This is mostly due to resistance mechanisms towards chemotherapy and to a response to immunotherapy bellow 15%. Notably, mutations in the *TP53* tumor suppressor gene correlate with a reduced response to chemotherapy in patients, an alteration of the immune tumor landscape, and a protein gain of function that favors cell proliferation due to the generation of neo-interactions. In this context, we have developed to complementary strategies. The first strategy aims at bypassing the need of the p53 pathway by using small molecules containing a transition metal (ruthenium, osmium) that procures the ability to modulate directly or upon light irradiation the cellular redox system, notably metabolic redox enzymes. Our results shows that several novel ruthenium complexes can be activated by light and that this leads to high cytotoxicity against cancer cells. The cytotoxicity correlates with induction of several effectors of the ER stress pathway (e.g., ATF4, ATF6, CHOP) involved in apoptosis and with immune cell death (e.g., CALR, HMGB1) that favors an anti-tumor immune response (e.g., phagocytosis by macrophages). Hence, these compounds represent interesting solution for photodynamic therapy and theragnostic that may improve response to immunotherapy. The second strategy aims at reactivating the p53 pathway, notably with small chemicals that bind to mutant p53 and restore partially their normal function. For instance, we are developing small molecules that act as chaperone for p53 and that bring back to p53 a Zn atom. We show that such molecules partially reactivate p53 ability to drive transcription of p53 target genes, facilitating chemotherapy response in cancer cells. Interestingly, these compounds show a reduced toxicity on healthy tissues, as tested on intestinal organoids.To further increase the selectivity of these small compounds we are developing vectorization strategies using liposomes and conjugation with HER2 or EGFR monoclonal antibodies/nanobodies to selectively target cancer cells expressing elevated level of HER2 and EGFR, which is frequently observed in cancer of the aerodigestive system.

Biography

Christian Gaiddon is Director of Research from the ''Centre National de la Recherche Scientifique'' (CNRS) and the head of a Biomedical research team from the ''Institut National de la Santé et de la Recherche Médicale'' (Inserm) at Strasbourg University, France. He has a strong expertise in cancer-related topics, working on molecular mechanisms involved in cancer aggressivity. More precisely, his work is focused on the p53 family and their role in the response of the tumor ecosystem to various stresses, including chemotherapy and extra/intracellular redox imbalances. In addition, he is applying the knowledge gathered for the development of innovative anticancer therapies either to reactivate the p53 pathway or to bypass it with original inorganic chemical compounds that induce the ER stress pathway/proteostasis. Prior to his appointment at CNRS, he investigated the p53 family as a Human Frontier postdoctoral fellow in Pr. C. Prives's lab at Columbia University, NYC. He earned his PhD in Molecular Pharmacology in Cancer and Neurobiology, Strasbourg University, France. He was awarded a French national prize for Innovation and was the founder/scientific advisor of Almetis, a biotech developing metal-based anticancer drugs.

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INNOVATIVE RADIOPHARMACEUTICS FOR IMAGING, TRACING AND TREATING OF HUMAN DISEASES

Miloš Petřík

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Innovative radiopharmaceuticals for imaging, tracing and treating of human diseases Miloš Petřík Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, Palacký University in Olomouc, Czech Republic The use of animals plays a central role in preclinical and translational biomedical research. In drug development, animal and other laboratory tests provide basic and indispensable information for further human studies. Recently, in vivo imaging of small animals has become an integral part of preclinical research. Prior to the widespread adoption of preclinical imaging, animal sacrifice was unavoidable in order to obtain relevant information about the pharmacokinetics and biodistribution of the drug under investigation. Small animal imaging however provides a noninvasive means of assaying biological structure and function in vivo, allowing follow-up of a specific disease or drug within the same animal, ultimately improving statistical analyses and reducing the number of animals required per experiment. These techniques are usually performed with imaging systems dedicated to imaging of small animals. These are complex devices that can combine different imaging modalities such as positron emission tomography (PET), single-photon emission computerized tomography (SPECT), computerized tomography (CT), magnetic resonance imaging (MRI), ultrasound and optical imaging. This presentation will focus on presenting the experience of the Small Animal Imaging Centre of the Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, Palacký University in Olomouc in the development of novel radiopharmaceuticals for imaging and treatment of human diseases using small animal imaging techniques.

Biography

Miloš Petřík received his PhD in 2008 from Charles University in Prague and worked as a postdoctoral fellow at the Medical University of Innsbruck before joining the Institute of Molecular and Translational Medicine (IMTM) in 2011. He is the head of the Small Animal Imaging Centre at the IMTM, holds a European Specialisation Certificate in Radiopharmacy and is the national coordinator of Imaging and Tracing platform for the European Infrastructure for Translational Medicine. He has published more than 50 articles in the field of nuclear medicine and molecular imaging

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THE TRANSMEMBRANE DOMAIN OF SINGLE PASS RECEPTORS AS THERAPEUTIC TARGETS

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The transmembrane domain (TMD) of single pass membrane receptors is actively contributing to receptor dimerization. It is therefore a crucial component of cell signaling by modulating the nature and the stability of TMD/TMD interactions in response to ligand binding. We have shown that the TMD of Neuropilin-1 (NRP1) exhibits a double GxxxGxxxG motive required to trigger migratory and proliferative behaviors in different cell types (Roth et al., 2008 Mol. Biol. Cell.; Nasarre et al., 2010 Oncogene; Arpel et al., 2016 Oncotarget). The biological functions of TMD have also been demonstrated for other cancer-associated receptors such as HER2 (Arpel et al., 2014 Cell Reports) or Plexin-A1 (Jacob et al., 2016 Oncotarget). From this extensive biological work we developed a systematic workflow including in silico, in vitro and in vivo approaches allowing for the design and validation of drug candidates being Membrane Targeting Peptides (MTP). Here, I will present examples of novel MTP with therapeutic potential in demyelinating diseases. Hence, I will introduce the results of our unique systematic screening of TMD interactions of the 58 Tyrosine kinase receptors.

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Biography

Dominique Bagnard is directing INSERM group research since 2003. Expert in neurobiology, brain diseases and neuro-oncology. He is professor at the University of Strasbourg, Director of Research (Medalis Director) of the Strasbourg Institute for Drug Design and Drug Development (IMS) and Dean of the engineer school ESBS (Ecole Supérieure de Biotechnologie de Strasbourg). Involved in scientific edition from the beginning of is carrier he is also the founder and Editor in Chief of the international journal Cell Adhesion and Migration (https://www.tandfonline.com/kcam20). His passion is Tech Transfer as seen with the two startup companies Peptimimesis Pharma and Adaptherapy developing his research.

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IMTM ACADEMIC DRUG DEVELOPMENT PROGRAMS: FROM MOLECULAR TARGETS TO CLINICAL DRUGS

Marian Hajdúch

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Biography

Scientist and medical professional mainly involved in molecular and translational medicine (disease area oncology and infectious diseases); long-term experience in project management; R&D and technology transfer activities, including the construction and management of large research infrastructures. Founding director of the Institute of Molecular and Translational Medicine, Palacky University in Olomouc, CZ. He has been involved as principal investigator, investigator or clinical site manager in 19 clinical trials; actively participated in the research and/or management of >50 national and international projects; established Cancer Research Czech Republic as a major charity to support cancer research in CZ; spin-off companies focused on manufacturing of molecular diagnostics, bioinformatics and drug development; leader/co-leader drug development initiatives with one registered drug on market, several products in clinical trials, >30 in vitro diagnostic products on market, several CE IVD certified. Former Chair of the Boards of National Director and current Czech National Director for European Translational Medicine Infrastructure (EATRIS-ERIC); participated in creation of national network for personalized medicine and cancer management policies. Published more than >350 papers, 17 books/chapters, >40 patents, >4900 SCI citations, H-index 36**.**

DESIGN AND DELIVERY OF MESSENGER RNA BASED-THERAPEUTICS

Chantal Pichon

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Recent advancements in messenger RNA therapeutics have led to the development of novel classes of RNA based-vaccines. Any antigenic protein can be encoded by messenger RNA (mRNA) allowing the development of preventive and therapeutic vaccines to fight against infections. Messenger RNA offers a strong safety compared to DNA because it cannot be integrated in host genome. The translation machinery being located in the cytosol, mRNA expression does not require nuclear import which is of benefit for hard to transfect cells as dendritic cells. By contrast to peptides, they lack MHC haplotype restriction. Moreover, messenger RNA can be recognized by pattern recognition receptors conferring them immunostimulatory properties. Different strategies have been proposed to improve the efficacy of mRNA-based vaccines. Advancements in the molecular virology of single-stranded RNA viruses have allowed the development of RNA replicons. They encode for antigens as well as RNA polymerase that allows RNA amplification within the cells. I will present current knowledge regarding crucial aspects-structure, stability, formulations, cellular delivery and translation- and in vivo applications of RNA-based vaccines. Promises and challenges for clinical trials will be also discussed.

Biography

Chantal Pichon is Professor at the University of Orleans (France) and senior member of the Institut Universitaire de France as Innovation chair laureate. She carries out her research activities at the Centre de Biophysique Moléculaire (CNRS-Orléans) and coordinates the team Cellular Signaling, Molecular Targets and Innovative Therapies. Her research at the interface of chemistry and biology focuses on the development of innovative therapies and nanomedicine with a strong focus on the exploitation of messenger RNAs as vaccines and biomedicines. Chantal Pichon has a track-record of 167 articles and 12 filed patents. She has obtained 26 academic and private contracts including 17 as coordinator (ANR, FP7 and Horizon Europe, Centre Val de Loire Region, BPI France, Sanofi, Ligue contre le cancer ....).

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BIOCOMPATIBLE PROTEIN-DELAMINATED NB2C MXENES FOR PHOTOTHERMAL THERAPY AND PHOTOACOUSTIC IMAGING

Jan Belza

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MXenes are a new class of two-dimensional transition metal carbides, nitrides and carbonitrides whose applications mainly include energy storage, electromagnetic interference shielding and water purification. However, their good biocompatibility and hydrophilic properties also offer possible uses of MXenes in biomedical applications such as bioimaging, drug delivery, antibacterial, tissue engineering, and photothermal therapy (PTT). Here we introduce Nb_2C MXene prepared by eco-friendly bovine serum albumin (BSA)-driven delamination, characterised by excellent colloidal stability under physiological conditions, biocompatibility and high near-infrared (NIR) absorption. We have demonstrated that BSA-delaminated Nb_2C is photostable and efficient for *in vitro* PTT in two cell lines using a 940 nm NIR source. With this *in vitro* model, we have employed laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) to quantify and image Nb_2C accumulated in a single cell. Therefore, we can determine the effective concentration of Nb_2C needed for *in vitro* PTT. Moreover, we have used this nanomaterial for *in vivo* photoacoustic imaging (PAI) in xenograft mice.

Biography

Jan Belza is a Ph.D. student in the Nanomaterials in biomedicine research group led by Dr. Kateřina Poláková at the Czech Advanced Technology and Research Institute. His Ph.D. project is supervised by Prof. Radek Zbořil. He received his bachelor's degree (2016) in biochemistry at Charles University in Prague. Afterwards, he graduated in Physical Chemistry (2018) at Palacký University in Olomouc. His research focuses on the interaction of nanomaterials with living organisms and the development of functional nanostructures for bioapplications.

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LIPID NANOPARTICLES FOR RNA DELIVERY – MORPHOLOGY REVEALED BY COARSE GRAINED SIMULATIONS

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RNA-based therapy covers a wide range of applications, from cancer therapy, treatment of inherited diseases up to vaccination. The encapsulation of RNAs into ionizable lipids (ILs) containing lipid nanoparticles (LNPs) enabled their safe targeted delivery, but for design of more efficient RNA-LNPs, molecular understanding of LNP-structure and IL-RNA interactions is needed.Here we simulated LNPs with composition corresponding to currently developed covid-19 vaccines. We observed, that in conditions acidobasically representing LNP preparation (acidic pH), lipids assembled around RNA into a hexagonal phase and formed a rough, non-spherical hydrated LNP.The change of pH to neutral conditions, representing the environment after LNP administration into human tissues drastically affected the morphology of LNPs. Immediately after IL deprotonation, LNP became spherical and in microseconds time scale, they got gradually dehydrated. Further, we observed lipid separation and creation of an IL-rich phase and a phase rich in ordered saturated phospholipids, that organized to be in contact with water or RNA. During the simulations in neutral conditions, majority of RNA was expelled from LNP, as it lost the favorable electrostatic interactions by neutralization of ILs and the RNA remaining inside LNP was surrounded by helper phospholipid.We present here the first ever simulation of self-assembly of LNPs containing ILs and their internal morphology. The simulations support the hypothesis of a solid electron-rich hexagonal phase in the LNP which hosts the RNA. We also give evidence for the fragility of LNPs in neutral conditions, that can explain still very limited efficiency in RNA delivery.

Biography

Markéta Paloncýová did her Ph.D. in physical chemistry (2016) at Palacký University in Olomouc focusing on molecular dynamics simulations of small-molecules and drug-metabolizing enzyme interactions with lipid membranes. She stayed in Olomouc for another year, studying the structure of carbon dots. Afterwards, she spent her post-doc at KTH, Stockholm, Sweden in the group Stefan Knippenberg, simulating photoisomerization of cyanine dyes in lipid membranes and then moved to the group of Patrick Norman, predicting the structure and CD spectra of supramolecular assemblies. Finally, she moved back to Czech Advanced Technology and Research Institute of Palacký University and focuses on simulations of lipid nanoparticles for RNA delivery.

Presenting author

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ACIDIC PH-DEPENDENT ASSEMBLY OF SKIN BARRIER LIPIDS

Kateřina Vávrová

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Lipid membrane remodeling belongs to the most fundamental processes in the body. The skin barrier lipids, which are ceramide-dominant and highly rigid, must attain an unusual multilamellar nanostructure with long periodicity to restrict water loss and prevent the entry of potentially harmful environmental factors. While this uncommon lipid rigidity makes sense for limiting permeability, it is less conceivable how such lipids attain their complex architecture. Our data suggest that the stratum corneum acidic pH, apart from regulating enzyme activities and keeping away pathogens, may also be a prerequisite for the multilamellar assembly of the barrier lipids. Atomic force microscopy on monolayers composed of synthetic or human SC lipids showed multilayer formation in an acidic but not neutral environment. X-ray diffraction, infrared spectroscopy, and permeability studies showed markedly altered lipid nanostructure and increased water loss at neutral compared to acidic pH. These findings are consistent with the altered organization of skin lipids and increased transepidermal water loss in conditions with inadequate skin acidification, e.g., in neonates, the elderly, and patients with atopic dermatitis.

Biography

Kateřina Vávrová
Affiliation Charles University, Faculty of Pharmacy, Hradec Králové, Czech Republic

Education
2003 PhD in Bioorganic chemistry, Charles University
1999 MSc in Pharmacy, Charles University

Professional Experience
Since 2022 Head of Dept. of Organic and Bioorganic Chemistry, Faculty of Pharmacy, CU
Since 2017 Full professor (Medicinal chemistry, Charles University)
2004-2005 visiting researcher at the University of Franche-Comte, Besancon, France

Major Interests
skin barrier lipids (lipid synthesis, analysis, and biophysics to understand their role in the skin permeability barrier) and transdermal and topical drug delivery

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MOLECULAR MECHANISMS REGULATING THE SURFACE MOBILITY OF NMDA RECEPTORS IN MAMMALIAN NEURONS

Martin Horák

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N-methyl-D-aspartate receptors (NMDARs) belong to a family of ionotropic glutamate receptors that play a key role in excitatory neurotransmission in the mammalian brain. The functional importance of NMDARs is underscored by the strikingly high number of pathogenic mutations identified to date, many of which are associated with severe neurological and neuropsychiatric disorders. NMDARs are heterotetramers composed of two GluN1 together with two GluN2 (GluN2A to GluN2D) and/or GluN3 (GluN3A and GluN3B) subunits. Surface NMDARs are subject to tight regulation at multiple levels, including lateral diffusion to/from the excitatory synapse. In general, to investigate the surface mobility of membrane receptors located on the surface of neuronal cells, we must deal with the obvious problem that the synaptic cleft is relatively small, which may discriminate against the use of larger fluorescent probes. Here, we characterized three probes that can be used to study the mobility of green/yellow fluorescent protein (GFP/YFP)-GluN subunits: i) a polyclonal rabbit anti-GFP antibody combined with a secondary antibody conjugated to quantum dots (QDs) with emission at 605 nm (aGFP-QD605), ii) an anti-GFP nanobody conjugated to QD525 (nGFP-QD525), and iii) an anti-GFP nanobody conjugated to QD605 (nGFP-QD605). Using fluorescence correlation spectroscopy (FCS) we found that the hydrodynamic diameter of nGFP-QD525 is slightly smaller than nGFP-QD605 (8.8±0.5 nm vs. 12.0±0.5 nm, respectively); however, the signal produced by QD605 is ~3x brighter than the signal produced by QD525, allowing us to localize QD605 with significantly higher accuracy (i.e. lower localization error) compared to QD525). Moreover, our analysis of the synaptic mobility of YFP-GluN1-1a showed that aGFP-QD605 has a significantly smaller diffusion coefficient compared to both nGFP-QD525 and nGFP-QD605, likely due to its larger size (the typical dimensions of IgG are approximately 14.5 nm × 8.5 nm × 4.0 nm whereas for nanobodies they are approximately 4.0 nm × 2.5 nm × 3.0 nm). Using nGFP-QD605 (which has the optimal combination of size and spatial accuracy), we found that compared to both GFP-GluN2A and GFP-GluN2B, GFP-GluN3A has reduced synaptic localisation, as well as an increased diffusion coefficient for all and only extrasynaptic trajectories. Our results show significant subunit-dependent differences in the mobility of NMDARs and also point to the possibility of further development of QD-based probes to study the mobility of surface NMDARs in mammalian neurons, which will be the focus of my talk.

Biography

Martin Horak has been studying N-methyl-D-aspartate receptors (NMDARs) in mammalian neurons for more than twenty years. His PhD thesis (2001-2005) with Prof. Ladislav Vyklicky Jr. in the Institute of Physiology of the CAS was focused mainly on the characterization of the molecular mechanism of action of the neurosteroid pregnenolone sulfate (PS) on NMDARs using whole-cell patch-clamp recordings with a rapid solution application system. Subsequently, he was awarded a postdoctoral fellowship with Robert J. Wenthold, a leading researcher in the field of glutamate receptors in the Laboratory of Neurochemistry at IDCD/NIH 2005-2010). In 2018, he established a new Department of Neurochemistry in the Institute of Experimental Medicine of the CAS.

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OPTICAL CONTROL OF TRIMERIC ION CHANNELS WITH CHEMICAL PHOTOSWITCHES

Thomas Grutter

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Recent chemical biology developments in the optogenetics field offer great opportunities for the optical control of ion channel activation, with exquisite temporal and spatial resolution. Inspired by these achievements, we have developed new and versatile approaches, called optogating and opto-tweezers, in which the gating machinery of trimeric ion channels, such as P2X receptors, was reprogrammed to respond to light. We demonstrated photocontrol of neuronal activity by a light-gated P2X receptor, in which the sensitivity to the natural ligand, ATP, was genetically removed. We also uncovered part of P2X gating and ion permeation mechanisms using these optical actuators. Finally, we extended this technology to Piezo channels, which are another class of trimeric, mechanically-activated ion channels. Chemical engineering thus provides not only clues on the biophysics of these proteins, but also valuable tools for interrogating the function of these ion channels in native tissues.

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Biography
Thomas Grutter studied chemistry and biology at the University of Strasbourg. He obtained his PhD in bio-organic chemistry in the laboratory of Prof. Maurice Goeldner in 2000. After a postdoc position at the Pasteur Institute in Paris, he joined the CNRS in 2003 in the laboratory of Prof. Jean-Pierre Changeux, where he used to work on pentameric ligand-gated ion channels. In 2007 he moved back to Strasbourg to set up his own research team at the Faculty of Pharmacy in Illkirch (Strasbourg) and obtained the accreditation to lead research projects (HDR). He was appointed Research Director at the CNRS in 2012, and Deputy Director of the CAMB laboratory in 2017. His research team focused on biophysical and molecular aspects of trimeric ion channels, in particular ATP-gated P2X and Piezo channels, by combining several approaches, such as patch-clamp electrophysiology and the use of molecular sensors. He also developed innovative (photo-)chemical tools applied to ion channels.

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TARGETING PROTEOTOXIC STRESS VIA NANOFORMULATED DIETHYLDITHIOCARBAMATE-COPPER COMPLEX

Martin Mistrík, Zdeněk Škrott

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Impaired protein homeostasis is typical for several human diseases, and proteotoxic stress is considered a hallmark of cancer and an attractive therapeutic target. Inhibition of the p97-NPL4 pathway, a vital part of protein degradation machinery, by disulfiram metabolite diethyldithiocarbamate-copper complex (CuET) represents an unorthodox yet promising and efficient way of cancer cell eradication. However, the clinical application of disulfiram is limited by its complicated metabolism leading to low and unpredictable levels of the active metabolite CuET. Direct administration of CuET is hindered by its poor pharmacokinetic properties and solubility. We developed a nano-formulated CuET by a reaction between dithiocarbamate and copper ions in suitable carriers, such as plasma proteins, immunoglobins, pharmaceutical polymers or nucleic acids, to overcome these limitations. The resulting nanoparticles are of size 50-100 nm and are very stable under different conditions. In vitro, nanoparticles target NPL4 protein and induce unresolvable proteotoxic stress leading to cancer cell toxicity, which is higher compared to other described formulations of CuET. The anti-tumour activity was further confirmed on various spheroids and mouse models. Given the simplicity of such nanoparticle production and the high versatility of carriers offering potential specific targeting and activity in different models, we are presenting an intriguing technology for further clinical development.

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MAKING ORDER OUR OF PROTEIN DISORDER

Vladimir Torbeev

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Intrinsically disordered proteins (IDPs) are highly abundant in eukaryotes and play key roles in molecular recognition, regulation and signalling. Gene transcription machinery is particularly rich in IDPs with most of the transcription factors possessing IDP domains. Thus, IDPs represent attractive targets to interfere with gene transcription. However, regulating the functions of IDPs by classical approaches using small molecules is challenging because IDPs do not have well-defined hydrophobic binding pockets. Furthermore, due to their malleable nature the structural characterization of IDPs is also difficult. Recently, my team introduced an approach to interfere with the complex formation formed by IDPs via conformational editing of an intrinsically disordered domain itself through the introduction of conformationally constrained non-canonical α-methylated amino acids [1,2]. A modified variant of the disordered activation domain 1 (AD1) from activator for thyroid and retinoid receptors (ACTR) was discovered that possessed an enhanced affinity to the nuclear coactivator binding domain (NCBD) of the cancer-related transcriptional co-activator CBP. In addition, using the best binding ACTR variant, we succeeded to crystallize the ACTR/NCBD complex for the first time and determined its high accuracy X-ray structure. Our results provide insights with atomic precision into properties of the "fuzzy" ACTR/NCBD protein complex - a truly peculiar class of protein complexes.

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Biography

Vladimir Torbeev received his Ph.D. degree in Chemistry from the University of Chicago under the direction of Prof. Stephen B. H. Kent for the work dedicated to total chemical synthesis and biophysical studies of HIV-1 protease. Then, he performed postdoctoral studies in the group of Prof. Donald Hilvert at ETH Zurich working on molecular mechanism of misfolding and aggregation of β2-microglobulin. In March 2014 he started his independent research group at the Institute for Supramolecular Science and Engineering at the University of Strasbourg. In September 2021 he became Professor of Biosystems Chemistry at École Supérieure de Biotechnologie de Strasbourg (ESBS) and joined research unit CNRS UMR 7242 "Biotechnology and Cellular Signalling". His current areas of research are intrinsically disordered proteins, protein design, protein aggregation and development of novel approaches for chemical synthesis of protein libraries.

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GOLD MARKERS FOR PROBING THE INTRACELLULAR MACHINERY IN LIVING CELLS

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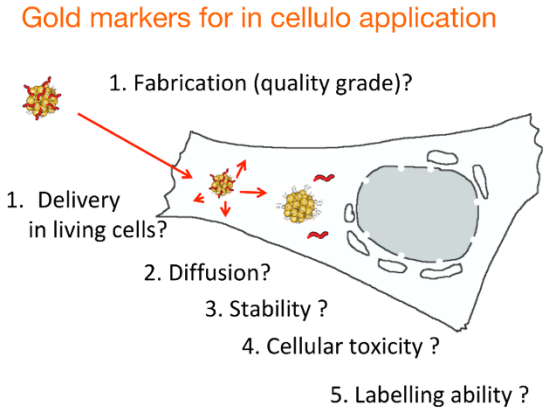
For high-resolution electron microscopy, conjugation of selective binders originating from the immune response arsenal to gold nanoparticles (AuNPs) as contrasting agents is the method



of choice to obtain labeling tools. However, the advances in microscopy technology have unraveled limitations of the classical AuNPs. Herein, we developed thiolate-coated AuNPs containing an inner core of gold atoms that was surrounded by an organic monolayer made of thioaminobenzoic acids (TAB) and anionic thionitrobenzoic acids (TNB).[1] The mixed TAB-,TNB-protected gold nanocluster reacted well in water with thiolated peptides or thiolate antibody derivatives, providing AuNPs that were functionalized with organic elements with targeting abilities.[2] The behavior of these functionalized gold nanoparticles was then assayed in presence of living cells and more specifically inside living cells using an electroporation procedure allowing transient plasma membrane permeability. Light and electron microscopy observations demonstrated inflow and diffusion of the gold nanoparticles into the cytosol as well as specific binding to their targets. Altogether, we will show that definable ligand-substituted gold nanoclusters can become promising detecting tools for cellular electro microscopy in a full cryo-EM procedure, opening the possibility to visualize the cellular machinery at unprecedented resolution.

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PHPMA POLYMER WITH CY7 AND CYTARABINE AS A THERANOSTIC AGENT FOR LYMPHOMA CANCER TREATMENT IN MICE MODEL

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pHPMA copolymers are widely used for its both specific delivery and controlled drug release in tumor targeting and treatment [1]. It was also proved, that various side chains of pHPMA polymer can influence its physico-chemical characteristics which leads to changes in tumor cell uptake [2]. Cytarabine is synthetic nucleoside used in clinical medicine for over 50 years. It contains arabinose instead of ribose or deoxyribose. Thanks to this it successfully inhibits DNA polymerase in various tumors like sarcoma or lymphoma [3]. In this study we prepared pHPMA polymer with bound cytarabine and Cy7 dye.We used pHPMA polymer, M_W = 42 000 g/mol with Cy7 3,9% and 12% of cytarabine. Two mice with tumor size approx 7 mm got the intraperitoneal application of 3,6 mg cytarabine / mouse and we measured photoacoustic signal at single wavelenght 755 and 800 nm and also we measured tumor size and via VEVO LAZR-X 3100 preclinical ultrasound with 3D scan in 0h, 2h, 4h, 24h, 48h, 72h and 1W timepoints. Tumor size and photoacoustic signal intensity were evaluated via VEVO lab software.Cytarabine has a great effectivity in cancer treatment, no matter if subject is human or animal. We supposed pHPMA copolymer would have specific uptake in the tumor due to the dense capillary network and this would enhance cytarabine anticancer effect of the mice tumor treatment. When signal distribution in various organs is compared, although most of the polymer is metabolized in the liver, still there´s plenty of cytarabine therapeutic effect in tumor.We have shown that the type of dye affected the distribution of the polymer in the body. We further demonstrated that a dose of 3.6 mg cytarabine per mouse is subtherapeutic and will only slow but not cure lymphoma growth. So far, this is a diligent experiment and the issue of polymer dosing and distribution in the body will be further investigated on a larger number of experimental animals.

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Biography

First Faculty of Medicine, Charles University,**2019- Center of Advanced Preclinical Imaging (CAPI) – Researcher** Writing articles, experience with operating devices for preclinical imaging MRI BRUKER ICON 1T, MR Solutions 7T, UZV / PA VEVO LAZR-x 3100, BRUKER XTREME for in vivo imaging, SPARK TECAN microplate reader for in vitro tests, evaluation of results - MS Excel, Origin, ImageJ, independent scientific work. **F**irst Faculty of Medicine, Charles University 2**020- PhD. Student in Medical Biophysics** Dissertation: „Use of upconversion nanoparticles for diagnosis and treatment“ The Faculty of Natural Science, Charles University

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SILICA-COATED MAGHEMITE NANOPARTICLES FOR BIOMEDICAL APPLICATIONS

Jean-Michel Siaugue

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Magnetic nanoparticles, used in biomedical applications like drug delivery, magnetic hyperthermia, magnetic imaging (MRI, MPI) or magnetic particles spectroscopy (MPS) based assays, are made of a superparamagnetic iron oxide core capped with an organic or inorganic layer. As such, aggregation is prevented and their physicochemical stability is improved. Precise surface bio-functionalization is also mandatory to allow highly selective chemical interactions, for example with cancer cells for drug delivery or with biological targets to quantify in biomedical assays.

In this context, several examples of surface functionalization of $\gamma Fe_2O_3@SiO_2$ core-shell nanoparticles were developed using strain promoted azide alkyne click chemistry (SPAAC).

In the first one those nanoparticles are functionalized either with a HaloTag ligand or with Green Fluorescent Protein (GFP), in order to interact specifically with intracellular proteins able to trigger different pathways in the cell. For that purpose, MNPs are then microinjected in the cell and show intra-cellular biased diffusion toward a micro-magnet. The magnet can then be used to displace target proteins attached to the MNPs inside the cell thus creating gradient protein concentration near the cell membrane. Studies are in progress to avoid the microinjection of nanoparticles in cells, as this is a method that cannot be used on a large number of cells. Two strategies are investigated to bypass the endocytosis pathway by which nanoparticles are internalised into cells, and to promote direct access to the cytosol by crossing the cell membrane

In the second one $\gamma Fe_2O_3@SiO_2$ core-shell nanoparticles are used to anchor single strand nucleic acid (ssDNA). Optimized SPAAC grafting protocol enables the grating of six different ssDNA, complementary of miRNA sequences specific of liver (miR 122), skeletal (miR 133b, 206) and/or cardiac (miR 208a, 133a, 1) muscles, as they are promising biomarkers. Magnetic separation of the complementary miRNA sequences in model buffer solution results in the rapid capture of miRNAs, corresponding to 50-60% of ssDNA's hybridization. Furthermore, capture experiments carried out in complex biological media (fetal bovine serum or rat plasma) reveal only a slight decrease in the amount of miRNA extracted. Finally mismatch experiments using miR 133a and 133b sequences, which differ only by one nucleic acid, indicate a fairly good selectivity. Dehybridization of captured miRNAs is now being studied in a lab-on-a-chip format using mild magnetic hyperthermia conditions to quantify miRNAs on the surface of microelectrodes, as part of the DIMELEC project, funded by the French National Research
Agency.

Biography

Jean-Michel Siaugue (ORCID N° 0000-0003-1217-9493) carried out his studies at the Ecole Supérieure de Physique et de Chimie Industrielles de Paris and received his Ph.D. from Université Pierre et Marie Curie (Paris VI) in 2000 under the supervision of Professor A. Guy. After postdoctoral training with Dr F. Taran and C. Mioskowski (Commisariat à l'Energie Atomique, Saclay), he joined Université Pierre et Marie Curie as assistant professor in the group of V. Cabuil in 2005. His current research interests concern biomedical applications of magnetic nanoparticles, especially their use in cellular engineering and in vitro diagnostics.

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MULTI-METALLIC COMPOUNDS AS MOLECULAR BARCODES

Miloslav Polášek

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Molecules offer an incredible potential to serve as information carriers, but our ability to read molecular code remains limited. For example, mass spectrometry can read the code from polymeric chains or from mixtures of molecules, but the code is destroyed during the reading process. On the other hand, non-destructive spectroscopic methods cannot read sequences from polymers. In this work we demonstrate a new method of encoding digital information into molecules based on paramagnetic lanthanide ions, which allows non-destructive reading with nuclear magnetic resonance (NMR). With specially designed molecular scaffolds, it is possible to combine magnetic susceptibility tensors of two or more lanthanides within one molecule. This allows programmable tuning of the NMR signal of the molecule, given by the choice and order (sequence) of the lanthanides. In reverse, the NMR signal can be decoded to reveal the encoded sequence. Moreover, the unique NMR signals can be further multiplexed to create a high number of digital codes from a few basic components. A current prototype molecular system is capable of 16-bit (65,535 codes) encoding. Reading the code with NMR in radiofrequency spectrum is contactless, non-destructive and repeatable, and thus shares favorable attributes with the macroscopic RFID technology. Advancements in miniaturization and development of new quantum-based detection systems are making paramagnetic encoding a viable concept for tagging macroscopic and microscopic objects.

Biography

Miloslav Polášek obtained his PhD title in 2009 at the Department of Inorganic Chemistry at Charles University in Prague, with a thesis on synthesis of gadolinium-based contrast agents for magnetic resonance imaging (MRI). During his 4-year post-doctoral stay at Massachusetts General Hospital in Boston, he worked on a collagen-targeted MRI contrast agent and its in-vivo applications to diagnose fibrosis in various organs. In 2013, Dr. Polášek joined the Institute of Organic Chemistry and Biochemistry (IOCB) in Prague, where he is investigating coordination compounds of lanthanides. In recent years, his team developed a new technology for separation of lutetium-177, a radioactive isotope used in cancer therapy, which has been licensed to US company SHINE. His current research interest focuses mainly on molecular tags, barcodes and information encoding at the molecular level for biomedical and technological applications.

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SMART NANOSYSTEMS FOR CANCER THERAPY AND BIOIMAGING

Xavier Le Guevel

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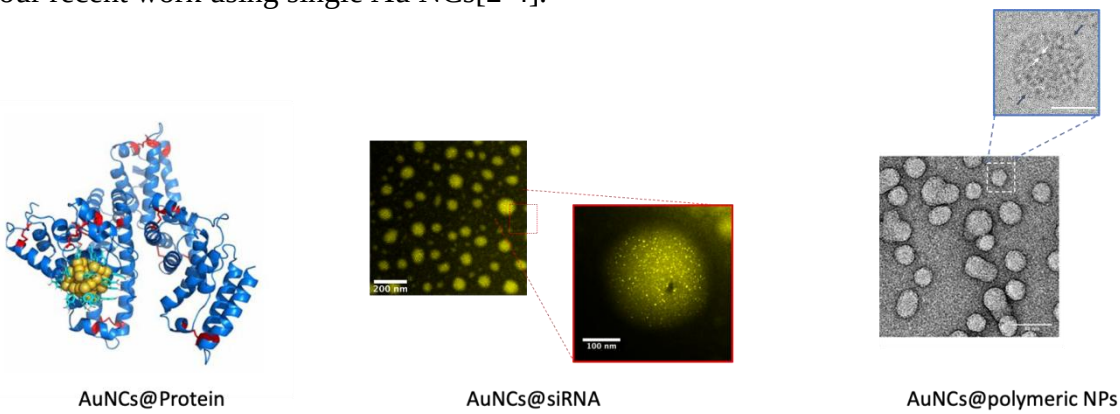
Multimodal nanosystems offer great promise for the early detection and the treatment of various cancers. Ultra-small gold nanoparticles called gold nanoclusters (AuNCs) with size lower than 3nm exhibit remarkable properties for their detection *in vivo* thanks to their photoluminescence in the broad infrared region (NIR-I :700-900nm; NIR-II: 900-1700nm) and the ability to activate them by light or X-ray to treat cancer[1].
In this context, with the expertise of producing a large library of AuNCs with tunable optical and physico-chemical properties, we designed different smart engineered nanosystems based on AuNCs. We demonstrated the ability to specifically label proteins with single atomically precise AuNCs and to assemble AuNCs using polymeric and siRNA scaffolds in order to develop nanosystems with enhanced optical capacity, capable of targeting cancer cells, and to deliver molecules of interests. We investigated the behavior of these smart nanosystems in different cancer cell lines (breast, lung, melanoma, glioblastoma) and explored their application as theranostic agents for radio/phototherapy and optical guided surgery based on our recent work using single Au NCs[2-4].



Biography
Dr Xavier Le Guével obtained his PhD in 2006 in Chemistry from the University of Tours (France). Following this, he did some postdoctoral fellowships in physics (Rome, Italy), biophotonics (Dublin, Ireland) and biotechnology (Saarbruecken, Germany) between 2006 and 2010 before starting as an independent researcher at the Nanomedicine Centre Bionand in Malaga (Spain). Since 2016, XLG has been a CNRS researcher at the Institute for Advanced Biosciences in Grenoble (France). XLG was PI on various private and public funded projects (Plan cancer, ARC, ANR, LCC, Merck Serono, Carlos Tercero) dedicated to the use of nanomaterials for diagnosis and therapy (50 articles, 4 patents, 2 chapters, 2537 citations, h=28). His work focuses on the development of new nanomaterials such as metal nanoclusters and optical instruments for medical applications and more specifically for cancer treatment and diagnosis from the fundamental research to pre-clinical application.

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FLUORINATED NANOGELS FOR IMAGE-QUIDED THERAPY

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Nanogels represent potentially interesting drug delivery systems. They may carry insoluble drugs, may respond to environment stimuli by the release of the drug at a specific site, and may bear a marker for non-invasive tracking by imaging methods. Besides fluorescence markers for optical imaging or radiolabels for PET/SPECT, labeling by fluorine for MRI can be used. Fluorine magnetic resonance imaging (^{19}F MRI) supplements anatomical ^{1}H MRI and provides information about the nanogel system location and its fate *in vivo*.
Moreover, nanogels may be 3D-printed, which expands the possibilities of their application.
We synthetized several types of polymeric fluorinated tracers, tested them both *in vitro* and *in vivo* and estimated detection limits for future use as a drug delivery system.
We tested a new material based on an already published thermoresponsive polymeric gel[1], which contained hydrophilic thermoresponsive and redox-sensitive monomers, both *in vitro* and *in vivo. In vitro* tests involved estimation of the detection limit by measurement of different aliquots in test tubes, *in vivo* tests were performed on rats; the polymer depot was injected into the muscle of an anesthetized rat and tracked by MRI.).

Biography
Vít Herynek (*1967) studied Biophysics and Chemical Physics at Faculty of Mathematics and Physics, Charles University and graduated in 1990. He received his PhD at First Faculty of Medicine, Charles University, in 1996; his thesis was titled Optimalization and Application of MR Spectroscopy and Imaging Methods. He gained research experience during his stay as a visiting fellow in National Institutes of Health – National Institute of Neurological Diseases and Stroke, Neuroimaging Branch, Bethesda, Maryland, USA, (1997 – 1999), where he participated in both clinical and experimental research related to contrast mechanisms in magnetic resonance imaging with special attention to iron storage proteins and iron oxide nanoparticles. He continued in this topic after his return to the Czech Republic in the Institute for Clinical and Experimental Medicine (1999 – 2018) and contributed to the area of cell labeling and in vivo cell tracking by magnetic resonance imaging using iron oxide nanoparticles, 19F labels and novel contrast agents. While MRI is still his main research interest, he mastered also other imaging methods, including bioluminescence, fluorescence, magnetic particle imaging, ultrasound and photoacoustic imaging at his current workplace in the Center for Advanced Preclinical Imaging at First Faculty of Medicine, Charles University (since 2018).

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