ANNUAL REPORT
FACULTY INSTITUTE BIOCEV
2016

BIOCEV

Biotechnology and Biomedicine Center of the Academy of Sciences
and Charles University in Vestec

CHARLES UNIVERSITY
First Faculty of Medicine

TABLE OF CONTENS

INTRODUCTORY WORDS

Dear readers and fellow scientists,

It is my pleasure to write few words to our annual report to summarize what has been achieved during the year 2016. BIOCEV is a joint project, in which the scientists from the Academy of Sciences and Charles University under one roof are solving most imminent tasks in biomedicine and biotechnology. The 1st Faculty of Medicine participates in this project of excellence by establishing its faculty research institute. Genesis of our stay in Biocev has been initiated by Project Biocev that provided start-up financing for teams that were destined to move into new building in 2016. That actually happened during first few months of the last year and shortly the teams settled in Vestec near Prague in their bright new labs. While there are teams that completely moved in (internal groups), there are also teams that keep ties with the mother institutions (external groups) and closely collaborate with them. In total, nine research groups are located in the faculty institute. All principal investigators communicate on daily-basis and establish new interactions with the research facilities and non-faculty lab teams within the BIOCEV. Thus original idea of bringing scientists with different expertize and background has become every day reality with potential of performing groundbreaking research. This is facilitated by the existence of Research Infrastructures and Core Facilities. Year 2016 was indeed very important from several aspects. Firstly, we have assembled together and started to organize our lives here with help of administration faculty office. Secondly, we have started to meet regularly on departmental meetings every month. Thirdly, we have agreed on and started to run our monthly departmental seminars; year 2016 was dedicated to presentations of principal investigators and their labs. Lastly, the research labs participate on the university projects such as Progres, UNCE and SVV either via new faculty institute (internal groups) or via original faculty institutes (external groups). As will be in detail provided in this Annual report, the laboratories published many research publications, some of them in very prestigious journals with higher impact factor. These publications were often a result of bright ideas and hard work with help of international collaborators and also in many cases involving patients via the participation of clinics & hospitals. I am fully convinced that the teams producing these exciting results will continue being productive in the future and possibly even improve thanks to very stimulating environment and presence of high-technology facilities.

To summarize my intro to the first Annual 2016 report I would like to cordially thank to all people who participated in the Project BIOCEV in the past and wish to this new faculty institute very productive and successful scientific life!

Prof. Tomáš Stopka MD, PhD
Head of the faculty institute

RESEARCH GROUPS

Internal research laboratories

STOPKA LAB

Page 5

6.462 5.373 4.411 3.234

PETRÁK LAB

Clinical Proteomic Lab

Page 9

5.134 4.031 3.867 3.867 2.486

KRÁL LAB

Page 13

4.055 2.693 2.213 0.7

KOSTROUCH LAB

Page 17

MIKULA LAB

Page 21

4.055

IF = impacted publications

External research laboratories

SMETANA LAB

Institute of Anatomy

Page 23

MĚLKOVÁ LAB

Institute of Immunology and Microbiology

Page 27

NEČAS LAB

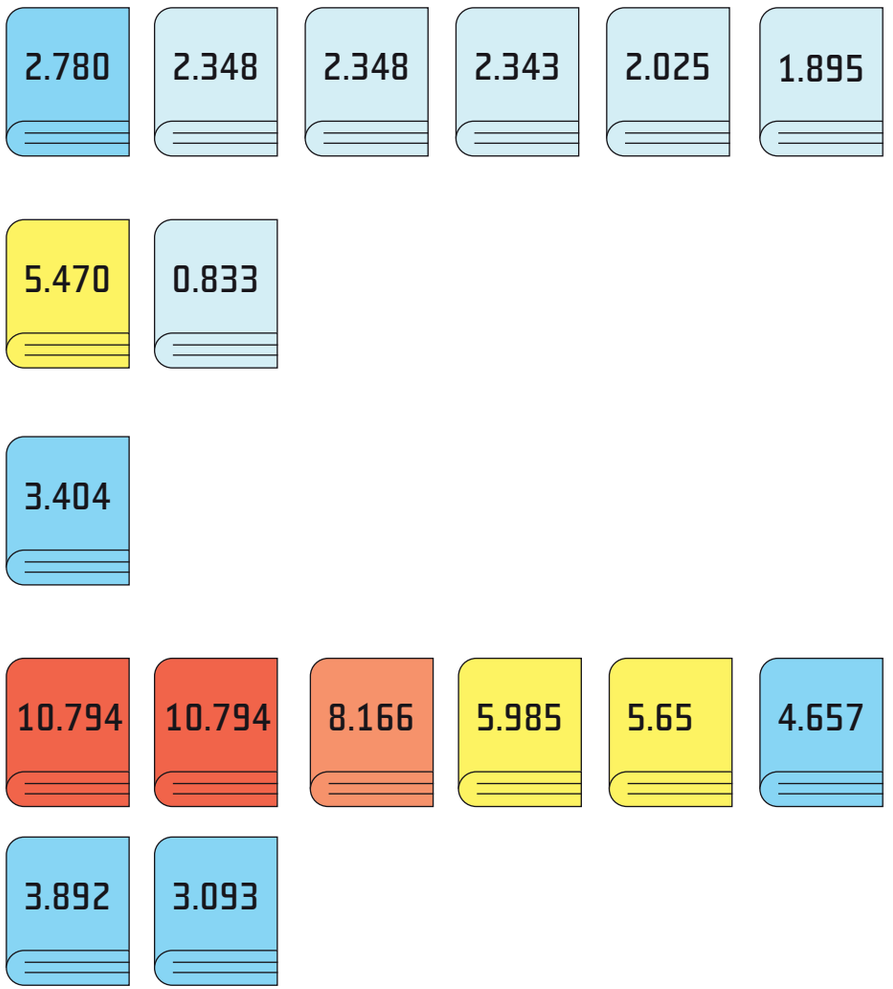
Institute of Pathological Physiology

Page 31

KMOCH / ZIKÁNOVÁ LAB

Institute of Inherited Metabolic Disorders

Page 35



STOPKA LAB

Head: Prof. MUDr. Tomáš Stopka, Ph.D.

T: +420 325 873 001 E: tomas.stopka@lf1.cuni.cz Room: B2.008

MEMBERS

Prof. Tomáš Stopka, M.D., Ph.D.
RNDr. Petra Bašová, Ph.D.
RNDr. Pavel Čabart, CSc.
MUDr. Nina Dusílková
Mgr. Juraj Kokavec, Ph.D.
Mgr. Vojtěch Kulvait
Kristina Léblová
MUDr. Ľubomír Minařík
Mgr. Helena Paszeková
MUDr. Kamila Polgárová
Mgr. Tereza Turková
Mgr. Shefali Thakur
RNDr. Jarmila Vargová
Mgr. Tomáš Zikmund

LAB SCOPE

Project focuses on studying the function of chromatin remodeling ISWI ATPase Smarca5 (Snf2h, MommeD4, Iswi) in the development of haematopoiesis from stem and progenitor cells and to understand their involvement in leukaemogenesis. Chromatin, a nucleoprotein complex engaged in the transfer of biological information, is made accessible (or inaccessible) upon activities of enzymes that belong to SWI/SNF2 family. SWI/SNF2 proteins, namely Smarca5, can regulate the interaction between DNA and histones and allow or block cell decisions imposed by recruitments of these factors. Importantly, Smarca5 interacts with several hematopoietic transcription factors, whose role is also a focus in our plans, as well as to understand target genetic programs of Smarca5-complexes.

RESEARCH FOCUS

- To understand mechanisms that during development are involved in regulating cell fate decisions at the level of chromatin and Smarca5.
- To elucidate role of Smarca5 in lineage-specific processes involving differentiation and lineage commitment using proposed set of transgenic animals that enable tissue specific knockout and overexpression.
- To understand how disruption of mechanisms involving Smarca5 and their partners may lead to hematologic malignancies.

From the left: Pavel Čabart, Tereza Turková, Tomáš Stopka, Juraj Kokavec, Tomáš Zikmund, Nina Dusílková, Kamila Polgárová, Petra Bašová, Helena Paszeková, Shefali Thakur

PUBLICATIONS

Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

6.462

Chromatin remodeling enzyme Snf2h/Smarca5 regulates embryonic lens differentiation and denucleation. He S, Limi S, McGreal RS, Xie Q, Brennan LA, Kantorow WL, Kokavec J, Majumdar R, Hou H Jr, Edelmann W, Liu W, Ashery-Padan R, Zavadil J, Kantorow M, Skoultchi AI, **Stopka T**, Cvekl A. Development. 2016 Jun 1;143(11):1937-47. doi: 10.1242/dev.135285. **N, B, I,**
(IF 6.462)

5.373

Distinct and overlapping DNMT1 interactions with multiple transcription factors in erythroid cells: Evidence for co-repressor functions. Papageorgiou DN, Karkoulia E, Amaral-Psarris A, Burda P, Kolodziej K, Demmers J, Bungert J, **Stopka T**, Strouboulis J. Biochimica et Biophysica Acta - Gene Regulatory Mechanisms. 2016 Dec;1859(12):1515-1526. doi: 10.1016/j.bbagrm.2016.09.007. **N, B, I, H** (IF 5.373)

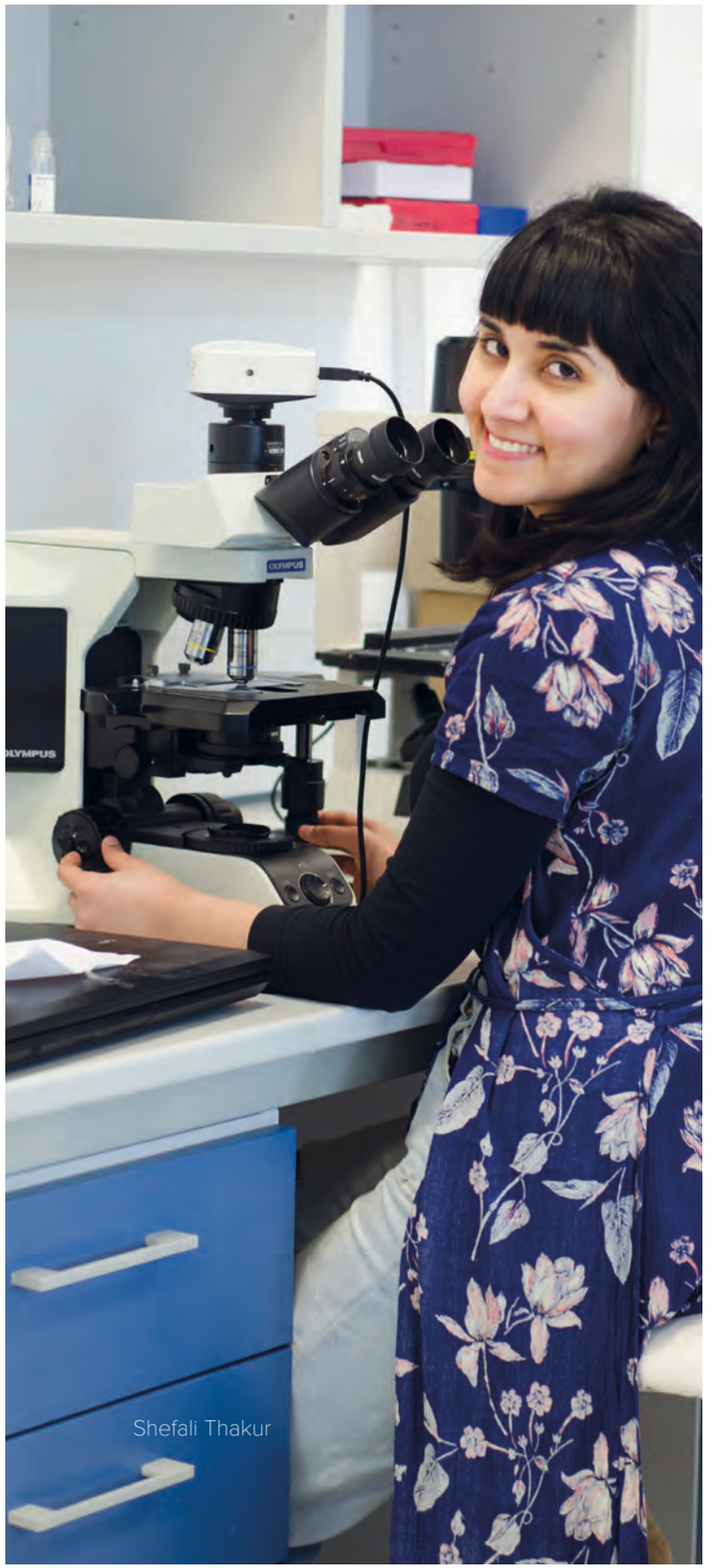
4.411

Differential expression, localization and activity of MARCKS between mantle cell lymphoma and chronic lymphocytic leukemia. Vargova J, Vargova K, Dusilkova N, Kulvait V, Pospisil V, Zavadil J, Trneny M, Klener P, **Stopka T**. Blood Cancer J. 2016 Sep 23;6(9):e475. doi: 10.1038/bcj.2016.80. **N, B, I, H**
(IF 4.411)

3.234

GATA-1 inhibits PU.1 gene via DNA and histone H3K9 Methylation of its Distal Enhancer in Erythroleukemia. Burda P, Vargova J, Curik N, Salek C, Papadopoulos GL, Strouboulis J, **Stopka T**. PLoS One. 2016 Mar 24;11(3):e0152234. doi: 10.1371/journal.pone.0152234. **N, B, I, H**
(IF 3.234)

Somatické mutace u myelodysplastického syndromu a jejich klinické využití. Stopka T. Myelodysplastic Syndrome NEWS. Ročník 4 / Číslo 2 / listopad 2016.**N**
(IF N/A)



Shefali Thakur

GRANTS

Regulation of hematopoietic stem cell differentiation by chromatin remodeling SWI/SNF2 ATPase Smarca5 (Snf2h) in mouse.
GA ČR 305/12/1033 (2012 – 2016)
Principal investigator: Stopka, Tomáš

Experimental pathology based on genetic manipulation of stem cells.
UNCE 204021 (2012 – 2017)
Principal investigator: Stopka, Tomáš

Identification of genetic events regulating aggressiveness of acute myeloid leukemia throughout the disease development.
GA ČR 16-05649S (2016 – 2018)
Principal investigator: Stopka, Tomáš

The molecular markers in diagnostics and therapy-monitoring of myelodysplastic syndrome patients treated by new modalities.
NV16-27790A (2016 – 2019)
Principal investigator: Stopka, Tomáš

Role of chromatin remodeling proteins in hematopoietic stem cells and during leukemogenesis.
LH15170 (2015 – 2017)
Principal investigator Stopka, Tomáš

Study of chromatin remodeling factor Smarca5 in murine hematopoiesis.
815316 (2016 – 2017)
Principal investigator Kokavec, Juraj

Directed deletion of putative oncogene SMARCA5 in tumor cells.
228316 (2016 – 2018)
Principal investigator Paszeková, Helena

COLLABORATION

New York Albert Einstein College of Medicine,
Laboratory of Prof. A.I. Skoultchi
Field of study: mouse genetics
Principal investigator: Stopka, Tomáš


From the left: Juraj Kokavec, Tezera Turková, Tomáš Zikmund


Juraj Kokavec

Clinical Proteomic Lab

PETRÁK LAB

Head: Doc. RNDr. Jiří Petrák, Ph.D.

T: +420 325 873 011 E: jiri.petrak@lf1.cuni.cz Room: B2.030

MEMBERS

Doc. RNDr. Jiří Petrák, Ph.D.
Mgr. Matěj Běhounek
Mgr. Eliška Doktorová
Mgr. Martin Chmel
Mgr. Ondřej Vít

LAB SCOPE

Our lab employs modern proteomic analyses to study global changes of cellular proteomes in order to describe molecular mechanisms of various human diseases. We analyze complex biological samples such as tissue samples, body fluids or cell cultures. Using various hi-res separation methods combined with fast and sensitive mass spectrometry we are able to monitor quantitative and qualitative changes of thousands of proteins in a single sample.

We use quantitative proteomic approaches to identify the key proteins and pathways involved in diverse biological processes such as molecular mechanisms underlying drug resistance in tumors or the molecular pathways responsible for heart failure. Proteomic methods also enable us to look for potential drug targets or to identify disease biomarkers - i.e. specifically altered proteins present in patient blood or other body fluids.

From the left: Matěj Běhounek, Eliška Doktorová, Ondřej Vít, Jiří Petrák, Martin Chmel

PUBLICATIONS

Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

5.135

Myocardial iron content and mitochondrial function in human heart failure: a direct tissue analysis. Melenovsky V, **Petrak J**, Mracek T, Benes J, Borlaug BA, Nuskova H, Pluhacek T, Spatenka J, Kovalcikova J, Drahota Z, Kautzner J, Pirk J, Houstek J. Eur J Heart Fail. 2016 Sep 19. doi: 10.1002/ejhf.640. **B, N, I, H**
(IF 5.135)

4.031

Changes in Myocardial Composition and Conduction Properties in Rat Heart Failure Model Induced by Chronic Volume Overload. Sedmera D, Neckar J, Benes J Jr, Pospisilova J, **Petrak J**, Sedlacek K, Melenovsky V. Front Physiol. 2016 Aug 25;7:367. doi: 10.3389/fphys.2016.00367. **B, H**
(IF 4.031)

3.867

Large-scale identification of membrane proteins based on analysis of trypsin-protected transmembrane segments. Vit O, Kadek A, Hausner J, Sklenar J, Harant K, Novak P, Scigelova M, Woffendin G and **Petrak J**. J Proteomics. 2016 Mar 11. pii: S1874-3919(16)30069-0. **B, I**
(IF 3.867)

3.867

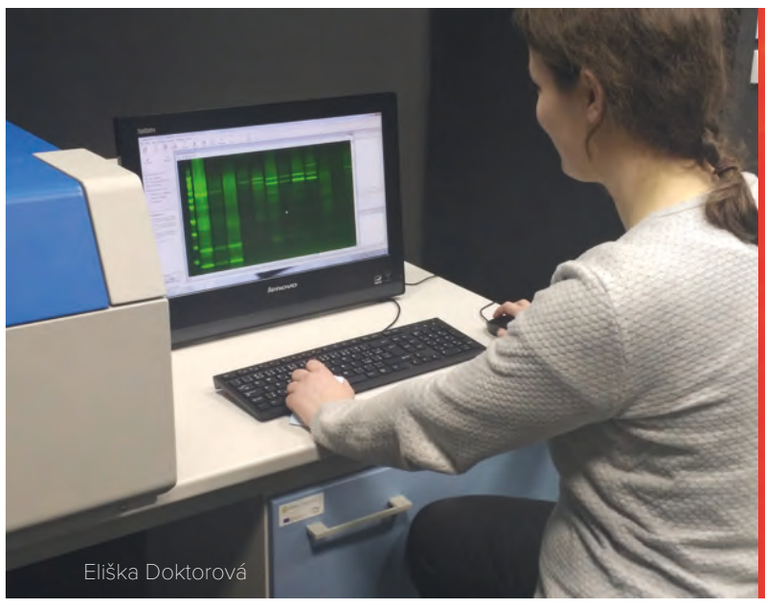
Integral membrane proteins in proteomics. How to break open the black box? Vit O, **Petrak J.** J Proteomics. 2016 Aug 13.
doi: 10.1016/j.jprot.2016.08.006. **B**
(IF 3.867)

2.486

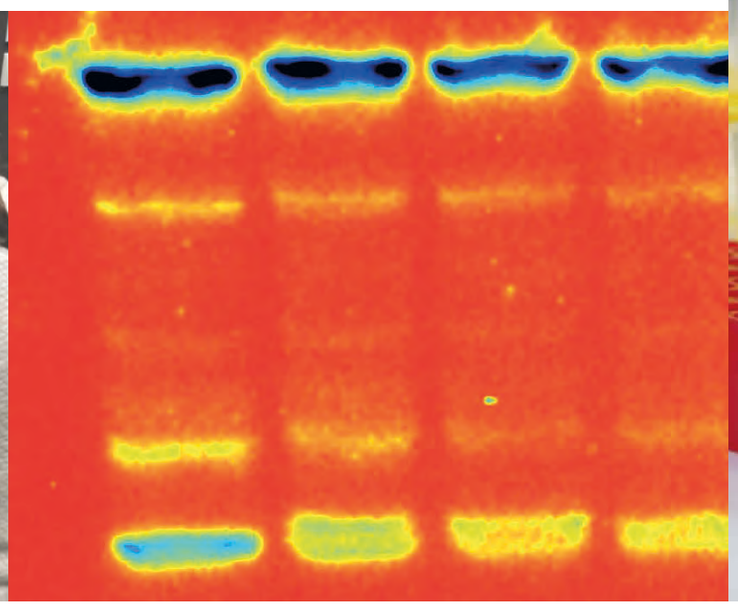
Proteomic analysis of imatinib-resistant CML-T1 cells reveals calcium homeostasis as a potential therapeutic target. Toman O, Kabickova T, Vit O, Fiser R, Machova Polakova K, Zach J, Linhartova J, Vyoral D and **Petrak J**. Oncology Reports. 2016 Sep;36(3):1258-68. doi: 10.3892/or.2016.4945. **B, H**
(IF 2.486)

GRANTS

The role of hepcidin in regulation of systemic and myocardial iron metabolism in heart failure.
GA ČR 15-14200S (2015 – 2017)
Principal investigator: Petrák, Jiří



Eliška Doktorová



KRÁL LAB

Head: Prof. RNDr. Vladimír Král, DSc.

T: +420 325 873 004 E: vladimir.kral@lf1.cuni.cz Room: B2.034

MEMBERS

Prof. RNDr. Vladimír Král, DSc.
Bc. Vojtěch Albert Borek
Ing. Martin Havlík, Ph.D.
Ing. Milan Jakubek, Ph.D.
Ing. Zdeněk Kejík, Ph.D.
Ing. Lucie Krčová
Ing. Miroslav Louma
Mgr. Alla Synytsya, Ph.D.
Doc. Mgr. Taťjana Šiškanová, CSc.
Mgr. Liudmila Vasina

LAB SCOPE

The main focus of our group is biochemical, cellular and molecular biological aspects of cell differentiation and oncogenic transformation dependent on proteases.

The aim of our group's research is to study molecular recognition, intermolecular interactions, and the use of this knowledge for the benefit of life.

We are preparing molecular systems for early diagnosis of diseases, preparing drug dosing systems and drug delivery systems for more effective and safe treatment. We exploit and discover new knowledge of supramolecular chemistry, nanotechnology, molecular engineering and other newly formed disciplines of modern science.

From the left: Lucie Krčová, Liudmila Vasina, Vojtěch Albert Borek, Zdeněk Kejík, Alla Synytsya, Vladimír Král

PUBLICATIONS

Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

4.055

Specific ligands based on Troger's base derivatives for the recognition of glycosaminoglycans. Kejik Z, Briza T, Havlik M, Dolensky B, Kaplanek R, Kralova J, Mikula I, Martasek P, **Kral V**. Dyes and Pigments. 2016 Nov, 134 (212-218).
doi: 10.1016/j.dyepig.2016.07.002. **B, N**
(IF 4.055)

2.693

Aluminium(III) sensing by pyridoxal hydrazone utilising the chelation enhanced fluorescence effect. Kejik Z, Kaplanek R, Havlik M, Briza T, Vavrinova D, Dolensky B, Martasek P, **Kral V**. Journal of Lumininescence. 2016, 180, 269-277.
doi: 10.1016/j.jlumin.2016.08.047. **B, N**
(IF 2.693)

2.213

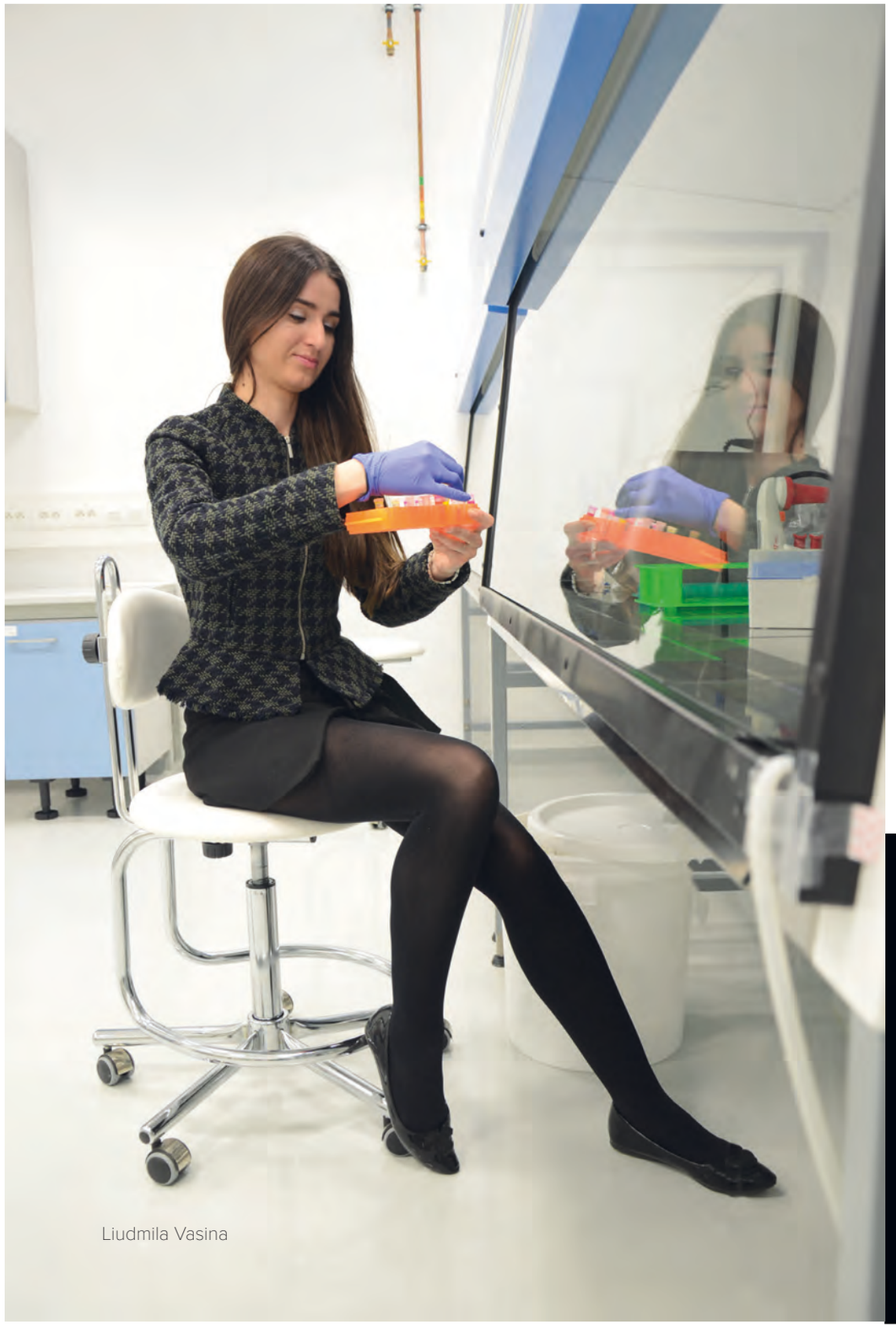
Large scale preparation of up- converting YF3:YbEr nanocrystals with various sizes by solvothermal syntheses using ionic liquid bmimCl. Bartunek V, Rak J, Pelankova B, Junkova J, Mezlikova M, **Kral V**, Kuchar M, Engstova H, Jezek P, Smucler R, Journal of Fluorine Chemistry. 2016 Aug, 188 (14-17).
doi: 10.1016/j.jfluchem.2016.05.015. **B, N, I, H**
(IF 2.213)

0.7

Multifunctional Bile Acid Derivatives as Efficient RNA Transporters (Carriers). Vasina L, Bhupendra C Reddy BC, Sievanen E, Kolehmainen E, **Kral V**.
Journal of Pharmaceutics & Drug Delivery Research. 2016,5:2.
doi: dx.doi.org/10.4172/2325-9604.1000147. **B, N, I**
(IF 0.7)

Supramolecular nanosized siRNA-carrier complexes for efficient into-cell transport. Vasina, L, **Kral V**, *Наука в современном мире* 2016, 5, 47-50. **B, N**
(IF N/A)

Milan Jakubek



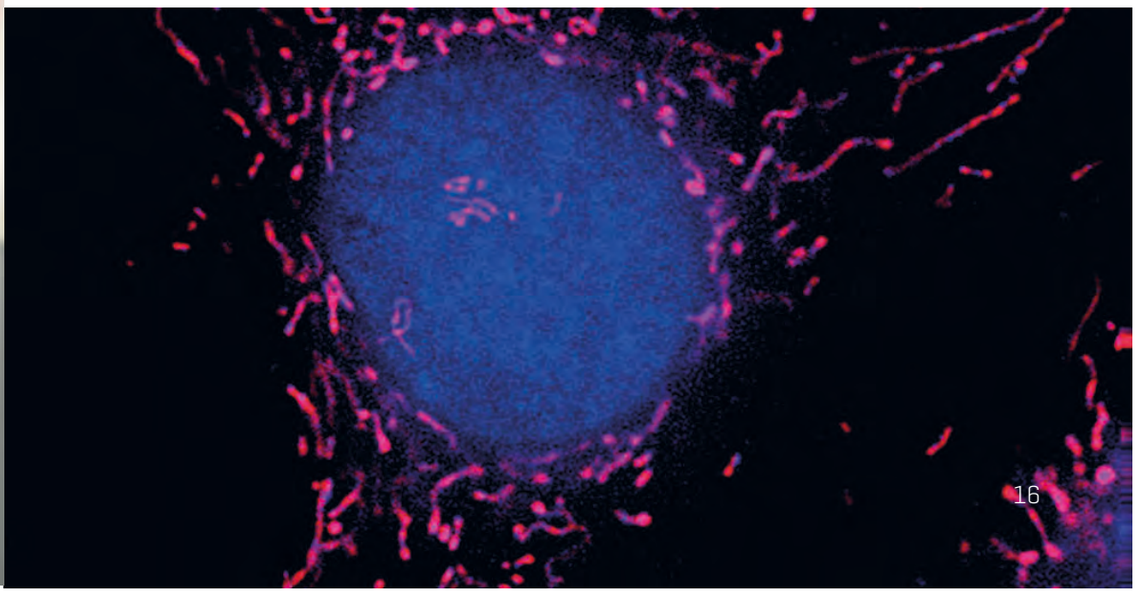
Liudmila Vasina

PATENT

Use of new types of pentamethinine salts with expanded quinoxaline unit in antitumor therapy.
306320

GRANTS

Nourishment and its influence on the epigenetic profile of the Czech Fleckvieh Breed.
QJ1610515 (2016 – 2018)
Principal investigator: Král, Vladimír



KOSTROUCH LAB

Head: MUDr. Zdeněk Kostrouch, CSc.

T: +420 325 873 020 E: zdenek.kostrouch@lf1.cuni.cz Room: B2.004

MEMBERS

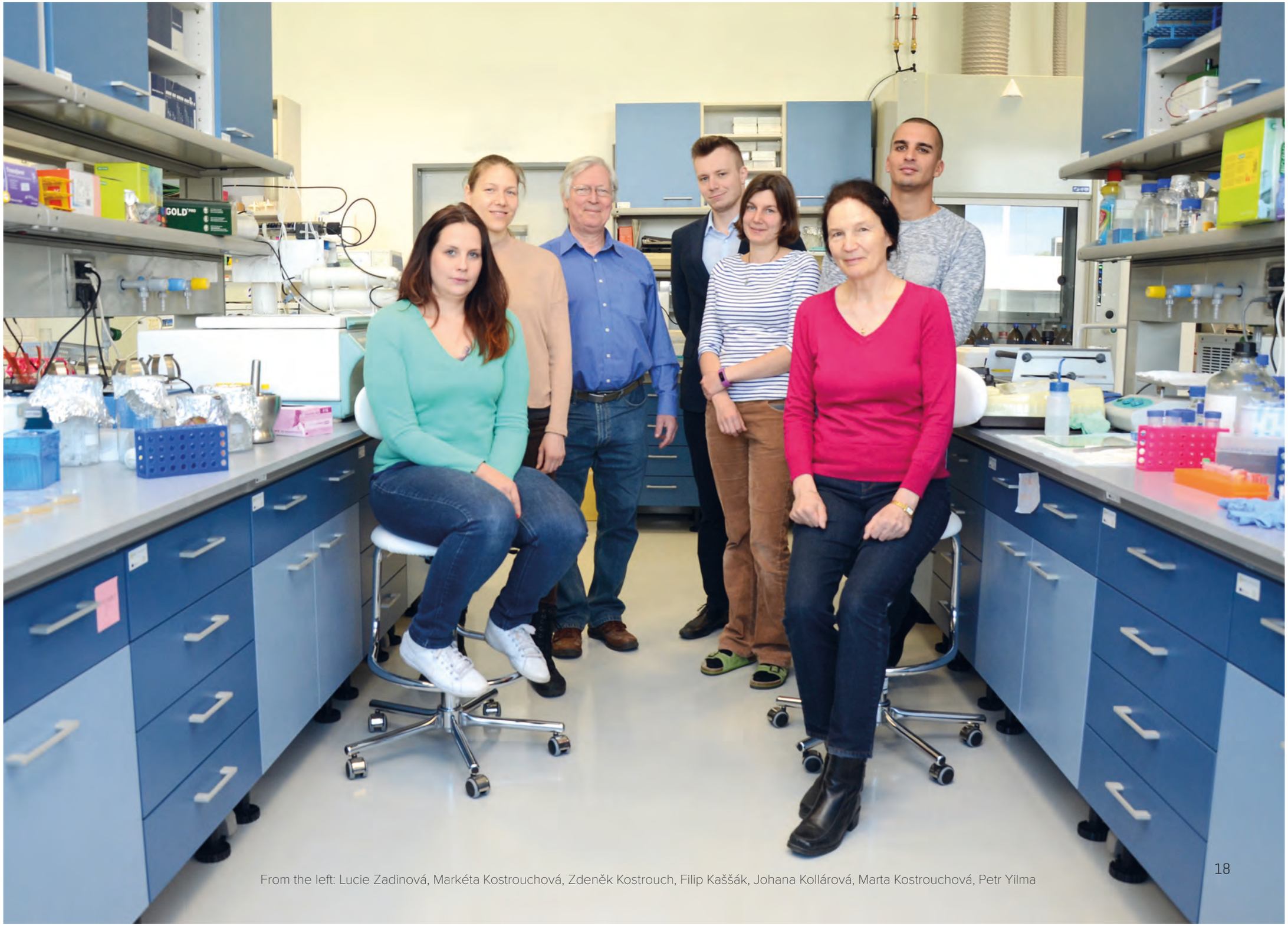
MUDr. Zdeněk Kostrouch, CSc.
Azzat Al Redouan, BSc.
MUDr. Ahmed Ali Chughtai
MUDr. Filip Kaššák
Ing. Johana Kollárová
MUDr. David Kostrouch, Ph.D.
MUDr. Markéta Kostrouchová
MUDr. Marta Kostrouchová, CSc.
Veronika Kostrouchová
MUDr. Jan Philipp Novotný
Hana Prouzová
MUDr. Kateřina Šušlíková
Ing. Petr Yilma
Lucie Zadinová
Mgr. Vladimír Zima

LAB SCOPE

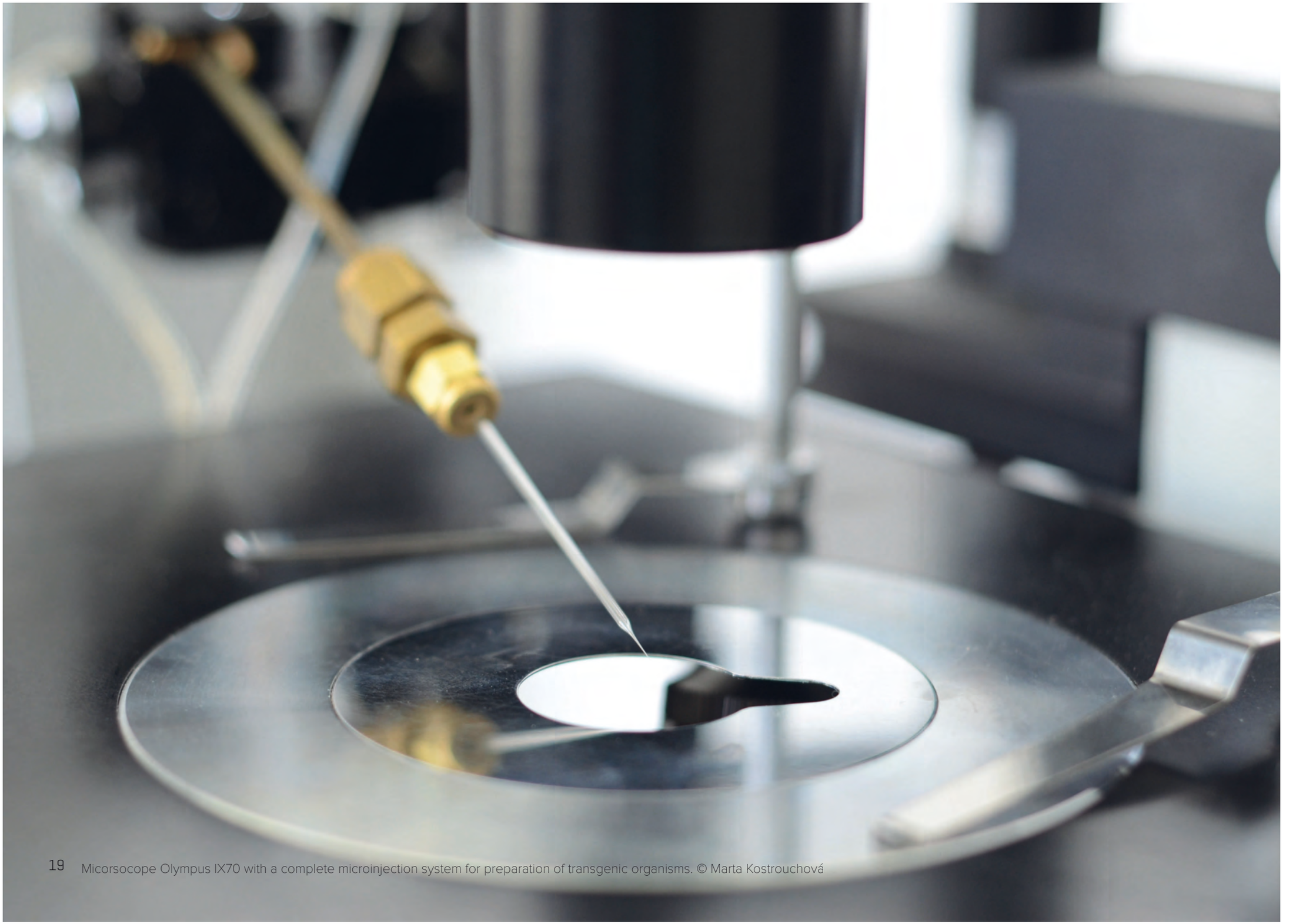
The aim of the research group is to use invertebrate model systems and advanced informatics for the identification and analysis of regulatory cascades that determine normal development and metabolism of metazoan organisms and play critical roles in human diseases. The projects focus on regulatory mechanisms involving nuclear receptors and proteins that transmit or modulate their function. Model systems used for this research include nematodes (Caenorhabditis elegans and other Rhabditidae), flatworms (Schmidtea mediterranea) and diploblastic species (Tripedalia cystophora, Aurelia aurita, corals, sea anemones, Placozoa) and Porifera. Parallel to model organisms, the research is conducted on mammalian cell cultures and on human samples.

RESEARCH FOCUS

- The identification of conserved regulatory mechanisms including nuclear receptors and proteins that transmit or modulate their function.
- The analysis of the parallel (orthologous) mechanisms in mammalian cells and human tissues, including cancers.



From the left: Lucie Zadinová, Markéta Kostrouchová, Zdeněk Kostrouch, Filip Kaššák, Johana Kollárová, Marta Kostrouchová, Petr Yilma

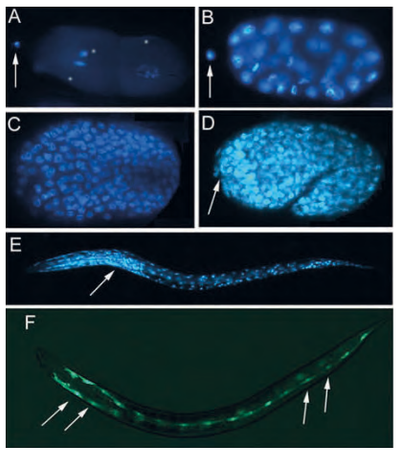


19 Micorsocope Olympus IX70 with a complete microinjection system for preparation of transgenic organisms. © Marta Kostrouchová

GRANTS

Gene expression at normal and pathologic states.
SVV 260257 (2016)
Principal investigator: Kostrouch, Zdeněk

Mikroskop Olympus IX70 s kompletním mikroinjekčním systémem pro přípravu transgenních organismů. © Marta Kostrouchová



C. elegans at various stages of embryonic (A to D) and larval development (E, F). Blue labeled nuclei are visualized by DAPI staning. Green marker in panel F visualizes a transgene consisting of a part of a nuclear receptor fused with the gene coding for green fluorescent protein. Arrows indicate polar bodies in A, B and D, neurons of the neuronal cord in E and seam cells expressing the transgene in F. © Marta Kostrouchová

MIKULA LAB

Head: Ing. Ivan Mikula, Ph.D.

T: +420 325 873 022 E: ivan.mikula@lf1.cuni.cz Room: B2.014

MEMBERS

Ing. Ivan Mikula, Ph.D.
Ing. Tomáš Bříza, Ph.D.
Doc. Ing. Petr Kačer, Ph.D.
Ing. Robert Kaplánek, Ph.D.
Ing. Kateřina Veselá, Ph.D.

LAB SCOPE

The research group is mainly focused on the structure-functional basis of gaseous molecule signaling. The second objective is to use analytical approaches to solving specific problems (eg. analysis of factors associated with obesity and metabolic disorders).

RESEARCH FOCUS

- Characterization of mammalian isoforms of NOS and HO, more precise definition of the NO and CO role in the individual physiological and pathophysiological processes.
- Determination of the complete structure of the NOS holoenzyme.
- Study of the reactivity and catalytic characteristics of bacterial NOSoxy-like proteins, clarification of their ability to bind different compounds, i.e. at close quarters of the haem (as it is in the L-Arg analogues in the mammalian NOS or in the iron ligands).
- Study of the physiological and pathophysiological functions of the newly described protein NOA1 (Nitric Oxide Associated protein 1).
- Identification of the factors responsible for the development of obesity in connection with metabolic disorders (Diabetes Mellitus Type 2).

PUBLICATIONS

Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

4.055

Specific ligands based on Troger's base derivatives for the recognition of glycosaminoglycans. Kejik Z, Briza T, Havlik M, Dolensky B, Kaplanek R, Kralova J, Mikula I, Martasek P, **Kral V**. Dyes and Pigments. 2016 Nov, 134 (212-218).
doi: 10.1016/j.dyepig.2016.07.002. **B, N**
(IF 4.055)

COLLABORATION

University of Maryland, USA (prof. C.S. Raman)

Charité Universitätsmedizin Berlin, Institute of Medical Genetics and Human Genetics, Berlin, Germany.
(Dr. Tomasz Zemojtel)

Fachhochschule Nordwestschweiz (FHNW), Basel, Schwitzerland. (prof. Dr. Berndt Joost)
Yerevan State University, Yerevan, Armenia (prof. Vladimir M. Aroutiounian)
Project DecoComp - Competence Centre for Decontamination and Sterilization Processes with Vapour Phase Hydrogen Peroxide.

Tomáš Bříza

External research group affiliated to Institute of Anatomy

SMETANA LAB

Head: Prof. MUDr. Karel Smetana, DrSc.

T: +420 325 873 021 E: karel.smetana@lf1.cuni.cz Room: B2.032

MEMBERS

Prof. MUDr. Karel Smetana. DrSc.
RNDr. Barbora Dvořánková, Ph.D.
MUDr. Ondřej Kodet, Ph.D.
MUDr. Lukáš Lacina, Ph.D.
Mgr. Karolína Strnadová
RNDr. Pavol Szabo, Ph.D.

LAB SCOPE

The laboratory project is aimed at studying possibilities of epidermal stem cell isolation.
The epidermal stem cells and the multipotent neural crest originated stem cells represent the most easily accessible stem cells in human body. The *in vitro* propagation and controlled differentiation will be investigated too.
Our interest is focused predominantly on study of the microenvironment of these cells under physiological and pathological conditions (cancer) that is necessary for their expansion *in vitro*.

RESEARCH FOCUS

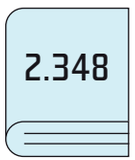
- Development of separation and cultivation methods for the preparation of stem cells from the human epidermis.
- Methods of the characterization and differentiation of the obtained cell types
- Study of the influence of the microenvironment on the stem cells function and their differentiation.
- Development of the new clinical applications.

From the left: Barbora Dvořánková, Lukáš Lacina, Karolína Strnadová, Pavol Szabo, Karel Smetana

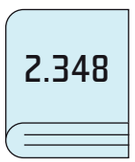
PUBLICATIONS

Affiliation indicated to Institute of Anatomy and Biocev
Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

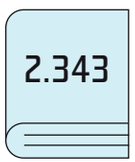
Simultaneous blocking of IL-6 and IL-8 is sufficient to fully inhibit CAF-induced human melanoma cell invasiveness. Jobe NP, Rosel D, Dvorankova B, Kodet O, Lacina L, Mateu R, **Smetana K Jr**, Brabek J. Histochem Cell Biol. 2016 Apr 21.
doi: 10.1007/s00418-016-1433-8. **B, N, H**
(IF 2.780)



Pharmacological activation of estrogen receptors-α and -β differentially modulates keratinocyte differentiation with functional impact on wound healing. Perzelova V, Sabol F, Vasilenko T, Novotny M, Kovac I, Slezak M, Durkac J, Holly M, Pilatova M, Szabo P, Varinska L, Criepokova Z, Kucera T, Kaltner H, Andre S, Gabius HJ, Mucaji P, **Smetana K Jr**, Gal P. Int J Mol Med. 2016 Jan;37(1):21-8.
doi: 10.3892/ijmm.2015.2351. **B, I, H**
(IF 2.348)

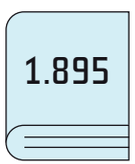


Functional differences between neonatal and adult fibroblasts and keratinocytes: Donor age affects epithelial-mesenchymal crosstalk *in vitro*. Mateu R, Zivicová V, Drobna Krejci E, Grim M, Strnad H, Vlcek C, Kolar M, Lacina L, Gal P, Borsky P, **Smetana K Jr** and Dvorankova B. Int J Mol Med. 2016 Oct;38(4):1063-74.
doi: 10.3892/ijmm. 2016.2706. **B, N, I, H**
(IF 2.348)

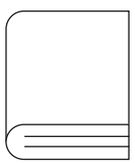


Intercellular crosstalk in human malignant melanoma. Dvorankova B, Szabo P, Kodet O, Strnadova H, Kolar M, Lacina L, Krejci E, Nanka O, Sedo A, **Smetana K Jr**. Protoplasma. 2016 Nov 3.
doi: 10.1007/s00709-016-1038-z. **B, N**
(IF 2.343)

Regulatory impact of amniotic membrane transplantation on presence of dhesion/growth-regulatory galectins-1 and -7 in corneal explants from Acanthamoeba keratitis patients: Clinical Note. Smorodinova N, Kaltner H, Jirsova K, Hrdlickova-Cela E, Andre S, Kucera T, **Smetana K Jr**, Gabius HJ. Curr. Eye Res. 2016 Jun; 46(1): 740-6.
doi: 10.3109/02713683.2015.1061022. **B, I, H**
(IF 2.025)



Ageing as an Important Risk Factor for Cancer. Smetana K Jr, Lacina L, Szabo P, Dvorankova B, Broz P, and Sedo A. ANTICANCER RESEARCH. 2016 Oct;36(10):5009-5017.
doi: 10.21873/anticanres.11069. **N, I, H**
(IF 1.895)



Fibroblasts as Drivers of Healing and Cancer Progression: From *In vitro* Experiments to Clinics. Krejci E, Dvorankova B, Szabo P, Nanka O, Strnad H, Kodet O, Lacina L, Kolar M and **Smetana K Jr**. Molecular Mechanisms of Skin Aging and Age-Related Diseases. 2016 June 18.
ISBN: 978-1-4987-0465-6. **B**
(IF N/A)

GRANTS

Assigned to Institute of Anatomy

Mechanisms of reprogramming of complex cellular responses.
UNCE 204013 (2012 – 2017)
Co-investigator: Smetana, Karel

The Sugar Code: from (bio)chemical concept to clinics.
PITN-GA-2012-317297 (2012 – 2016)
Co-investigator: Smetana, Karel

Tumor microenvironment of head and neck carcinoma: Prognostic significance of extracellular matrix produced by tumor-associated fibroblasts.
AZV15-28933A (2015 – 2018)
Co-Investigator: Smetana, Karel

Microenvironment of malignant melanoma as a factor of tumor aggressiveness.
GA ČR 16-05534S (2016 – 2018)
Principal investigator: Smetana, Karel

Complex oncological programme
PRVOUK-27 (2012 – 2016)
Co-investigator: Smetana, Karel

Cellular and molecular characteristics of neonatal human skin: consequences for skin healing.
GA ČR 13-20293S (2013 – 2016)
Principal investigator: Dvořánková, Barbora

ERK pathway activation as a prognostic tool and a prospective therapeutic target in head and neck squamous cell carcinoma and malignant melanoma.
AZV 16-29032A (2016 – 2019)
Co-investigator: Lacina, Lukáš

COLLABORATION

Institute of Physiological Chemistry, Ludwiga-Maximiliana University, München, Germany, Field of study: endogenous lectin

Institute of Medical Biology, Agency for Science, Technology and Research (A*STAR), Singapore, Field of study: epithelial-mesenchymal interaction

Department of Information and Electronic Materials Engineering, Paichai University, Daejeon, Korea, Field of study: biocompatibility of metals

Karolína Strnadová

Pavol Szabo

Lukáš Lacina

External research group affiliated to Institute of Immunology and Microbiology

MĚLKOVÁ LAB

Head: MUDr. Zora Mělková, Ph.D.

T: +420 325 873 014 E: zora.melkova@lf1.cuni.cz Room: B2.031

MEMBERS

MUDr. Zora Mělková, Ph.D.
RNDr. Josef Bodor, CSc.
RNDr. Věra Hájková
Monika Kaplanová
Ing. Michaela Madleňáková

LAB SCOPE

The focus of the lab research in BIOCEV consists in the studies of interactions of the viruses, namely HIV-1, with the host. Specifically, we have been exploring the role of redox stress in HIV-1 latency reversal and its potential use for HIV-1 cure.

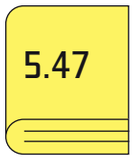
RESEARCH FOCUS

- To characterize the molecular mechanism of action of redox-modulating agents on reactivation of the latent HIV-1 and to verify the results obtained in vitro in tissue cultures also in primary peripheral lymphocytes of healthy donors and HIV-1 positive patients ex vivo.
- To assess the effects of Normosang, a heme arginate containing drug used to treat acute attacks of hepatic porphyrias, in HIV-1 positive patients.
- To assess the effects of Normosang on the size of the latent pool and its potential use for HIV-1 cure.

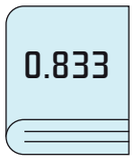
From the left: Josef Bodor, Michaela Madleňáková, Monika Kaplanová, Zora Mělková, Věra Hájková

PUBLICATIONS

Affiliation indicated to Institute of Immunology and Microbiology
Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**



Protein expression from unintegrated HIV-1 DNA introduces bias in primary in vitro latency models. Bonczkowski P, De Scheerder MA, Malatinkova E, Borch A, **Melkova Z**, Koenig R, De Spiegelaere W, Vandekerckhove L. Scientific Reports, 2016 Dec 2;6:38329. doi: 10.1038/srep38329.
(IF 5.47)



Iron Overload Causes Alterations of E-Cadherin in the Liver. Fujikura Y, Krijt J, Povysil C, **Melkova Z**, Prikryl P, Vokurka M, Necas E. Folia Biol (Praha). 2016;62(3):95-102.
(IF 0.833)

GRANTS

Assigned to Institute of Immunology and Microbiology

Studies of infectious diseases and their causative agents
SVV 2016, 260260 (2016)
Principal investigator: Mělková, Zora

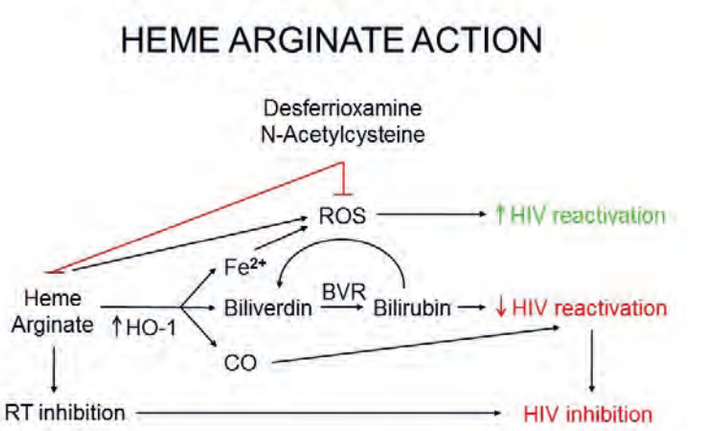


Fig. 1. Scheme of action of heme arginate. Heme inhibits reverse transcription, leading to HIV-1 inhibition. Heme is decomposed by the action of HO-1 into Fe2+, CO and biliverdin that is further converted to bilirubin by biliverdin reductase. Heme- and iron-mediated Fenton reaction generates reactive oxygen species (ROS), leading to reactivation of the latent HIV-1. This reaction might be exploited for latency reversal and HIV-1 cure. The reactivation can be inhibited by the antioxidant N-Acetyl cysteine or iron chelator Desferrioxamine as well as by CO and bilirubin.

External research group affiliated to Institute of Patological Physiology

NEČAS LAB

Head: Prof. MUDr. Emanuel Nečas, DrSc.

T: +420 325 873 013 E: emanuel.necas@lf1.cuni.cz Room: B2.035

MEMBERS

Prof. MUDr. Emanuel Nečas, DrSc.
Ing. Tomáš Heizer
Mgr. Nicol Renešová

LAB SCOPE

Research is focused on cellular and molecular responses of the haematopoietic tissue to injury. It is based on our recent results which demonstrated that not only stem cells, but also the whole spectrum of progenitor cells (including those from the very bottom of the stem cell – progenitor cell developmental hierarchy) respond to bone marrow injury. Our research is focused on the cell signalling and the key transcription factors which activate the latent potential of myeloidbiased progenitors to rapidly respond to bone marrow injury. The response includes a transient switch from the differentiationlinked cell division to the selfrenewal-linked one. In parallel, attention is also paid to the external microenvironmental cues that induce the switch.

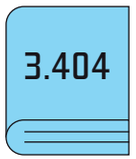
The research is original in integrating the latent potential of haematopoietic progenitor cells to respond to tissue injury with control of the cells function executed by external microenvironmental factors, and specific intracellular signalling. The research is expected to provide new information on the functional organisation of the very complex tissue of bone marrow, i.e.

The tissue composed of specific stroma with control and supportive roles, and the executive component - the haematopoietic stem and progenitor cells. This research requires that the haematopoietic tissue is primarily studied *in situ,* for which we have developed appropriate and well defined experimental approaches.

From the left: Nicol Renešová, Emanuel Nečas, Tomáš Heizer

PUBLICATIONS

Affiliation indicated to Institute of Pathological Physiology
Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

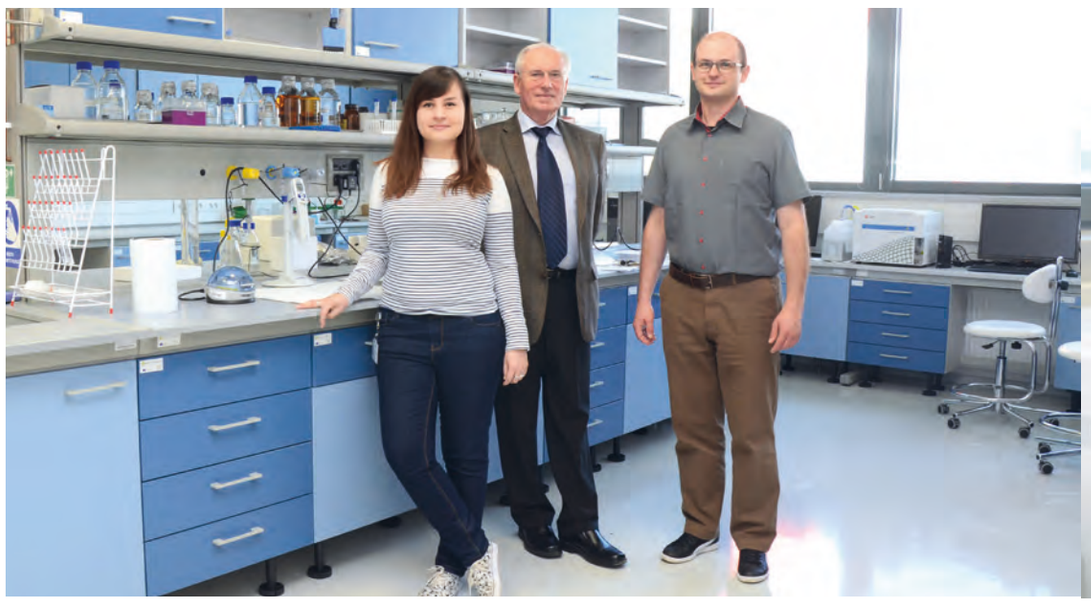


Low c-Kit Expression Level Induced by Stem Cell Factor Does Not Compromise Transplantation of Hematopoietic Stem Cells. Chen CL, Faltusova K, Molik M, Savvulidi F, Chang KT, **Necas E**. Biol Blood Marrow Transplant. 2016 Jul;22(7):1167-72. doi: 10.1016/j.bbmt. 2016.03.017. **B, I**
(IF 3.404)

GRANTS

Assigned to Institute of Pathological Physiology

Self-renewal of haematopoietic stem cells in regenerating haematopoiesis.
GA ČR 14-25515S (2014 – 2016)
Principal investigator: Nečas, Emanuel



Kmoch / Zikánová LAB

PUBLICATIONS

Affiliation indicated to Institute of Inherited Metabolic Disorders
Dedicated to project Biocev = **B**, NPU II = **N**, international collaboration = **I**, collaboration with hospital = **H**

10.794

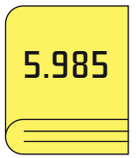
Autosomal-Dominant Corneal Endothelial Dystrophies CHED1 and PPCD1 Are Allelic Disorders Caused by Non-coding Mutations in the Promoter of OVOL2. Davidson AE, Liskova P, Evans CJ, Dudakova L, Noskova L, Pontikos N, Hartmannova H, Hodanova K, Stranecky V, Kozmik Z, Levis HJ, Idigo N, Sasai N, Maher GJ, Bellingham J, Veli N, Ebenezer ND, Cheetham ME, Daniels JT, Thaung CM, Jirsova K, Plagnol V, Filipec M, **Kmoch S**, Tuft SJ, Hardcastle AJ. Am J Hum Genet. 2016 Jan 7;98(1):75-89. doi: 10.1016/j.ajhg.2015.11.018. **B, I, H**
(IF 10.794)

10.794

Heterozygous Loss-of-Function SEC61A1 Mutations Cause Autosomal-Dominant Tubulo-Interstitial and Glomerulocystic Kidney Disease with Anemia. Bolar NA, Golzio C, Zivna M, Hayot G, Van Hemelrijk C, Schepers D, Vandeweyer G, Hoischen A, Huyghe JR, Raes A, Matthys E, Sys E, Azou M, Gubler MC, Praet M, Van Camp G, McFadden K, Pediaditakis I, Pristoupilova A, Hodanova K, Vyletal P, Hartmannova H, Stranecky V, Hulkova H, Baresova V, Jedlickova I, Sovova J, Hnizda A, Kidd K, Bleyer AJ, Spong RS, Vande Walle J, Mortier G, Brunner H, Van Laer L, **Kmoch S**, Katsanis N, Loeys BL. Am J Hum Genet. 2016 Jul 7;(1):174-187. doi: 10.1016/j.ajhg.2016.05.028. **N, I**
(IF 10.794)

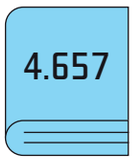
8.166

Diagnosis and misdiagnosis of adult neuronal ceroid lipofuscinosis (Kufs disease). Berkovic SF, Staropoli JF, Carpenter S, Oliver KL, **Kmoch S**, Anderson GW, Damiano JA, Hildebrand MS, Sims KB, Cotman SL, Bahlo M, Smith KR, Cadieux-Dion M, Cossette P, Jedlickova I, Pristoupilova A, Mole SE. Neurology. 2016 Aug 9;87(6):579-84. doi: 10.1212/ WNL.0000000000002943. **N, I**
(IF 8.166)



Acadian variant of Fanconi syndrome is caused by mitochondrial respiratory chain complex I deficiency due to a non-coding mutation in complex I assembly factor NDUFAF6. Hartmannova H, Piherova L, Tauchmannova K, Kidd K, Acott PD, Crocker JF, Oussedik Y, Mallet M, Hodanova K, Stranecky V, Pristoupilova A, Baresova V, Jedlickova I, Zivna M, Sovova J, Hulkova H, Robins V, Vrbacky M, Pecina P, Kaplanova V, Houstek J, Mracek T, Thibeault Y, Bleyer AJ, **Kmoch S**. Hum Mol Genet. 2016 Sep 15;25(18):4062-4079. doi: 10.1093/hmg/ddw245. **B, N, I**
(IF: 5.985)

The clinical, biochemical and genetic features associated with RMND1-related mitochondrial disease. Ng YS, Alston CL, Diodato D, Morris AA, Ulrick N, **Kmoch S**, Houstek J, Martinelli D, Haghighi A, Atiq M, Gamero MA, Garcia-Martinez E, Kratochvilova H, Santra S, Brown RM, Brown GK, Ragge N, Monavari A, Pysden K, Ravn K, Casey JP, Khan A, Chakrapani A, Vassallo G, Simons C, McKeever K, O'Sullivan S, Childs AM, Østergaard E, Vanderver A, Goldstein A, Vogt J, Taylor RW, McFarland R. J Med Genet. 2016 Jul 13. doi: 10.1136/jmedgenet-2016-103910. **B, I**
(IF 5.650)



Tamm Horsfall Glycoprotein and Uromodulin: It Is All about the Tubules! Bleyer AJ, **Kmoch S**. Clin J Am Soc Nephrol. 2016 Jan7;11(1):6-8. doi: 10.2215/CJN.12201115. **B, I**
(IF 4.657)

Hereditary truncating mutations of DNA repair and other genes in BRCA1/BRCA2/PALB2- negatively tested breast cancer patients. Lhota F, Zemankova P, Kleiblova P, Soukupova J, Vocka M, Stranecky V, Janatova M, Hartmannova H, Hodanova K, **Kmoch S**,
Kleibl Z. Clin Genet. 2016 Oct;90(4):324-33. doi: 10.1111/cge.12748. **B**
(IF 3.892)

CRISPR-Cas9 induced mutations along de novo purine synthesis in HeLa cells result in accumulation of individual enzyme substrates and affect purinosome formation. Baresova V, Krijt M, Skopova V, Souckova O, **Kmoch S**, Zikanova M, Mol Genet Metab. 2016 Nov; 119(3):270-277. doi: 10.1016/j.ymgme.2016.08.004. **B, N, H**
(IF 3.093)

EDUCATION

Postgradual – recent graduates

Doctoral program

Ing. Milan Jakubek, Ph.D.
Tutor - Prof. RNDr. Vladimír Král, DSc.
Disertation thesis “Preparation, studies and application of new multi-binding ligands“
Defended November 2016

MUDr. David Kostrouch, Ph.D.
Tutor - MUDr. Zdeněk Kostrouch, CSc.
Disertation thesis “The role of evolutionarily conserved proteins BIR-1/Survivin and SKP-1 in the regulation of gene expression”
Defended December 2016

Praskash Shankaran, Ph.D.
Tutor - MUDr. Zora Mělková, Ph.D.
Disertation thesis “Effects of heme arginate in HIV-1 acute infection and in latency reversal”
Defended September 2016

Master program

Mgr. Matěj Běhounek
Tutor - RNDr. Kamila Balušíková, Ph.D.
Master thesis “Cell death as a result of iron-induced cellular damage”
defended September 2016

Mgr. Tereza Turková
Tutor - Prof. MUDr. Tomáš Stopka, Ph.D.
Master thesis “Generation of the Mouse Model to Delineate Function of Chromatin Remodeling Gene Smarca5 (Snf2h)”
defended September 2016

Bachelor program

Bc. Hana Pilná
Tutor - MUDr. Zora Mělková, Ph.D.
Bachelor thesis “Experimental and clinically used vaccines based on vaccinia virus” defended June 2016

Participation of pregradual and postgradual students on research conferences

Mgr. Ondřej Vít, Mgr. Eliška Doktorová, Mgr. Matěj Běhounek, Mgr. Martin Chmel:
EMBL Conference „Proteomics in Cell Biology and Disease Mechanism“, Heidelberg, SRN, 14.-17.9.2016.

“Clonal Architecture of MDS Somatic Mutations Dynamically Changes during Azacitidine Therapy and Has Very Limited Potential to Predict Patient Outcome.” **Kamila Polgarova, Vojtech Kulvait**, Karina Vargova, Lubomir Minarik, Nina Dusilkova, Zuzana Zemanova, Anna Jonasova, and Tomas Stopka. 58th ASH meeting, San Diego, CA (poster).

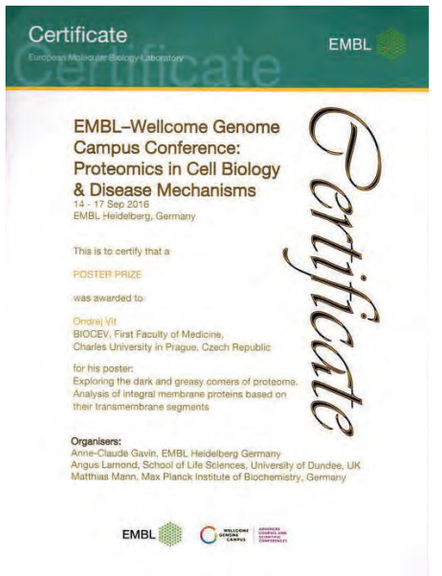
Myristoylated Alanine-Rich C-Kinase Substrate (MARCKS) Is a New Biomarker for Mantle Cell Lymphoma: Expression, Localization, and Phosphorylation Study. Tomas Stopka, **Jarmila Vargova**, Karina Vargova, **Nina Dusilkova, Vojtech Kulvait**, Vit Pospisil, Jiri Zavadil, Marek Trneny, and Pavel Klener. 58th ASH meeting, San Diego, CA (poster).

„Migration of glioblastoma cells in vitro is influenced by stromal fibroblasts from human melanoma“. **Rosana Mateu, M.Sc.** Conference EMBL „Tumor Microenvironment and Signaling“, Heidelberg, SRN, 3.-6.4.2016. (poster)

„Cancer-associated fibroblasts are not formed from cancer cells“. **MUDr. Alžběta Mifková**: Conference EMBL „Tumor Microenvironment and Signaling“, Heidelberg, SRN, 3.- 6.4.2016. (poster)

„Characterization of plasma and cell-associated virus load and its correlation with redox state and heme metabolism in HIV-1-infected patients“. **Ing. Michaela Madleňáková**. 27th Congress of the Czechoslovak Society of Microbiology, Prague, 7.-9. 9. 2016. (poster)

„Quantitative evaluation of siRNA transport using novel carriers“. **Mgr. Liudmila Vasina**, J. Králova, V. Král. The 12th International Congress of Cell Biology (ICCB), Prague, 21.-25.7.2016. (poster)



EMBL Conference: Ondrej Vit was awarded a POSTER PRIZE for his poster “Exploring dark and greasy corners of proteome. Analysis of integral membrane proteins based on their transmembrane segments.”

EVENTS

G3 Talks

November 10th, 2016

This one-day conference was organized by 1st Faculty of Medicine, Charles University and the Institute of Hematology and Blood Transfusion, and it aimed to research devoded to recent discoveries in hematology and molecular biology, presenting two invited lectures:

1. CHROMOTHRIPSIS: POTENTIAL MECHANISMS AND IMPACT IN HUMAN REPRODUCTION
   Assoc. Prof. Franck Pellestor, Arnauld de Villeneuve University Hospital & INSERM, Montpellier, France.
2. IN VIVO GENERATION OF TRANSPLATABLE HUMAN ORGANS FROM HUMAN INDUCED PLURIPOTENT STEM CELLS (hiPSc), Dr. Romain Desprat, Saint Eloi-CHU Hospital & INSERM, Montpellier, France.

G3 Symposium

April 4th, 2016

The G3 symposium was organized by the 1st Faculty of Medicine, Charles University and the Institute of Hematology and Blood Transfusion with the main focus on recent discoveries ina field of resisance in chronic myeloid leukemia and gene expression during normal hemaopoiesis, presenting two invited lectures:

1. Drug resistence in chronic myeloid leukemia. Some old and new insights.
   Prof. Michael Deininger, M.D., Ph.D.
   Division of Hematology and Hematologic Malignancies, University of Utah, Huntsman Cancer Institute, Salt Lake City, USA
2. Variation of gene expression during normal hematopoiesis
   Prof. Eric Bouhassira, Ph.D.
   Department of Cell Biology and Medicine, Albert Einstein College of Medicine, New York, USA


Eric Bouhassira

Michael Deininger

CONTACTS

BIOCEV, 1. LF UK
Průmyslová 595
252 50, Vestec

+420 325 873 031
biocev@lf1.cuni.cz
biocev.lf1.cuni.cz

HEAD
Prof. MUDr. Tomáš Stopka, Ph.D.

DEPUTY
Doc. RNDr. Jiří Petrák, Ph.D.

OFFICE AND ADMINISTRATION
Ivana Nikodymová

OFFICE AND ADMINISTRATION
Ing. Lucie Vyšatová

TECHNICAL ADMINISTRATOR
Martin Ouvín

BIOCEV

CHARLES UNIVERSITY
First Faculty of Medicine