INSTITUTE OF MACROMOLECULAR CHEMISTRY
CZECH ACADEMY OF SCIENCES

Institute of Macromolecular Chemistry
Czech Academy of Sciences
Heyrovského nám. 2, 162 00 Prague 6
Czech Republic

BOOK OF ABSTRACTS AND PROGRAMME

Czech Academy of Sciences

NiCR

Prague Meeting on Tumor Therapy and Imaging

19 – 21 March 2023
Prague, Czech Republic

Conference Chairmen

Tomáš Etrych, PhD, DSc, Institute of Macromolecular Chemistry CAS

Eva Koziolová Randárová, PhD, Institute of Macromolecular Chemistry CAS

Organized by

Institute of Macromolecular Chemistry CAS
Heyrovského nám. 2
162 00 Prague 6
Czech Republic

We would like to thank for the auspice:

Czech Academy of Sciences

NiCR

Funded by the European Union
NextGenerationEU

CZECH RECOVERY PLAN

MINISTRY OF EDUCATION, YOUTH AND SPORTS

We would like to thank our sponsors:

technoprocur cz

SHIMADZU
Excellence in Science

avantor™

Prague Meeting on Tumor Therapy and Imaging 2023 - Programme

SUNDAY March 19th, 2023

18:30 – 21:00	**Welcome reception** at Institute of Macromolecular Chemistry CAS

MONDAY March 20th, 2023

8:50 – 9:00	**Tomáš Etrych**, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic* Introduction
1st section: *New materials*	
Chair: Tomáš Etrych	
9:00 – 9:30	**Jonathan A. Coulter**, *School of Pharmacy, Queen's University Belfast, BT9 BL, UK* Achieving Impact from University Research – A nanotechnology tale
9:30 – 10:00	**Ian Teasdale**, *Johannes Kepler University, Linz, Austria* Phosphorus-based polymers as a tunable, biodegradable platform for polymer therapeutics
10:00 – 10:20	**Libor Kostka**, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic* Polymerization platform for synthesis of multi-arm carriers
10:20 – 10:40	**Pavla Bojarová**, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic* Glycopolymers targeting galectins in biomedicine
10:40 – 11:00	Posters and coffee
2nd section: *Cancer metabolism and microenvironment*	
Chair: Eva Randárová	
11:00 – 11:30	**Karel Smetana**, *Charles University, 1st Faculty of Medicine, Institute of Anatomy, Prague and BIOCEV, Vestec, Czech Republic* Role of cancer-associated fibroblasts in cancer microenvironment
11:30 – 12:00	**Alexander Detappe**, *Institut de Cancérologie Strasbourg Europe, Strasbourg, France* Molecular bottlebrush prodrugs as mono- and triplex combination therapies for multiple myeloma
12:00 – 12:20	**Juan Bautista De Sanctis**, *Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic* Effect of ASA nanopolymers on tumour antigen expression in human cell lines
12:20 – 12:40	**Marek Kovář**, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic* Linear and star HPMA copolymer conjugates bearing doxorubicin and ritonavir derivate overcomes P-gp and STAT3-mediated tumor chemoresistance
12:40 – 12:50	**Future directions in cancer targets** – discussion led by Marek Kovář
12:50 – 14:10	Lunch

3rd section: *Chemotherapy*	
Chair: Jun Fang	
14:10 – 14:40	**Danuta Radzioch**, *McGill University Health Centre, Montreal, Canada* Magnetically-guided chemotherapy-carrying magneto-aerotactic bacteria induces immune cells infiltration and their activation resulting in inhibition of colorectal cancer growth
14:40 – 15:00	**Yohann Corvis**, *Université Paris Cité, CNRS, INSERM, UTCBS lab, Paris, France* Nanocrystals engineering for anticancer therapies
15:00 – 15:20	**Milada Šírová**, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic* Polymer carrier of cytotoxic drugs with P-gp overcoming capacity in the treament of chemoresistant tumors
15:20 – 15:50	**Marián Hajdúch**, *Institute of Molecular and Translational Medicine, Faculty of Medicine and Dentistry, Palacky University, Olomouc, Czech Republic* Academic driven drug development: From molecular targets to proof-of-concept clinical trials
15:50 – 16:20	Posters and coffee

4th section: *Directions beyond cancer*	
Chair: Nathalie Mignet	
16:20 – 16:40	**Kazumi Yokomizo**, *Faculty of Pharmaceutical Sciences, Sojo University, Kumamoto, Japan* Application of polymeric micelle nanocarrier to microbes and infections
16:40 – 17:00	**Makoto Anraku**, *Faculty of Pharmaceutical Sciences, Sojo University, Kumamoto, Japan* The preparation and validation of chitosan tablets that rapidly disperse and disintegrate as an oral adsorbent in the treatment of lifestyle-related diseases
17:00 – 17:20	**Eva Randárová**, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic* Polymer-based drug delivery systems for treatment and diagnosis of inflammatory diseases
17:20 – 17:40	**Tomáš Špringer**, *Institute of Photonics and Electronics of the Czech Academy of Sciences, Prague, Czech Republic* pH-triggered drug release from nanocarriers investigated by surface plasmon resonance biosensor
	Dinner at Břevnov Monastery

TUESDAY March 21st, 2023

1st section: *Theranostics*	
Chair: Steffen Hackbarth	
9:00 – 9:30	**Carolina de Aguiar Ferreira**, *Departments of Radiology, Pharmacology & Toxicology and Biomedical Engineering, Michigan State University, USA* Exploring Biological Applications of Radionuclides: From Cancer Theranostics to Tumor Immunology
9:30 – 10:00	**Jean-Luc Coll**, *Team Cancer Targets and Experimental Therapeutics, Univ. Grenoble Alpes, INSERM U1209, CNRS UMR5309, Institute for Advanced Biosciences, Grenoble, France* NIR-I and NIR-II optically active nanosystems and their use for theranostic treatment of cancer
10:00 – 10:20	**Kirakci Kaplan**, *Institute of Inorganic Chemistry of the Czech Academy of Sciences, Husinec–Řež, Czech Republic* Octahedral Molybdenum Cluster Complexes for Photodynamic Applications
10:20 – 10:40	**Petr Hermann**, *Department of Inorganic Chemistry, Faculty of Science, Universita Karlova, Prague, Czech Republic* Macrocyclic chelators for metal radioisotopes and influence of phosphorus acid pendant arms.
10:40 – 11:00	Posters and coffee

2nd section: *PDT*	
Chair: Jean-Luc Coll	
11:00 – 11:30	**Steffen Hackbarth**, *Photobiophysics, Institute of Physics, Humboldt-Universität zu Berlin, Germany* Sometimes less is more – How photosensitization in vivo depends on intensity
11:30 – 12:00	**Jun Fang**, *Faculty of Pharmaceutical Sciences, Sojo University, Japan* Polymeric nano-probes for tumor-targeted photodynamic therapy and imaging
12:00 – 12:20	**Marina Tavares**, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic* pH-Responsive Polymer Nanomedicines for Tumor-Targeted Photodynamic Therapy and Imaging
12:20 – 12:50	**Kamil Lang**, *Institute of Inorganic Chemistry of the Czech Academy of Sciences, Husinec–Řež, Czech Republic* Molybdenum nanoclusters for X ray-induced photodynamics
12:50 – 14:10	Lunch

3rd section: *Imaging*	
Chair: Carolina Ferreira	
14:10 – 14:40	**Nathalie Mignet**, *Université Paris Cité, CNRS, INSERM, UTCBS lab, Paris, France* Bioconjugates made of albumin as targeted imaging agent
14:40 – 15:00	**Eliška Grosmanová**, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic* Synthesis of polymer-based multifunctional nanotherapeutics decorated with antimicrobial, cell-penetrating, targeting or therapeutic oligopeptides
15:00 – 15:20	**Martin Kaňa**, *Department of Otorhinolaryngology and Head and Neck Surgery, 1st Medical Faculty, Charles University and University Hospital Motol, Czech Republic* Intraoperative Fluorescence-Guided Surgery of Malignant Head-and-neck Tumors and Metastases
15:20 – 15:40	**Dora Konečná**, *Institute of Biochemistry and Experimental Oncology 1st Medical Faculty, Charles University and Department of Neurosurgery, Military University Hospital Prague, Czech Republic* Protease-activated probes for the visualization of glioblastoma
15:40 – 15:50	**Future directions in imaging and theranostics** – discussion led by Carolina de Aguiar Ferreira
15:50 – 16:10	Closing of the meeting and coffee

Presented posters

Kateřina Běhalová, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic*
Antitumor activity of HPMA polymeric conjugates bearing HIV protease inhibitor derivatives

Alena Braunová, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Micellar copolymers with P-gp inhibition for treatment of resistant solid tumors

Natálie Klusová, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic*
Anti-tumor and immunomodulatory effect of polymeric conjugates based on HPMA carrying gemcitabine

Kevin Kotalík, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Water-soluble polymer conjugates with 5-aminolevulinic acid intended for photodynamic therapy

Alena Libánská, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Size-switchable polymer-based nanomedicines in the advanced therapy of rheumatoid arthritis

Ondřej Lidický, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Biocompatible polymers as tool for the antibody drug conjugate concept improvement

Dana Mareková, *Institute of Experimental Medicine, Czech Academy of Sciences, Prague, Czech Republic*
Biological evaluation of upconversion nanoparticles

Robert Pola, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Cytarabine nanotherapeutics with increased stability and different rate of hydrolytic release for highly effective antitumor therapy

Tomáš Přibyl, *University of Chemistry and Technology, Prague, Czech Republic*
Formulation of molybdenum clusters for photodynamic cancer therapy

Sára Pytlíková, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Hydrophilic polymer-pirarubicin conjugates for cancer treatment

Anna Rumlerová, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
Polymer conjugates with antimicrobial peptides

Johanne Seguine, *Université Paris Cité, CNRS, INSERM, UTCBS lab, Paris, France*
Development and evaluation of optical imaging probes for tumor targeting

Daniil Starenko, *Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic*
Polymeric conjugates with retroviral protease inhibitors as a potential way of overcoming chemoresistance in P-glycoprotein expressing tumors

Karolína Turnovcová, *Institute of Experimental Medicine, Czech Academy of Sciences, Prague, Czech Republic*
Modeling of drug delivery to brain in vitro

Alžběta Turnovská, *Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic*
HPMA-based conjugates with porphyrins for photodynamic therapy and tumour imaging

Abstracts

Achieving Impact from University Research – A nanotechnology tale

Jonathan A. Coulter

School of Pharmacy, Queen's University Belfast, BT9 BL

High-Z materials in the nanoparticle form are proven pre-clinical sensitisers to ionising radiation. Yet clinical translation has been slow, mainly compounded by issues that include formulation complexity, lack of target site accumulation, unexpected toxicity, regulatory misalignment, compromised IP and limited clinical adoption. However, early consideration of these factors can offset many of these barriers. Using the example of radiation dose modifying nanoparticles I will illustrate examples of specific formulations which have succeeded in this space, while detailing how informed clinical considerations and inter-disciplinary collaboration has assisted the research efforts of our group in overcoming many of these challenges.

Biography

Dr Jonathan Coulter is a Reader (Associate Professor) in Nanotherapeutics within the School of Pharmacy, Queen's University Belfast. Jonathan was appointed as a PI at Lecturer level in the School of Pharmacy in June 2012. Dr Coulter's research focuses on identifying novel approaches to increase the effectiveness of radiotherapy while limiting damage to surrounding normal tissue. This is achieved via two key approaches: i) taking advantage of the unique biological features of the tumour to achieve therapeutic benefit, or ii) exploiting the unique physical properties of common materials to produce tiny particles called nanoparticles, which in turn act as potent sensitisers to radiotherapy. To date Jonathan has secured >£4 M in research income as PI/CoI, published >65 research papers/book chapters and achieved approximately 3200 citations of his work. He is past Chair of the Association of Radiation Research (UK) and a committee member of the Irish Radiation Research Society.

j.coulter@qub.ac.uk

Phosphorus-based polymers as a tunable, biodegradable platform for polymer therapeutics

Ian Teasdale

Johannes Kepler University, Linz Austria

Although biopolymers such as DNA and RNA are built with a phosphorus backbone, nearly all reported polymer-based drug delivery systems are based on combinations of carbon, nitrogen and oxygen. Furthermore, phosphorus-nitrogen bonds are known in biochemistry to hydrolyse readily. Indeed, this hydrolysis reaction is the basis of many biochemical processes, for example, the transfer of phosphate from phosphocreatine to regenerate ATP from ADP. This sensitivity to hydrolysis can be used to prepare biodegradable synthetic polymers with phosphorus backbones, whereby substituents on the phosphorus centre control the degradation rate. Importantly recent developments allow controlled polymerisations of the major phosphorus-based polymers, polyphosphoesters, polyphosphazenes and polyphosphoramidates. The high valency of the phosphorus coupled with controlled polymerisation techniques allows facile access to multiarmed and bottlebrush polymers. As the size, shape and chemical function are critical parameters when designing tumour- and organ-targeting nanomedicines, this makes them ideal candidates for degradable polymers for therapeutic applications. Herein we describe recent developments in tuning their architectural and chemical properties towards polymers for imaging and drug delivery.

Biography

Ian Teasdale completed his PhD in chemistry in 2008 at the University of Manchester (UK). A postdoc position at the Institute of Polymer Chemistry at the Johannes Kepler University Linz (Austria) was followed by an assistant professorship and then promotion to associate professor in polymer chemistry. He is currently interested in synthetic polymer chemistry with a particular research focus on inorganic polymers (including silicon, phosphorus, boron and transition metals), their use as degradable polymers and their application in biomedical applications.

ian.teasdale@jku.at

Polymerization platform for synthesis of multi-arm carriers

Libor Kostka

M. Hrochová, L. Kotrchová, T. Etrych

Institute of Macromolecular Chemistry Czech Academy of Sciences, Dpt. of Biomedical Polymers, Heyrovskeho nam. 2, Prague, 162 00

Biodegradable polymer-based therapeutics have recently become essential drug delivery carriers for various bioactive compounds. Biodegradable and biocompatible polymer-based systems fulfill the requirements of these therapeutics because they enable to obtain the polymer systems with optimized blood circulation, pharmacokinetics, biodegradability, and renal excretion. Here we describe an adaptable polymerization platform employed for the synthesis of long-circulating, stimulus-sensitive, and biodegradable therapeutics or theragnostic. We designed and successfully synthesized four novel chain transfer agents (CTA) for the reversible addition−fragmentation chain transfer (RAFT) polymerization, allowing the straightforward synthesis of hydrolytically labile copolymer structures, i.e., *N*-(2- hydroxypropyl)methacrylamide (HPMA)-based bio-degradable block copolymers. The setup of the controlled RAFT polymerization using the novel CTAs enables controlling the half-life of the hydrolytic degradation of polymer precursors in a wide time range from 5 hours to 21 days. Emphasis will be placed on diblock structures. However, the synthesis of 3 and 4-arm structures will also be shown.

Moreover, the antitumor drug pirarubicin (THP) was successfully conjugated to the diblock copolymers via a pH-sensitive hydrazone bond, and *in vitro* and *in vivo* experiments were performed. Polymer conjugates demonstrated superior antitumor efficacy in comparison to basic linear polymer-based conjugates.

The adaptable polymerization platform design allows tuning the biodegradability rate to select stimuli-sensitive drug bonding, optimize the pharmacokinetics to increase the therapy outcome, and target the system. Thus, targeted or theragnostic polymer conjugates could be advantageously prepared.

Biography

L. Kostka completed his Ph.D. from the University of Chemistry and Technology Prague in 2011. He is the group leader in prof. Etrych's department of Biomedical Polymers at IMC CAS. He has published more than 45 papers in reputed international journals, which were cited more than 680 times; ResearcherID H-4182-2014. His research focuses on new synthetic routes for new polymeric structures and materials usable for medical applications, especially for drug delivery or diagnosis.

kostka@imc.cas.cz

Glycopolymers targeting galectins in biomedicine

Pavla Bojarová[1]

Marina R. Tavares,[2] *David Vrbata,*[1] *Marcela Filipová,*[2] *Vladimír Křen,*[1] *Tomáš Etrych*[2]*, Petr Chytil*[2]

[1] Institute of Microbiology of the Czech Academy of Sciences, Prague, Czech Republic
[2] Institute of Macromolecular Chemistry of the Czech Academy of Sciences, Prague, Czech Republic

Galectins are human lectins involved in pathological processes such as cancerogenesis, inflammation or cardiopathologies [1]. Their targeting can be used both in diagnostics and therapy. Galectins bind β-galactoside-terminated glycans but there are structural preferences, and, consequently, different degrees of selectivity between individual galectins, depending on their carbohydrate-binding domains [2]. Selective high-affinity glycopolymers can target active galectins both *in vitro* and *in vivo*, and serve as tools in biomedical research and even clinical applications. The affinity of glycopolymers to galectins may be enhanced by an apt architecture of the multivalent carrier [3] and the linker type [4]. Tailoring of the carbohydrate ligand structure affords glycopolymers with low nanomolar and even picomolar affinities to galectins [5] and high selectivities.

The present contribution describes the design of novel glycopolymers targeting galectins, in particular galectin-1 and galectin-3, and the determination of their activities by novel methods [6] at multiple levels, from pure inter-molecular interaction to anti-tumor activity in *in vitro* assays with galectin-overexpressing cancer cells [5,7]. These compounds represent a novel research direction, prospective for combined immunotherapy of cancer.

References:
[1] V. Heine et al. *Biotechnol. Adv*. **2022**, *58*, 107928.
[2] D. Laaf et al. *Trends Biotechnol*. **2019**, *37*, 402.
[3] M. R. Tavares et al. *Biomacromolecules* **2020**, *21*, 641.
[4] P. Bojarová et al. *J. Nanotechnol*. **2018**, *16*, 73.
[5] D. Vrbata et al. *J. Med. Chem*. **2022**, *65*, 3866.
[6] L. Bumba et al. *Int. J. Mol. Sci*. **2018**, *19*, 372.
[7] M. Filipová et al. *Biomacromolecules* **2020**, *21*, 3122.
Support from the grant project 22-00262S by the Czech Science Foundation is gratefully acknowledged.

Biography

Pavla Bojarová is the Deputy Head of the Laboratory of Biotransformation at the Institute of Microbiology of the Czech Academy of Sciences. In 2006 she obtained her Ph.D. in biochemistry at the Faculty of Sciences, Charles University in Prague, and she spent her postdoctoral stay at the University of Melbourne, Australia. She habilitated at the Faculty of Biomedical Engineering, Czech Technical University in Prague, in 2020. Her main research interests include chemo-enzymatic synthesis of carbohydrates and glycoconjugates using engineered carbohydrate-active enzymes, development and implementation of novel methods for assessment of lectin-carbohydrate interactions, and their applications in biomedicinal research.

bojarova@biomed.cas.cz

Role of cancer-associated fibroblasts in the cancer microenvironment

Karel Smetana, Jr.[1]

Lukáš Lacina[1]*, Pavol Szabo*[1]*, and Michal Kolář*[2]

[1]Charles University, 1st Faculty of Medicine, Institute of Anatomy, Prague and BIOCEV, Vestec,
[2]Institute of Molecular Genetics of the Czech Academy of Sciences, Prague, Czech Republic

Cancer incidence is increasing worldwide. This dismal trend is evident in highly developed countries where it coincides with population ageing. One of the new ideas to better understand cancer biology is the conception of cancer as an organ, where the biological properties of cancer cells are influenced by noncancer cells forming the complex ecosystem. Cancer-associated fibroblasts (CAFs) are a critical component of tumour stroma due to the production of extracellular matrix and paracrine secretion of growth factors and cytokines affecting cancer cells. CAFs can originate from local tumour-surrounding fibroblasts or mesenchymal stem cells. Alternatively, CAFs can originate by the transition from macrophages, endothelial cells, and probably even cancer cells. CAFs are responsible for the participation in the maintenance of sustained proinflammatory micromilieu that positively affects the low differentiation status of cancer cells, their proliferation, and migration. Bioactive factors produced by CAFs, such as IL-6 and IL-8 (CXCL8), are actively recognised by specific membrane receptors of cancer cells and influence their properties. We suggest that the targeting of CAFs, as well as of signalling cascades activated by their products, represents a promising strategy and basis for the novel generation of cancer therapy.

Biography

Karel Smetana completed his PhD at Charles University in Prague. He is the head emeritus of the Institute of Anatomy, 1st Faculty of Medicine, Charles University in Prague. He is also the scientific coordinator of the Centre for Tumour Ecology excellent research project funded by the European Union. His research focuses on cancer as an ecosystem and predominantly on the role of CAFs. Prof. Smetana has published over 250 papers in renowned international journals, which were cited more than 2500 times. HI=35.

karel.smetana@lf1.cuni.cz

Molecular bottlebrush prodrugs as mono- and triplex combination therapies for multiple myeloma

Alexandre Detappe

Institut de Cancérologie Strasbourg Europe, Member ITI Institut du Médicament Strasbourg, Affiliate Member, IPHC UMR7178, 3 rue de la porte de l'hôpital, 67000 Strasbourg, France

Cancer therapies often have narrow therapeutic indexes and involve potentially suboptimal combinations due to the dissimilar physical properties of drug molecules. Nanomedicine platforms could address these challenges, but it remains unclear whether synergistic free-drug ratios translate to nanocarriers and whether nanocarriers with multiple drugs outperform mixtures of single-drug nanocarriers at the same dose. Here we report a bottlebrush prodrug (BPD) platform designed to answer these questions in the context of multiple myeloma therapy. We show that proteasome inhibitor (bortezomib)-based BPD monotherapy slows tumour progression in vivo and that mixtures of bortezomib, pomalidomide and dexamethasone BPDs exhibit in vitro synergistic, additive or antagonistic patterns, respectively, distinct from their corresponding free-drug counterparts. BPDs carrying a statistical mixture of three drugs in a synergistic ratio outperform the free-drug combination at the same ratio as well as a mixture of single-drug BPDs in the same ratio. Our results address unanswered questions in the field of nanomedicine, offering design principles for combination nanomedicines and strategies for improving current front-line monotherapies and combination therapies for multiple myeloma.

Biography

After a PhD at the University of Lyon (2017) and a postdoctoral fellowship at the Massachusetts Institute of Technology and Harvard Medical School in nanomedicine (2019), Dr. Alexandre Detappe joined the Institut de Cancérologie Strasbourg-Europe (ICANS) as the group leader of the nanotranslational research laboratory. Since 2020, Dr. Detappe was appointed Prof in Medicine at the University of Strasbourg. His lab, funded in part by an ERC Starting grant, develops new approaches in nanomedicine and immunotherapy to improve the targeting efficiency and specificity of the nanoparticles toward several cell populations.

a.detappe@icans.eu

Effect of acetylsalicylic acid nanopolymer on tumour antigen expression in human cell lines

Juan Bautista De Sanctis[1]

Eva Randárová[2], *Markéta Frejková*[2], *Jenny Valentina Garmendia*[1], *Ivo Frydrych*[1], *Tomáš Etrych*[2]

[1] Institute of Molecular and Translational Medicine. Faculty of Medicine and Dentistry. Palacky University. Olomouc.
[2] Institute of Macromolecular Chemistry, Czech Academy of Sciences. Prague.

Tumour antigen expression is crucial for identifying and eliminating tumour cells by the immune system. Natural Killer (NK) cells and cytotoxic T CD8 cells are predominantly involved in tumour cell lysis. Both cell types share a non-major histocompatibility complex recognition of tumour antigens defined by specific activating receptors NKG2C or NKG2D or inhibitory receptors. The expression of ligands of NKG2C/NKG2D receptors renders the tumour cells susceptible to cytotoxic lysis. The study aimed to determine the effect of a nanopolymer containing acetylsalicylic acid (ASA) on the expression of tumour antigens MIC A/B and ULBP1 and ULBP2-5 (ligands of NKG2C/NKG2D receptors). The incubation was performed for 24 hr in DMED-0.1 % serum, polymer, 2 and 5 mg/ml. The ASA polymer induced a significant two and three-fold expression of MICA/B antigen on the HCT116 colon carcinoma cell line and A549 lung epithelial cell line, not affecting mutated HCT116 (p 53 KO) or the leukemic cells K562, CMT3. A significant twofold increase in ULBP1 expression was observed only in HCT116 cells. The rise in both tumour antigens resulted in increased lysis of this treated tumour cell line by cytotoxic immune cells compared to non-treated cells. The A549 cell lines were partially susceptible to lysis. No difference was observed with the mutated HCT116 or the leukemic cell lines. Conclusion: The ASA nanopolymer can induce antigen expression in HCT116 and A549 cell lines, not affecting normal cells or other cell lines.

Biography

Juan Bautista De Sanctis PhD 1991 in Physiological Sciences, Biochemistry and Immunology. Universidad Central de Venezuela, Caracas. In academic position since 1991, full professor since 2009, at the Institute of Immunology, Faculty of Medicine. Universidad Central de Venezuela. Ex-Director of the Institute 2012-2018. From 2018 Senior Research at the Insitute of Molecular and Translational Medicine and CATRIN member. Palacky University.

Fields: inflammation, immunology, lipid metabolism, cancer, cystic fibrosis, genetics, pharmacology, natural products. Publications 157, h index 29. Associate editor of Frontiers of Immunology, soluble factors and cytokines, Frontiers in Genetics and Immunogenetics, Immunogenetics, Section Editor of Current Pharmaceutical Design, Editorial board member of Immuno.

juanbautista.desanctis@upol.cz

Linear and star HPMA copolymer conjugates bearing doxorubicin and ritonavir derivate overcomes P-gp and STAT3-mediated tumor chemoresistance

Marek Kovář[1]

Ladislav Sivak,[1] *Vladimir Subr,*[2] *Jirina Kovarova,*[1] *Barbora Dvorakova,*[1] *Milada Sirova,*[1] *Blanka Rihova,*[1] *Eva Randarova,*[2] *Michal Kraus,*[1] *Jakub Tomala,*[1] *Martin Studenovsky,*[2] *Michaela Vondrackova,*[1] *Radislav Sedlacek,*[3] *Petr Makovicky,*[3] *Jitka Fucikova,*[4,5] *Sarka Vosahlikova,*[5] *Radek Spisek,*[4,5] *Libor Kostka,*[2] *Tomas Etrych*[2,]

[1] Institute of Microbiology, Czech Academy of Sciences
[2] Institute of Macromolecular Chemistry, Czech Academy of Sciences
[3] Czech Center of Phenogenomics, Institute of Molecular Genetics, Czech Academy of Sciences
[4] Charles University, 2nd Faculty of Medicine and University Hospital Motol
[5] Sotio

Here, we describe a polymer biomaterial composed of the antiretroviral drug ritonavir derivative (5-methyl-4-oxohexanoic acid ritonavir ester; RD), covalently bound to linear HPMA copolymer carrier via a pH-sensitive hydrazone bond (P-RD). Apart from being more potent inhibitor of P-glycoprotein in comparison to ritonavir, we found RD to have considerable cytostatic activity in six mice (IC_{50} ~ 2.3 - 17.4 μM) and six human (IC_{50} ~ 4.3 - 8.7 μM) cancer cell lines cells *in vitro*. Importantly, RD inhibits STAT3 phosphorylation and expression of the NF-κB p65 subunit, Bcl-2 and Mcl-1. RD also dampens chymotrypsin-like and trypsin-like proteasome activity and induces ER stress as documented by induction of PERK phosphorylation and expression of ATF4 and CHOP. P-RD nanomedicine showed considerable antitumor activity in CT26 and B16F10 tumor-bearing mice, which, moreover, synergized with IL-2-based immunotherapy. P-RD proved very promising therapeutic activity also in human FaDu xenografts. Next, we designed high molecular weight HPMA copolymer conjugates with a PAMAM dendrimer core bearing both doxorubicin (Dox) and RD (Star-RD+Dox) thus increasing the circulation half-life to maximize simultaneous delivery of Dox and RD into the tumor. Star-RD inhibited P-gp activity, potently sensitizing both low and high P-gp expressing cancer cells to the cytostatic and pro-apoptotic activity of Dox *in vitro*. Star-RD+Dox possessed higher cytostatic and pro-apoptotic activities compared to Star-Dox and the equivalent mixture of Star-Dox and Star-RD *in vitro*. Importantly, Star-RD+Dox was found to have superior antitumor activity in terms of tumor growth inhibition and increased survival of mice bearing P-gp expressing tumors.

Biography

Marek Kovar completed his Ph.D. in immunology at the Institute of Microbiology, Czech Academy of Sciences, working on anticancer drug-delivery systems based on HPMA copolymers. He spent his postdoc at The Scripps Research Institute (La Jolla, California, USA) in the laboratory of Prof. Jonathan Sprent. He returned back to IMIC in 2006. He is the PI in the Laboratory of Tumor Immunology which is focused on drug delivery systems based on polymeric drug carriers as well as cancer immunology and immunotherapy.

makovar@biomed.cas.cz

Magnetically-guided chemotherapy-carrying magneto-aerotactic bacteria induces immune cells infiltration and their activation resulting in inhibition of colorectal cancer growth

Danuta Radzioch[1]

Yong Zhong Xu[1,2], *Mahmood Mohammadi*[3], *Samira Taherkhani*[3], *Thusanth Thuraisingam*[1], *Sylwia Jancik*[1,4], *Juhi Shah*[1], *Daciana Catalina Dumut*[1,2], *Marian Hajduch*[4] *and Sylvain Martel*[3,5]

[1] The Research Institute of the McGill University Health Centre; [2]Department of Medicine, McGill University, Montréal, Canada; [3] NanoRobotics Laboratory, Department of Computer and Software Eng., Institute of Biomedical Engineering, Polytechnique Montréal, Canada; [4]Institute of Molecular and Translational Medicine, Olomouc, Czech Republic [5]Bioengineering Department, McGill University, Montréal, Canada

Optimal therapeutic efficacy of targeted chemotherapy has yet to be realized for most solid tumour malignancies. Our previous work reported the development and characterization of a novel computer-assisted and magnetically-guided bacterial complex containing vectors for the improvement of chemotherapy delivery resulting in the improvement of therapeutic index of nanocarriers inside tumour hypoxic regions (*Nature Nanotechnology* doi:10.1038/nnano.2016.137).

The vectors are laboratory-enhanced magneto-aerotactic bacterium (Bn1-S^{TM}) with liposomal SN-38 attached to their surface (Bn1-S-Complex). Peritumoural injection with magnetic guidance of Bn1-S-Complexes carrying a low total dose of 25 µg SN-38/kg every second day significantly inhibited extremely fast-growing syngeneic colorectal cancer model MC-38 in immunocompetent mice and caused regression or complete disappearance of HCT116 xenograft in immunodeficient animals. In the absence of Bn1-S-mediated delivery, equivalent doses peritumoural liposomal SN-38 or systemic CPT-11 did not significantly impact tumour growth. Targeted Bn1-S-Complex treatment resulted in increased apoptosis-related protein expression; immune cell infiltration including macrophages, granulocytes, T cells and NK cells and increased IL-1β and TNFα expression.

Active robotic propulsion-navigation-homing capabilities embedded in each microscopic carrier using therapeutic-loaded live magneto-aerotactic bacteria guided by weak directional magnetic fields and decreasing oxygen gradients towards deeply located tumor hypoxic cells. Targeting hypoxic areas resulted in better distribution throughout the tumor and a much better retention due to the lower oxygen levels sought by the bacteria compared to the higher oxygen levels found in surrounding tissues. This study not only provides further interesting observations unique aspects of this entirely new approach of treatment in the field of cancer therapy.

Biography

Dr. Danuta Radzioch, Professor, McGill University, Department of Medicine, Faculty of Medicine and Health Sciences, McGill University Scientist, RI-MUHC , Infectious Diseases and Immunity in Global Health Program at the Centre for Translational Biology Department of Medicine . Dr. Radzioch laboratory research focuses on the molecular mechanisms involved in the regulation of inflammatory response in asthma, cystic fibrosis, and cancer. Preclinical studies testing novel anti-inflammatory drugs on cystic fibrosis lung disease, allergic asthma, and colon cancer in vitro and in vivo, pharmacological intervention which enables to normalize fatty acids metabolism distortion during chronic bacterial infections in cystic fibrosis, chronic allergic responses, acute spinal cord injuries leading to permanent motor dysfunction. Dr Radzioch has published more than 190 papers in reputed international journals, which were cited more than 10693 times**; H-Index: 59: i10-Index: 136** (Google Scholar Feb 26, 2023).

danuta.radzioch@gmail.com

Nanocrystals engineering for anticancer therapies

Yohann Corvis[*]
Panpan Ma, Luis Castillo Henríquez, Feras Oyoun, Pierre de Begon de Larouzière, Brice Martin, Yiqian Wang, Markéta Bláhová, Alena Braunová, Khair Alhareth, Johanne Seguin, Bich-Thuy Doan, Tomáš Etrych, Nathalie Mignet

[*]Université Paris Cité, CNRS, Inserm, Chemical and Biological Technologies for Health Group (UTCBS, utcbs.u-paris.fr), Health Faculty, 4 avenue de l'Observatoire, 75 006 Paris, France.

During drug development, various processes involving the physicochemical modulation of active pharmaceutical ingredients (APIs) allow to overcome bioavailability issues. Their engineering optimizes the therapeutic efficacy of drugs with enhanced safety profile, targeting efficiency, and suitability for administration through various routes. Among them, nanocrystallization stands out as it maximizes the loading of the API dispersed in liquid or solid dosage forms.

UTCBS laboratory pioneered the solvent/anti-solvent bottom-up approach using a minimal amount of polymer as a stabilizer to develop etoposide nanocrystals (NCs) for anticancer therapies. Surprisingly, since the first commercialized NC preparation of an API in 1982, no antitumoral NC-based drug has been marketed. By contrast, about 20 NC drugs have been approved by the Food and Drug Administration, including only three marketed products for parenteral delivery. Therefore, the latter reinforces UTCBS' endeavors on developing anticancer drug NCs and the legitimacy of these nanoparticles as potent forthcoming delivery systems for nanomedicines.

Solvent/anti-solvent nanoprecipitation method optimization has been performed by screening various parameters, such as the nature of the API and the stabilizing agent, their relative mass ratio, and solvent-to-antisolvent volume ratio. Furthermore, an automated approach has been implemented for the robust preparation of crystalline nanoparticles and scale-up of the process considering green chemistry concerns. Based on promising results, APIs with various therapeutic indications have been chosen for formulating unprecedented nanocrystalline multiphase systems. Additionally, we aim to engineer NCs with tunable properties endowed with pharmaceutical, biomedical, or diagnostic functions as third and fourth generations of nanomedicines for personalized therapies.

Biography

Yohann Corvis holds an engineering doctorate in physical chemistry, material sciences and process (Lorraine University, 2005). His doctoral work dealt with the elaboration of biocatalytic surfaces by self-assembly of (bio)organic systems on protein-coated surfaces. After two years of postdoctoral studies at Warsaw University, Metz University, and IFPen Rueil-Malmaison Institute, he was recruited to the School of Pharmacy of Paris (Faculty of Health, Université Paris Cité) in 2008 as an Associate Professor in the physical chemistry of drugs research area; there, he obtained his accreditation to supervise research in 2013. Since 2021, he was promoted as Full Professor at the same University. He currently works in the CNRS/Inserm group "Chemical and Biological Techniques for Health" (director: Nathalie Mignet) on state of matter of raw pharmaceutical materials, characterization of intermolecular interactions, and the formulation of final products such as nanomedicines for anesthetic, antitumor, and anti-inflammatory therapies, from pre-formulation to *in vivo* evaluation of the formulated systems.

yohann.corvis@u-paris.fr

Polymer carrier of cytotoxic drugs with pH-overcoming capacity in the treatment of chemoresistant tumors

Milada Šírová [1]

Martin Kaňa[1], *Alena Braunová*[2], *Markéta Frejková*[2], *Tomáš Etrych*[2], *Blanka Říhová*[1], *Marek Kovář*[1]

[1] Institute of Microbiology, Czech Academy of Sciences, Prague, Czech Republic
[2] Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic

Chemotherapy is still the mainstay of cancer therapy. Indeed, cancer cells often fail to respond to chemotherapeutic regimens because of either inherent or acquired resistance. This is possibly the most important factor that determines success or failure of cancer therapy. One of the mechanisms developed during the treatment is an increased drug clearance by the transporter-facilitated efflux, resulting in (multi)drug resistance (MDR). It can be conferred by overexpression of transporters, such as adenosine triphosphate binding cassette (ABC) pumps, from which P-gp is probably the most prominent. Some recently developed nanodrug delivery systems may represent a significant approach for overcoming this resistance.

Here, we used an amphiphilic diblock polymer nanotherapeutics containing a hydrophilic block based on the *N*-(2-hydroxypropyl)methacrylamide (HPMA) copolymer and a hydrophobic poly(propylene oxide) block (PPO). The amphiphilic character of the diblock polymer ensures self-assembly into micelles with hydrodynamic radius Rh ~15 nm in aqueous solutions. The carrier serves simultaneously as a drug delivery system and an inhibitor of MDR. Doxorubicin (Dox) was bound to the diblock polymer through a pH-sensitive hydrazone bond, enabling prolonged circulation in blood, tumor-specific delivery of Dox and subsequent stimuli-sensitive controlled release within the tumor mass at a decreased pH. The presence of PPO in the polymer carrier leads to inhibition of P-gp, depolarization of mitochondrial membrane potential, and ATP loss in the target cells. *In vivo*, the diblock polymer system proved an excellent EPR-driven therapeutic activity. Importantly, significant therapeutic outcome was seen also in chemoresistant tumors characterized by inherently elevated P-gp expression.

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, served as 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.

sirova@biomed.cas.cz

Application of polymeric micelle nanocarrier to microbes and infections

Kazumi Yokomizo

Faculty of Pharmaceutical Sciences, Sojo University, Kumamoto, Japan

Biofilms extremely reduce the penetration of antimicrobials into biofilms that allows microbial living-region in biofilms to survive antimicrobial treatment, and causes persistent microbial infections. New micellar and star polymer-drug conjugates are designed for enhanced biofilm penetration and accumulation and release of antimicrobial in the microbial living-region in biofilms. The therapeutic efficacy of the conjugates is based on three mechanisms of selectivity toward biofilms: I) drug accumulation in infected site driven by enhanced permeability and retention (EPR) effect, II) drug penetration and accumulation in microbial biofilms enhanced by electrostatic targeting at acidic pH toward negatively charged bacterial cell surfaces, III) antimicrobial release due to degradation of the micelle core by bacterial enzymes. *In vitro* study, microbial biofilms on peg lids are used for antimicrobial activity of drug to biofilms. *In vivo* study, infectious mouse model is used for therapeutic efficacy of the conjugates.

Biography

Kazumi Yokomizo has completed his Ph.D. at Kumamoto University in Japan. He is a professor of Laboratory of Microbiology & Oncology at the Faculty of Pharmaceutical Sciences, Sojo University. He has published more than 90 papers in reputed international journals, which were cited more than 1,270 times. His research focus is based on the application of natural products to antimicrobials.

yoko0514@ph.sojo-u.ac.jp

The preparation and validation of chitosan tablets that rapidly disperse and disintegrate as an oral adsorbent in the treatment of lifestyle-related diseases

Makoto Anraku

Faculty of Pharmaceutical Sciences, Sojo University, Kumamoto, Japan

A carrier and an oral absorbent for the treatment of chronic diseases in the form of a tablet were prepared from granulated chitosan (G-CS) particles. The resulting tablet was highly dispersible and disintegrated rapidly in aqueous media. The non-granulated chitosan (N-CS) powder partially crystallized during wet granulation to give G-CS crystalline particles. The rate of penetration of water into G-CS aggregates was markedly faster than that for N-CS aggregates, as evidenced by the ease of disintegration of the tablets. The rapid disintegration and dispersion of the tablets *in vivo* were confirmed by MRI measurements after the oral administration of both tablets to rats. Some ureic toxins were adsorbed more strongly to G-CS tablets than to N-CS tablets. The results suggest that G-CS tablets have great potential for use as a fast disintegrating carrier and as an oral adsorbent in lifestyle-related diseases[1)].

We next investigated the hepatic protective and antioxidant effects of granulated chitosan tablets (G-CST) or non-granulated chitosan tablets (N-CST) after oral administration to SHRSP5/Dmcr rats that are fed a high-fat and high-cholesterol diet develop hepatic lesions that are similar to those observed in human NASH pathology for 4 weeks. The administration of G-CST resulted in a significant decrease in hepatic injury, and oxidative stress, compared with the N-CST or non-treatment. We, therefore, conclude that G-CST exerts anti-hepatic and antioxidative effects not only by adsorbing lipid substances but also by reforming the community of intestinal microflora in the intestinal tract.

1) Anraku M, et al., *Carbohydr Polym*. 2021.

Biography

Makoto Anraku has completed his Ph.D. at Kumamoto University in Japan. He is a professor of pharmaceutical formulation at the Faculty of Pharmaceutical Sciences, Sojo University. He has published more than 90 papers in reputed international journals, which were cited more than 2,800 times. His research focus is based on the application of albumin and natural polymers to formulation materials.

anraku@ph.sojo-u.ac.jp

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

Eva Randárová[a]

Alena Libánská[a], *Júlia Kudláčová*[1], *Gilles Renault*[b], *Tomáš Etrych*[a]

[a] Institute of Macromolecular Chemistry, Czech Academy of Sciences, Prague, Czech Republic
[b] Institut Cochin, Université de Paris, INSERM, CNRS, 75014 Paris, France

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

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

Biography

Eva Randárová (Koziolová) 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 30 papers in reputed international journals and presented her work at numerous international conferences. Researcher ID: 0000-0002-1586-9871, H-index 13.

randarova@imc.cas.cz

pH-triggered drug release from nanocarriers investigated by surface plasmon resonance biosensor

Tomáš Špringer[1]

Lucie Peštová[1], *Alena Libanská*[2], *Tomáš Etrych*[2], *Jiří Homola*[1]

[1] Institute of Photonics and Electronics of the Czech Academy of Sciences, Chaberská 1014/57, 182 51 Prague, Czech Republic
[2] Institute of Macromolecular Chemistry of the Czech Academy of Sciences, Heyrovského nám. 2, 162 06 Prague, Czech Republic

Controlled drug delivery systems represent a rapidly growing scientific field in which the drug is typically bound to a nanocarrier, such as a polymer. The drug is often bound via stimuli-sensitive linkers (e.g., pH sensitivity), which enable their release in a spatiotemporally controlled manner, improving their therapeutic efficacy and reducing their systemic side effects. To characterize the release of drugs from nanocarriers, conventional analytical methods, such as fluorescence and UV-Vis absorption spectroscopy, are typically used. Since these methods require a multi-step preparation procedure (incubation, collection, extraction, etc.), new techniques are needed to simplify the drug release characterization.

Herein, a surface plasmon resonance (SPR) biosensor is presented as a new and promising method for monitoring the stimuli-triggered release of drugs from nanocarriers. In particular, the release of drugs with anti-cancer and anti-inflammatory effects (e.g., 5-aminolevulinic acid hexyl ester, doxorubicin, and dexamethasone) bound to a polymer nanocarrier via pH-sensitive linkers is studied. In an SPR experiment, the biotinylated drug-loaded polymers are attached to a streptavidin-coated sensor surface via the streptavidin-biotin interaction and the drug release is triggered by injecting a buffer with a low pH. We demonstrate that the SPR biosensor method enables direct and real-time monitoring of the drug release for both fast and slow release processes, making it an attractive approach for the drug release characterization. This work is supported by the project National Institute for Cancer Research (Programme EXCELES, ID Project No. LX22NPO5102) - Funded by the European Union – Next Generation EU.

Biography

Tomáš Špringer completed his Ph.D. in 2015 (Biophysics, Faculty of Mathematics and Physics, Charles University, Prague). He is a research scientist in the group Optical biosensors (prof. Homola) at the Institute of Photonics and Electronics, Czech Academy of Sciences. He has published more than 24 papers in reputed international journals, which were cited more than 600 times. His research is focused on developing surface plasmon resonance (SPR) biosensors for medical applications.

springer@ufe.cz

Exploring Biological Applications of Radionuclides: from Cancer Theranostics to Tumor Immunology

Carolina de Aguiar Ferreira

Assistant Professor, Departments of Radiology, Pharmacology & Toxicology and Biomedical Engineering, Michigan State University

Radiopharmaceutical Therapy (RPT) is a radiation therapy modality consisting of systemic delivery of radioactive atoms to induce DNA damage in tumor cells. RPT agents target specific receptors or molecular cues overexpressed in tumor cells or the microenvironment. Recent developments in understanding of radionuclide chemistry and physical characteristics of radionuclides, as well as biological insights on appropriate and specific molecular targets, have promoted increased use of RPT, especially within a theranostic approach. Herein, we will demonstrate antibody and small molecule based RPT theranostics. Furthermore, most studies have focused on maximizing the radiation dose delivered to tumor cells using a maximum tolerable dosing approach based on normal tissue toxicity. However, this paradigm assumes that a tumor cannot be overdosed, generally ignoring the presence and importance of the tumor microenvironment. Overwhelming preclinical and clinical data indicate that anti-tumor effects of radiation are partly mediated by radiation-induced immunological effects. We will then discuss immunomodulatory effects of RPT with alpha vs beta emitters.

Biography

Dr. Carolina de Aguiar Ferreira has received a PharmD and an M.Sc. in Material and Nuclear Sciences from renowned Brazilian Universities, and a Ph.D. degree in Biomedical Engineering from UW-Madison, without losing focus on what made her interested in research in the first place: making people's lives better. Dr. Carolina Ferreira has published more than 40 peer-reviewed articles in high-impact journals and won three Young Investigator Awards from the Society of Nuclear Medicine and Molecular Imaging (SNMMI), and made the SNMMI's "Ones to Watch" list in 2021. She is an Assistant Professor at Michigan State University and her research focus on the use of radiation as a solution for healthcare problems. Her lab utilizes radiolabeled compounds for non-invasive detection of diseases and the immune system as well as for cancer therapy and modulation of the immune system.

deaguia1@msu.edu

Bioconjugates made of albumin as targeted imaging agent

Nathalie Mignet

J. Seguin, R. Gahoual, D. Scherman, Y. Zhang

Université Paris Cité, CNRS, INSERM, UTCBS lab, 4 avenue de l'observatoire, 75006 Paris, France

Albumin is a common endogenous protein which is relatively easy to chemically modify. In the past, we were interested in targeting asialoglycoprotein receptors to evaluate the liver function. Using SPECT[1] and optical imaging[2], we observed a fast accumulation in the liver starting after 2 minutes while no accumulation was observed for the non-targeted albumin. We also confirmed that mostly ASGR cells were targeted, and not Kupffer cells. Using the same chemistry, we were interested in the application of a new bioconjugate to imaging-guided surgery. In order to enhance the visualization of tumor margins, we developed a new imaging probe composed of human serum albumin linked to the Sialyl Lewis X ligand[3] and Cyanine 5 to target E-selectin. The bioconjugate obtained was characterized using size exclusion liquid chromatography and mass spectrometry in order to demonstrate the effective grafting of the ligands and the colloidal stability of the protein[4]. The *in vitro* and *in vivo* evaluation of the S-Cyal compound proved the interest of the active targeting and the usefulness of the probe in a context of tumor resection.

[1]doi: 10.1021/bc900275f; [2]doi: 10.1039/c8nr04163f; [3]doi: 10.1016/j.carres.2013.11.012; [4]doi: 10.1016/j.nano.2019.02.011

Biography

Dr Nathalie MIGNET is Research Director for the CNRS in France. She is the leader of the UTCBS lab deeply involved in Nanomedicine and Biotherapeutics at the Université de Paris Cité in Paris, France. Her laboratory is interested in investigating novel nano-autoassembled systems, non-viral cell engineering and local-immunotherapeutic strategies. Dr Mignet is one of the founder and the former president (2014-2020) of the French Society for nanomedicine. She is part of the editorial board of DDTR (Drug Delivery and Translational Research), International J. Pharmaceutics, Nanotheranostic and Pharmaceutics. She is also counsellor for the French alliance "Technologies For Health".

nathalie.mignet@parisdescartes.fr

Octahedral Molybdenum Cluster Complexes for Photodynamic Applications

Kaplan Kirakci

Institute of Inorganic Chemistry of the Czech Academy of Sciences, 250 68 Husinec-Řež, Czech Republic

Octahedral molybdenum cluster complexes, denoted $[\{Mo_6X^i_8\}L^a_6]^n$, are nanometer-sized metallic aggregates stabilized by eight strongly bonded halogen (Cl, Br, I) inner ligands and six apical ligands of inorganic or organic nature. When irradiated by UV or visible light up to the green spectral region, these complexes form long-lived triplet states that relax via a red-NIR phosphorescence or by energy transfer to molecular oxygen, forming the cytotoxic singlet oxygen with high quantum yields. Contrasting with typical photosensitizers such as porphyrinoids, their excited states are not quenched in the solid state, as the electronic density of those states is mainly localized on the $\{Mo_6X_8\}^{4+}$ cluster core. Moreover, these complexes display high resistance to photobleaching due to their metallic nature. These properties have led to the use of these complexes as photosensitizers for biological applications whether as standalone molecules or incorporated into functional (nano)materials. Herein, recent developments regarding the design of octahedral molybdenum cluster complexes towards photodynamic therapy or photoinactivation of bacteria will be summarized.

Biography

Kaplan Kirakci has completed his PhD from University of Rennes 1 in 2006. After a post-doctoral stay at University Jaime 1 in Castellon de la Plana, Spain, he joined the Materials Chemistry department of the Institute of Inorganic Chemistry in 2009. He has published more than 50 papers in reputed international journals, which were cited more than 1400 times. His research is focusing on octahedral molybdenum cluster complexes and related (nano)materials for applications as photosensitizers for PDT, X-ray induced PDT, and photoinactivation of bacteria.

kaplan@iic.cas.cz

Macrocyclic chelators for metal radioisotopes and influence of phosphorus acid pendant arms

Petr Hermann

Department of Inorganic Chemistry, Faculty of Science, Universita Karlova, Hlavova 2030, 12843 Prague 2, Czech Republic

Metal-based radiopharmaceuticals are emerging cancer drugs, e.g. Lutathera® and Pluvicto® (both with 177-Lu) for treatment of neuroendocrine and prostate cancers, respectively. Metal radioisotopes have various physical characteristics (emitting particle, half-life, particle energy etc.) and each metal ion has different chemical and "biological" properties. No chelator satisfies all requirements and, thus, each metal radioisotope requires an appropriate chelator, mostly a macrocyclic ligand, to be used in vivo. In the lecture, properties of ligands/complexes important for metal-based radiopharmaceuticals will be highlighted. Coordination chemistry of macrocyclic polyamines with phosphonic/phosphinic acid pendant(s) and advantages of the ligand design over acetate pendants will be explained. These acidic pendants maintain coordination modes of acetates. They accelerate metal ion coordination/radiolabeling but preserve kinetic inertness of the complexes. The ligands can improve thermodynamic selectivity for a particular metal ion due to larger ligand cavity due to bulky phosphorus atom(s). The phosphorus acid groups are hydrophilic and enable conjugation through the phosphorus atom, away from the macrocycle metal-binding site. Examples of utilizations of the chelators for metal radioisotopes (64-Cu, 68-Ga, 177-Lu) as well as conjugations and targeting will be presented.

Biography

Petr Hermann completed his PhD at Universita Karlova in 1994. He spent two years with Louis Quin at University of Massachusetts, Amherst, working on organophosphorus chemistry. He was a one-year Fulbright Scholar (2010) at University of California, Berkeley (with K. N. Raymond, chemistry of hydroxy-pyridones). He became a full professor in 2011 and now he leads a research group focusing on synthesis and coordination chemistry (thermodynamics, kinetics, solution/solid-state structure of the complexes) of macrocycles with phosphorus acid pendant arms. The complexes can be used as MRI contrast agents or as radiopharmaceuticals.

petrh@natur.cuni.cz

Sometimes less is more – How photosensitization *in vivo* depends on intensity

Steffen Hackbarth

Photobiophysics, Institute of Physics, Humboldt-Universität zu Berlin, Germany

What makes photodynamic therapy (PDT) so powerful is that a single non-toxic photosensitizer can turn thousands of oxygen molecules into highly reactive singlet oxygen. Unfortunately, there is one – so far not really noticed - flaw in the plan: oxygen is a single-use consumable in this treatment. Any singlet oxygen that reacts with cellular components has to be replaced for continuation of treatment, but the local supply *in vivo* is limited.

At first sight, this statement is not so surprising, but what makes it so important, is the scale.

Oxygen consumption during a typical PDT treatment exceeds that of the cell metabolism in the treated tissue many times over. Consequently, this causes instant anoxia and both oxygen replenishment and photosensitization in such cases are limited to the blood vessels and their direct vicinity. The presentation will illustrate the experimental pathway to this insight, using time-resolved optical detection of singlet oxygen and photosensitizer phosphorescence at unprecedented sensitivity. We report experimental results using excitation intensities sufficiently low to avoid anoxia and compare them with results gained with intensities above the limit, giving proof for the described effect. Both the reported findings and the developed technology open up new opportunities for PDT drug and treatment optimization as well as new diagnostic methods, including *in situ* supervision during the treatment.

Biography

Steffen Hackbarth received his Ph.D. degree in experimental physics from HU Berlin in 2000. Ever since, he has worked in the field of time-resolved spectroscopy in the ps to ms time range with a special focus on the triplet processes of photosensitizers. He is head of an independent research group at Humboldt University in Berlin. His research is dedicated to molecular photobiophysics, with a focus on fundamental research in the field of photosensitization, drug delivery and diffusion processes during Photodynamic Therapy. Technical developments focus on singlet oxygen and other luminescence detection *in vivo* or other heterogeneous environments at highest sensitivity.

hacky@physik.hu-berlin.de

Polymeric nano-probes for tumor-targeted photodynamic therapy and imaging

Jun Fang[1]

Vladimír Šubr[2], *Waliul Islam*[3], *Steffen Hackbarth*[4], *Rayhanul Islam*[1], *Tomas Etrych*[2]

[1]Faculty of Pharmaceutical Sciences, Sojo University, Japan; [2]Institute of Macromolecular Chemistry, Czech Republic Academy of Science; [3]Graduate School of Medical Sciences, Kumamoto University, Kumamoto, Japan; [4]Institute of Physics, Photobiophysics, Humboldt University of Berlin.

Use of macromolecular anticancer agents or so-called nanomedicine is a promising strategy to target vascularized solid tumors by utilizing the enhanced permeability and retention (EPR) effect. Because of the high tumor accumulation, it can be applied not only to cancer therapy, but also to tumor imaging/diagnosis, namely theranostics. In this regard, we have been focused on the development of tumor-targeted polymeric nano-probes for photodynamic therapy (PDT) and tumor imaging in the past decades. The first challenge is the *N*-(2-hydroxypropyl)methacrylamide (HPMA) polymer conjugated zinc protoporphrin IX (PZP) that is a potent inhibitor of antioxidative, antiapoptotic enzyme heme oxygenase-1 (HO-1) highly expressed in many tumors. As the micelle formation of 80 nm, PZP showed highly selective tumor accumulation resulting in remarkable anticancer PDT and tumor imaging effect in different solid tumor models. Along this line, recently we synthesized a HPMA conjugated pyropheophorbide-a (P-PyF) via amide bond, which showed a mean particle size of ~26 nm. Potent $^1O_2$ production and PDT effect were observed by irradiation at ~420 nm. Irradiation using longer wavelength light (i.e., ~ 680 nm) has less impact, but exhibited superior in vivo tumor imaging effect. In vivo studies showed a high accumulation in tumor resulting in remarkable antitumor, and clear tumor imaging profiles. More recently, we successfully developed a HPMA conjugate pyropheophorbide-a with hydrozone bond (P-hyd-PyF), which exhibited slow and tumor environment responsive release profiles. Interestingly, P-PyF showed a unique distribution profiles with very high tumor/liver ratio. Consequently, further superior PDT and imaging effect was achieve compared to P-PyF.

Biography

Jun Fang has completed his PhD at Kumamoto University Medical School in 2003 and 2-year postdoctoral studies from Duke University Medical Center. He is the Associate Professor of Faculty of Pharmaceutical Science at Sojo University, Japan. His major research topic is development of innovative strategies to target solid tumor for therapy and imaging, based on EPR effect and nanotechnology; particularly focusing on tumor targeted photodynamic therapy and the drug delivery system of carbon monoxide (CO) for inflammatory diseases. He has published more than 100 papers in reputed journals and has been selected as a "Highly Cited Researcher" from 2014 to 2018 in the field of Pharmacology and Toxicology.

fangjun@ph.sojo-u.ac.jp

pH-Responsive Polymer Nanomedicines for Tumor-Targeted Photodynamic Therapy and Imaging

Marina Rodrigues Tavares

Institute of Macromolecular Chemistry of the Czech Academy of Sciences, Prague, Czech Republic

Photodynamic therapy (PDT) has gained attention for the treatment of solid tumors, using light as a stimulus to activate photosensitizers and oxygen to generate cytotoxic singlet oxygen ($^1O_2$). Here, water-soluble *N*-(2-hydroxypropyl)methacrylamide copolymers (pHPMA) were used to design and synthesize micellar conjugates carrying pyropheophorbide-a (PyF) attached by pH-sensitive hydrazone bonds, enabling the stimuli-sensitive activation of the PDT effect. Various spacers were used to conjugate PyF to pHPMA, e.g., the aliphatic 5-hydroxy-2-pentanone or the aromatic moieties 4-(4-hydroxyphenyl)-2-butanone, 4-hydroxybenzaldehyde, and 1-(4-(hydroxymethyl) phenyl)ethanone. The aromatic moiety closer to the hydrazone bond clearly brought a higher stability to the system and slower hydrolysis. The study proved the clear benefit of the stimulus-sensitivity behavior for the tumor-targeted delivery of such nanomedicines, i.e., excellent anti-tumor efficacy and huge tumor-imaging potential. The theranostics with aliphatic linker showed selective tumor accumulation in the mouse sarcoma S180 tumor model and their beneficial tissue distribution dynamics reduced liver accumulation, resulting in a superior PDT effect due to the specific PyF release in the acidic tumor environment. Once in the tumor, illumination at λ_{exc} = 420 nm and a low dose of PyF reached an excellent therapeutic effect due to the $^1O_2$ generation, proving the potential of such theranostics.

Biography

Marina R. Tavares has completed her Ph.D. in Macromolecular Chemistry at the University of Chemistry and Technology of Prague, with a collaborative period at the School of Pharmaceutical Sciences at Sojo University, Japan. She also completed her Masters's in Polymer Science and Bachelor's degree in Pharmacy at the Federal University of Rio de Janeiro, Brazil, with a collaborative period at the School of Pharmacy at Trinity College Dublin, Ireland. She has published thirteen papers in reputed international journals and participated in the preparation of three patent applications. Her main scientific interests rely on the area of polymer biomaterials focusing on: tumor-targeted nanomedicines, polymer-based theranostics for photodynamic therapy and tumor imaging, stimuli-responsive drug delivery systems, and immuno-oncotherapy. All of the approaches include the synthesis of polymer carriers via controlled polymerization techniques.

tavares@imc.cas.cz

Molybdenum nanoclusters for X ray-induced photodynamics

Kamil Lang

Institute of Inorganic Chemistry of the Czech Academy of Sciences, Řež 1001, 250 68 Husinec-Řež, Czech Republic

The convergence of radiotherapy and photodynamic therapy (PDT) has led to the recent emergence of a modality called X-ray induced PDT. This approach relies on the use of scintillating nanoparticles that, upon exposure to X-rays, emit luminescence in the visible region, which, in turn, activates conjugated photosensitizers *via* energy transfer and ends up with the production of singlet oxygen $O_2(^1\Delta_g)$. Utilizing phosphorescent triplet states of molybdenum nanoclusters to generate singlet oxygen offers new possibilities for PDT applications. In this context, we prepared a series molybdenum cluster complexes $[\{M_6I_8\}L^a_6]^{2-}$ and simplified the architecture of radiosensitizing systems. Modulation of the apical ligands L^a allows for tunability of cellular uptake, colocalization, and cytotoxicity of these complexes. One such complex was utilized to prepare water-stable nanoparticles. A robust radiosensitizing effect of the nanoparticles was demonstrated *in vitro* against TRAMP-C2 murine prostatic carcinoma cells at typical therapeutic X-ray doses. I will delineate properties of these complexes, their photodynamic activity, and antiproliferative effects upon X-ray irradiation. The reported results highlight the relevancy of molecular nanocluster chemistry in medical applications.

Biography

Kamil Lang received his PhD from the Institute of Inorganic Chemistry of the Czech Academy of Sciences (IIC). 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, and reactive oxygen species with focus on singlet oxygen. He is a coauthor of 160 papers in impacted journals.

lang@iic.cas.cz

NIR-I and NIR-II optically active nanosystems and their use for theranostic treatment of cancer

Jean-Luc Coll

Mans Broekgaarden, Anne-Laure Bulin, Virginie Faure, Amandine Hurbin, Véronique Josserand, Xavier Le Guevel, & Lucie Sancey

Team Cancer Targets and Experimental Therapeutics, Univ. Grenoble Alpes, INSERM U1209, CNRS UMR5309, Institute for Advanced Biosciences, Grenoble, France

Theranostic nanoparticles (TN) are a new type of nanomedical device that combine diagnostic and therapeutic capabilities for the treatment of diseases and in particular cancer. They are made from a variety of materials, including metals, polymers, and lipids, and they are designed to be safe and biocompatible. TN offer a range of advantages, such as improved drug delivery, targeted drug release, and enhanced imaging capabilities. They can be used as contrast agents to precisely detect and delineate the region to treat using MRI, X-rays, Near-infrared light or ultrasounds. But in addition, NT can be remotely and precisely activated on site using non-ionizing and/or ionizing radiations to specifically deliver therapeutic activities to the diseased cells, allowing for more effective treatments with fewer side effects.

Our team is developing multifunctional theranostic particles targeting tumor cells and/or the tumor microenvironment. We particularly focus on optical-based systems for their detection and possible on site(s) activation. Optical imaging can also be combined with ultrasonic imaging modalities and provide additional information (photoacoustics).

Our 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. These nanosystems can also be used intraoperatively for optical guided surgery of cancer.

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. JL Coll is author of >200 international publications and of 5 patents (2 licensed); PubMed

jean-luc.coll@univ-grenoble-alpes.fr

Synthesis of polymer-based multifunctional nanotherapeutics decorated with antimicrobial, cell-penetrating, targeting or therapeutic oligopeptides

Eliška Grosmanová

Institute of Macromolecular Chemistry, Czech Academy of Sciences, Heyrovského nám. 2, 162 00 Prague 6, Czech Republic

Short peptides (up to 30 residues) bring a huge diversity of structures and variety in mechanism of action. Their main disadvantage when administered into the human body is their rapid degradation by enzymes and therefore lack of efficacy. It has been repeatedly reported that attachment of a low-molecular-weight "cargo" to a biocompatible polymer carrier often leads to improved pharmacokinetics, protection of the cargo from degradation, lower non-specific toxicity and improved therapeutic efficacy. Such polymer-peptide conjugates may contain along the polymer chain i) targeting, ii) cell-penetrating, iii) antimicrobial, or iv) therapeutic peptides.

First, novel biocompatible polymer nanocarriers based on *N*-(2-hydroxypropyl)methacrylamide with antimicrobial effect, or enhanced tumor-accumulation and/or penetration have been designed and successfully synthesized. Subsequently, the prepared fluorescently labeled polymer-peptide nanosystems were evaluated *in vitro* using microbiological methods. The affinity of the polymer conjugates to bacterial or cellular membranes and receptors was studied depending on the particular structure of the attached peptides. Prepared polymer-peptide nanosystems showed enhanced uptake by tumor cell due to the presence of respective peptides. Moreover, the selected polymer-peptide conjugates were evaluated *in vivo.* The results indicate that these multifunctional systems could serve for further preclinical evaluation as candidates for visualization or treatment of tumors or a new direction for the treatment of highly resistant bacterial diseases.

Biography

Eliska Grosmanova completed her PhD studies at the University of Chemical Technology and the Institute of Macromolecular chemistry (IMC), CAS in 2022. She is a postdoctoral researcher at the Department of Biomedical Polymers, IMC CAS in Prague. She has published 9 papers in international journals, which have been cited more than 80 times. Her research focus is based on solid-phase peptide synthesis and preparation of polymer-based therapeutics and diagnostics.

grosmanova@imc.cas.cz

Intraoperative Fluorescence-Guided Surgery of Malignant Head-and-neck Tumors and Metastases

Martin Kaňa[1]

Pola R.[2], *Grosmanová E.* [2], *Pankrác J.*[3], *Henry M.*[4], *Coll J.L.* [4], *Bouček J.* [1], *Etrych T.* [2]

[1] Department of Otorhinolaryngology and Head and Neck Surgery, 1st Medical Faculty, Charles University and University Hospital Motol, Czech Republic
[2] Institute of Macromolecular Chemistry, Czech Academy of Sciences, Czech Republic
[3] Center for Advanced Preclinical Imaging (CAPI), First Faculty of Medicine, Charles University, Czech Republic
[4] Univ. Grenoble Alpes, INSERM U1209, CNRS UMR5309, Cancer Target and Experimental Therapeutics, Institute for Advanced Biosciences, Grenoble, France

Precise and complete tumor removal is essential to ensure good prognosis and quality of life in patients with head and neck malignancies. Only few modalities are available to reliably detect malignant tissue intraoperatively. Fluorescence-guided surgery has potential to improve surgical outcomes by facilitating tumor-margin delineation, detection of residual malignant tissue and sentinel lymph nodes. The polymer probes based on N-(2-hydroxypropyl)methacrylamide (HPMA) copolymer with Cy7 near-infrared dye bound via various stimuli-sensitive spacers were proved to preferably accumulate in tumor tissue. The polymer probes with most favorable tumor-to-healthy tissue ratio were employed for cytoreductive surgery in CAL33-luc and FaDu-RFP peritoneal carcinomatosis murine model. The best results were provided by the HPMA-H-OPB-Cy7 copolymer with a pH-sensitive spacer, as it was able to markedly improve tumor detection during cytoreductive surgery. Moreover, we determined the efficacy of fluorescence-guided tumor resection in CAL33-luc orthotopic head and neck tumor model. The mice treated with fluorescence-guided surgery had prolonged disease free survival and slower tumor growth when compared to mice after the bright-light surgery. In conclusion, fluorescence guided surgery using stimuli-sensitive activable HPMA-Cy7 based probes is safe and feasible and might be of added value for treatment of head and neck tumors.

Biography

Martin Kaňa M.D., works as an attending physician at the Department of Otorinolaryngology and Head and Neck Surgery of 1st Faculty of Medicine and Motol University Hospital and is a student of the doctoral study programme Experimental surgery at the 1st Faculty of Medicine, Prague. The topic of his doctoral studies is focused on the drug delivery systems research, overcoming of multi-drug resistence in head and neck cancer and fluorescence-guided surgery.

katman@atlas.cz

Protease-activated probes for the visualization of glioblastoma

Dora Konečná[1,2]

P. Výmola[2], N. Ternerová2, N. Ternerová[2], D. Výmolová[2], E. Garcia-Borja[2], R. Mateu[2], F. Šroubek[3], J. Pankrác[4], J.C. Widen[5], M. Bogyo[5], D. Netuka[1], A. Šedo[2], P. Bušek[2]

[1]Dept. of Neurosurgery and Neurooncology, Military University Hospital, Prague
[2]Inst. of Biochemistry and Experimental Oncology, 1st Faculty of Medicine, Charles University, Prague,
[3]Inst. of Information Theory and Automation, Czech Academy of Sciences, Prague
[4]Center of Advanced Preclinical Imaging, 1st Faculty of Medicine Charles University, Prague
[5]Dept. of Pathology, Stanford University School of Medicine, Stanford

Fluorescence-guided surgery using 5-aminolevulinic acid (ALA) is used to identify tumor margins to improve the radicality of glioblastoma (GBM) resection. However, there are limitations to the use of ALA. Recently, molecularly targeted near-infrared protease-activated probes have been developed for the visualization of tumor tissue, but their application in GBM remains unexplored. The aim of this work was to evaluate the ability of single- and double-substrate probes to be specifically activated in brain tumor tissue and to compare the most promising candidate with ALA. The activation of probes was evaluated in glioma cell lines, macrophages, orthotopic mouse models, and in human GBM tissue. Tumor to normal brain tissue ratio (TNR) was determined using spectrofluorimery and image analysis. All probes visualized experimental GBMs with a minimum signal generated in non-tumorous brain tissue, TNR and signal intensity were highest for 6QC-ICG. 6QC-ICG was cleaved in glioma cells and macrophages *in vitro* and the resulting fluorophore accumulated intracellularly. Furthermore, 6QC-ICG was activated in the human GBM biopsy material. A comparison with ALA revealed a similar or even higher TNR for 6QC-ICG in GBM. In summary, 6QC-ICG is activated by glioma cells and tumor-associated macrophages, leading to a high contrast between tumor and brain tissue, which is superior to that of ALA. 6QC-ICG has the potential to be used for the intraoperative detection of GBM.

Biography

Dora Konečná has graduated from the 1st Faculty of Medicine, Charles University in 2019. She is a resident at Military University Hospital in Prague and a Ph.D. student of biochemistry and patobiochemistry at the 1st Faculty of Medicine, Charles University. Her research focuses on experimental visualization and treatment agents and their testing in preclinical GBM models.

dora.konecna@lf1.cuni.cz