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CONTENTS

Foreword	6
Introduction	8

Natural sciences

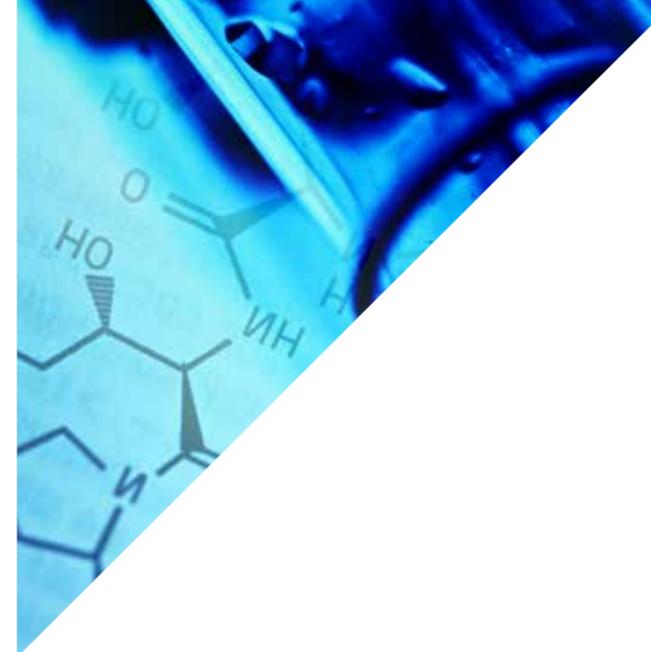
From magnetoactive coordinarion compounds to functional materials / APVV-0014-11	12
Comparative and functional analysis of nuclear telomeres / APVV-0035-11	14
Antitumour effect of biologically active ligands of nuclear retinoid X receptor heterodimers in tissue carcinoma cell lines / APVV-0160-11	16
NANOTIP- Tip-induced SPM processes: Imaging and nanomanipulation / APVV-0207-11	18
Towards increased sensitivity of cancer detection and selectivity of cancer treatment: biophotonic nanotechnology applications / APVV-0242-11	20
Preparation of nanostructured interfaces, their integration with bioelements and subsequent use / APVV-0282-11	22
Kinetics of electron and ion processes for fusion plasma and electric discharges / APVV-0733-11	24
Understanding of Plant Adaptation in the Radioactive Chernobyl Area / APVV-0740-11	26

Technical sciences

Crystal elements of X-ray optics for beam compression and expansion / APVV-0308-11	30
New semiconductor detectors of neutrons / APVV-0321-11	32
Research into new and newly emerging risks of industrial technologies within integrated safety as a precondition for management of sustainable development / APVV-0337-11	34
Monolithic Integration of Depletion-and Enhancement-mode InAlN/GaN HFET Transistors / APVV-0367-11	36
Study of systems and controllers of fractional, variable, and distributed order: methods, algorithms, and tools for modeling, simulation, analysis and synthesis / APVV-0482-11	38
Application of progressive tool coatings for increasing the effectiveness and productivity of forming sheets made of modern materials / APVV-0682-11	40

Medical sciences

Identification of biomarkers associated with treatment resistance in testicular germ cell tumors / APVV-0016-11	44
Effects of Hypoxia on Molecular Pathways related to Increased Cardiovascular Risk in Patients with Sleep Apnea and their Reversal by Therapy / APVV-0134-11	46
Possibilities of the stent restenosis and thrombosis prediction in patients with acute coronary syndrome undergoing percutaneous coronary intervention / APVV-0222-11	48
Proton radiation-induced cardiovascular toxicity (pathphysiology and prevention) / APVV-0241-11	50
Inactivation of endogenous surfactant: molecular, tissue and functional aspects of injury to the respiratory system / APVV-0435-11	52
Modified biomaterials and cell therapy for promoting regeneration of injured spinal cord / APVV-0472-11	54
Carbonic anhydrase IX as a functional component of cancer progression: the role in epithelial-mesenchymal transition and intercellular signaling / APVV-0658-11	56



Agricultural sciences

Integrated system of evaluation of the agricultural soils quality and potential of the simplified ways of their cultivation / APVV-0131-11	60
The possibility of beech stand tending rationalization based on evaluation of long-term thinning research / APVV-0262-11	62
Application of biotechnological methods for conservation of animal genetic resources / APVV-0556-11	64
Species boundary delimitation in fish parasites: morphology versus genes and chromosomes / APVV-0653-11	66
Biotechnological preparation of new types of functional cereals and cereal products enriched with polyunsaturated fatty acids and pigments / APVV-0662-11	68
Biological active and valuable components of cereals, pseudocereals and forages for functional foods production / APVV-0758-11	70

Social sciences

Social determinants of health in school-aged children / APVV-0032-11	74
Social, emotional and cognitive mirror image of autism from interdisciplinary perspective / APVV 0254-11	76
Optimization of the Processes of Development and Evaluation of Digital Educational Programmes and Electronic Learning Tools / APVV-0266-11	78
Regionalism and its contribution to universal public international law / APVV-0823-11	80
Global Commodity Prices, Price Transmission, and Food Security / APVV-0894-11	82

Humanities

Slovakia in the 19th century / APVV-0119-11	86
Patočka's Asubjective Phenomenology and History of Philosophy / APVV-0480-11	88
State borders and identities in modern Slovak history in Central European context / APVV-0628-11	90
Contribution of Slovakia for Economic and Social Development of European Metal Age / APVV-0736-11	92



FOREWORD

Dear friends,

We would like to invite you to read the second edition of publications Research projects with excellent level in which the Slovak Research and Development Agency (SRDA) presents the solutions of projects for all those who are interested to learn more about the support of research in Slovakia.

In this publication you may find out about the implementation and results of several years of work of Slovak experts in the projects in the period 2012-2016 in basic and applied research in natural, technical, medical, agricultural, social sciences and humanities. Of course, the publication in its content may hardly compete and be compared with the electronic resources of the newest information, which is much faster and more up to date. However, it has several advantages as it has allowed us to summarize and the balance, what the whole research teams participating organizations and the scientific community in Slovakia were dealing with.

Slovak Research and Development Agency for its 11 years of existence has become an important part of the national system of support for basic and applied research and development in Slovakia. On the territory of research and development it is may prove very difficult to find someone who would not know the name of our agency, which makes us very pleased.

Finally, allow us to thank for all the work and effort of researchers of the projects presented in the publication, as well as all those who contributed to the preparation of the second edition of the publication Research projects with excellent level 2017.

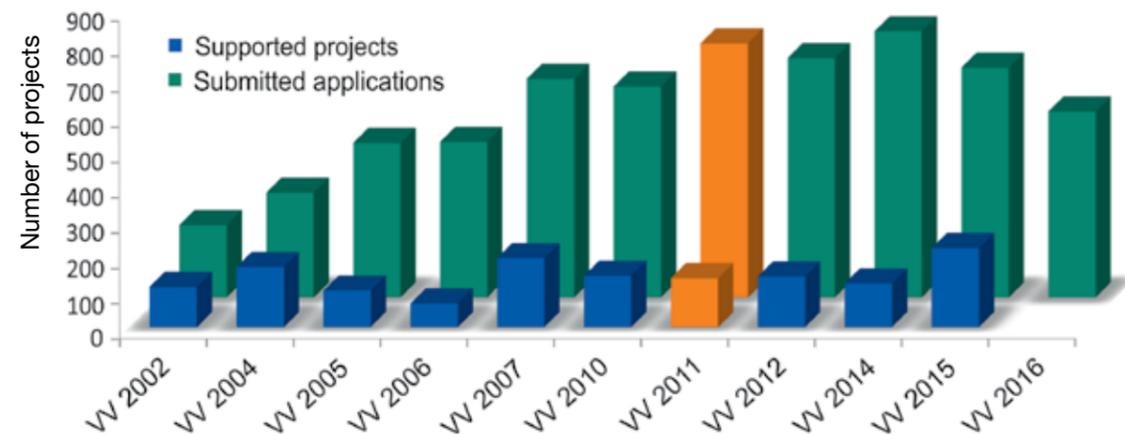


Ing. Martina Hasayová, PhD.
Director



prof. RNDr. Jozef Masarik, DrSc.
Chairperson

INTRODUCTION



SUMMARY OF APPLICATIONS SUBMITTED AND SUPPORTED PROJECTS IN THE GENERAL CALLS IN THE YEARS 2002-2016

The projects presented in this publication have been submitted within the general call to the Slovak Research and Development Agency in 2011 marked GC2011.

General Call GC 2011 had no limitations on the substantive focus of the projects. Specific focus, objectives and contents of the research and development were determined by the applicants themselves. Applications could be submitted by legal entities as well as natural persons – entrepreneurs without limitation as per sector of research and development.

864 applications for funding were received and registered as part of the public call PC 2011, in order to resolve research and development projects and 166 applications were supported. Start of the project solution was 1. July 2012. Latest date of completion of project solutions was 31. December 2015.

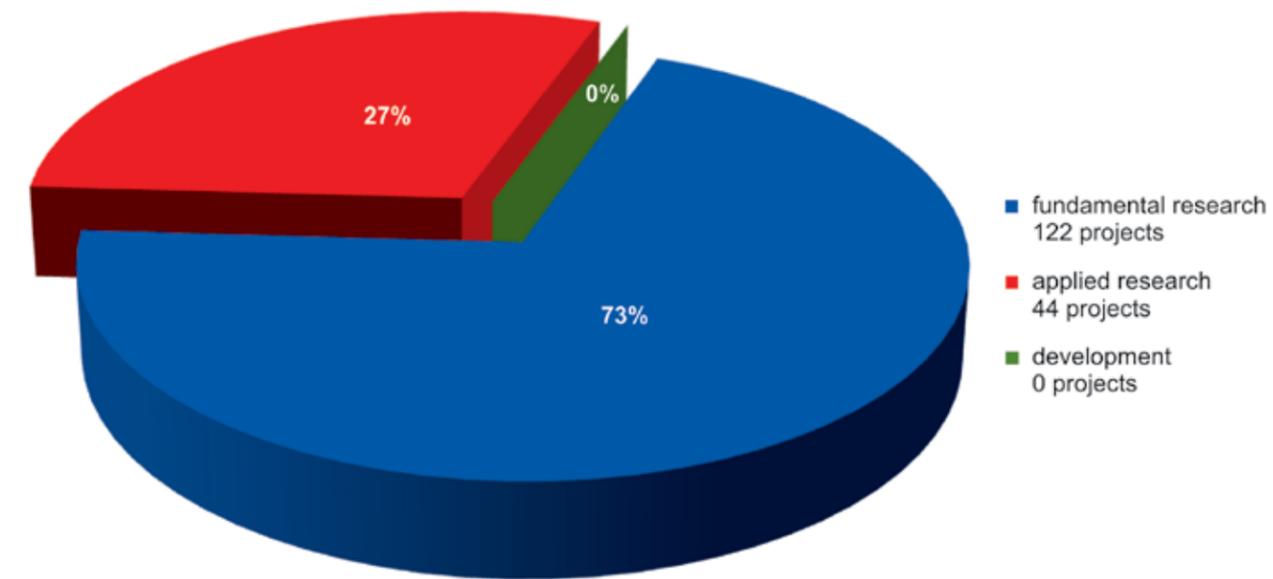
In 2016 subsequently completed projects were evaluated by different scientific councils on the basis of the final reports on projects submitted by the principal investigator within 30 days of the end of solution.

Success rate of applications supported by GC2011 as per scientific departments.

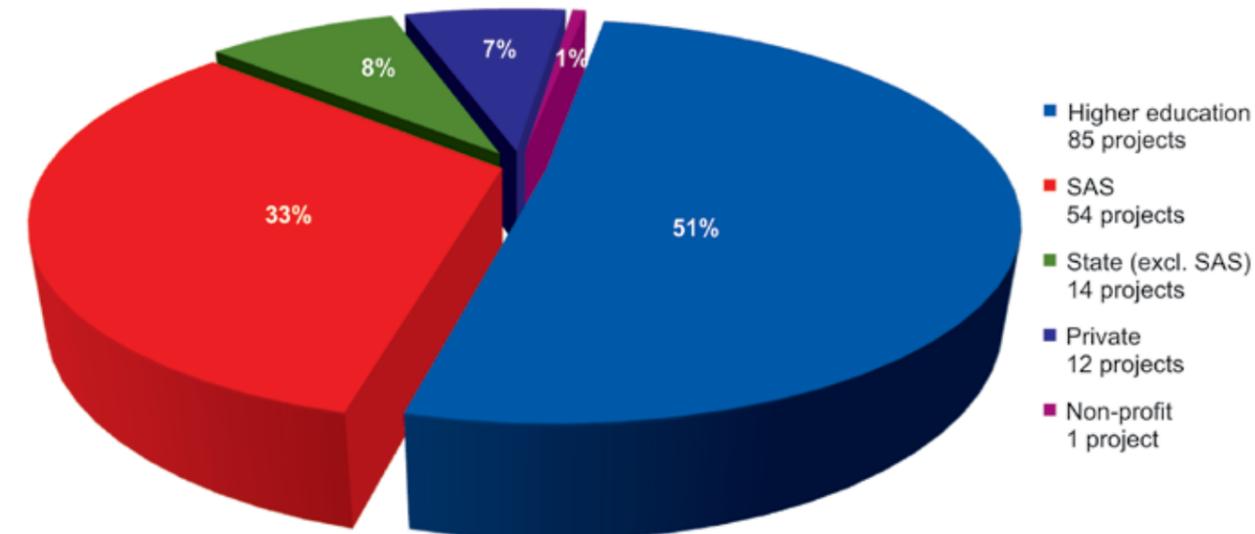
Department of Science and Technology	Registered applications	Financed projects	Success Rate (%)
Natural sciences	201	49	24,4
Technical sciences	296	50	16,9
Medical sciences	93	21	22,6
Agricultural sciences	119	19	16,0
Social sciences	111	20	18,0
Humanities	44	7	15,9
Total	864	166	19,2

In this publication the Slovak Research and Development Agency presents the selection of the most successful completed and subsequently evaluated projects from the general call GC 2011 in all sectors of Slovak science and technology.

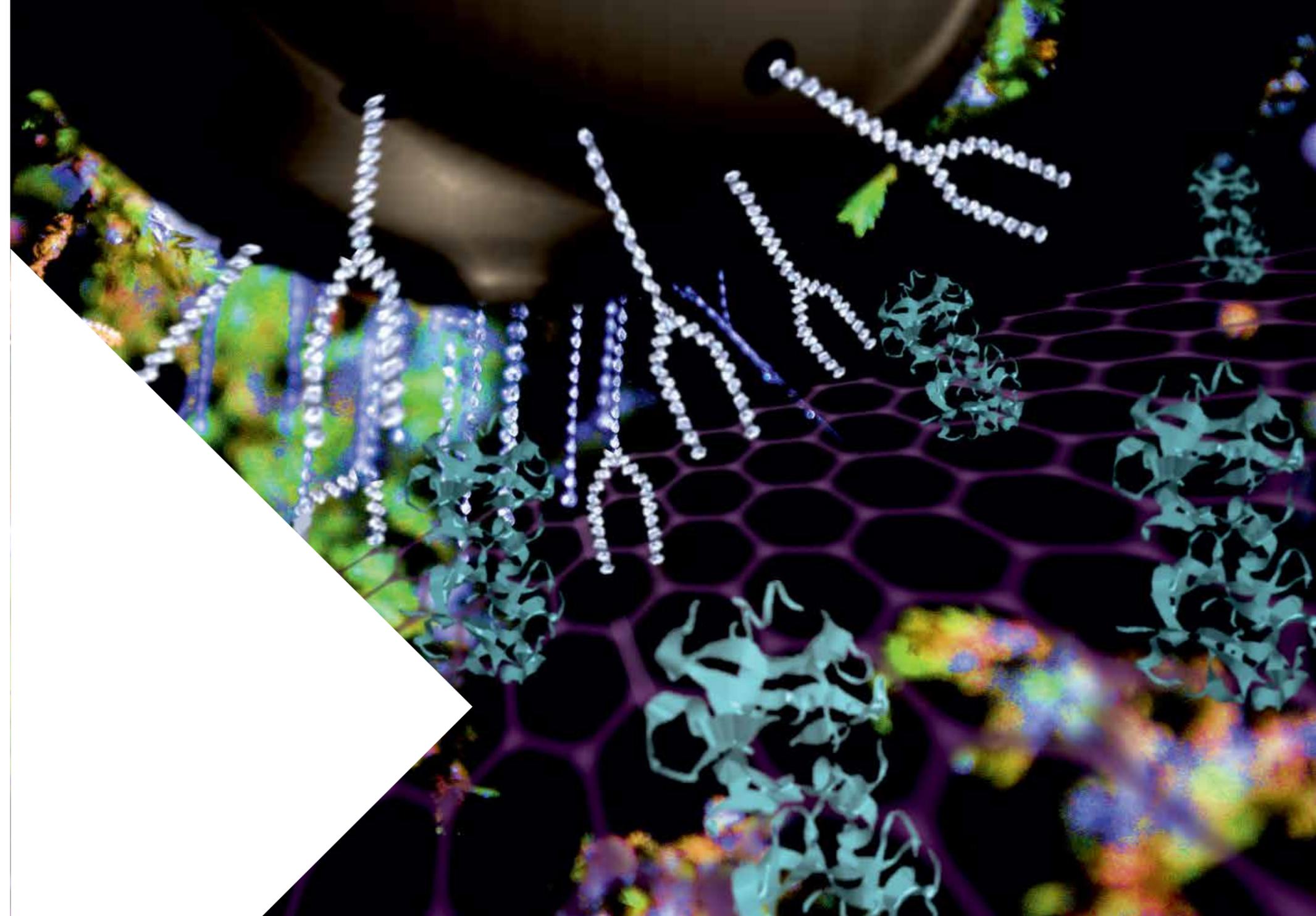
PERCENTAGE RATE OF PROJECTS SUPPORTED AS PER THE NATURE OF THE RESEARCH

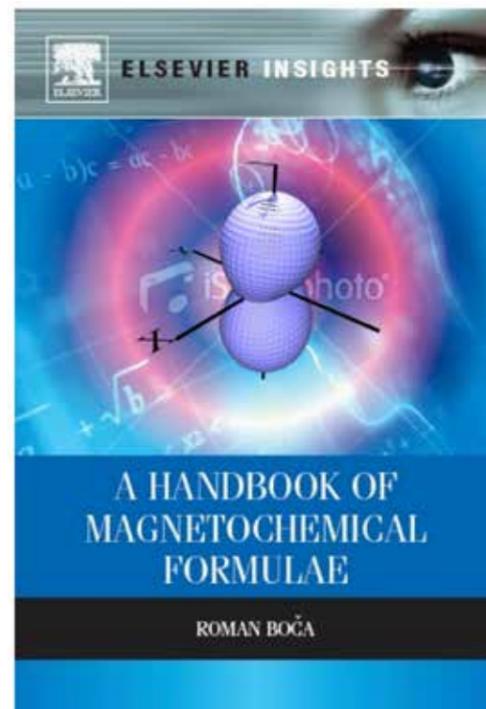


BREAKDOWN OF FUNDED PROJECTS AS PER SECTOR

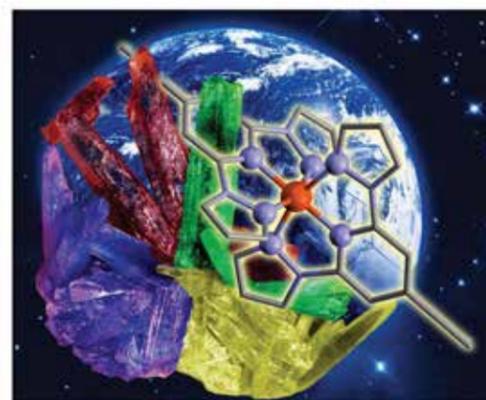


▼
NATURAL
SCIENCES





Monograph.



FROM MAGNETOACTIVE COORDINATION COMPOUNDS TO FUNCTIONAL MATERIALS

Principal investigator:
Applicant organisation:

prof. Ing. Roman Boča, DrSc.
Faculty of Chemical and Food Technology,
Slovak University of Technology in Bratislava
Participating organisations:
Faculty of Natural Sciences, University of SS Cyril and Methodius in Trnava
Faculty of Natural Sciences, Pavol Jozef Šafárik University in Košice
Term of solution:
Budget from agency:
Project ID:

Subject of research

The project studies new physical phenomena associated with the nanomagnetism of new chemical objects. Project activities involved the chemical synthesis of polynuclear transition metal complexes showing molecule-based magnetism, single-molecule magnetism and spin transitions, new modified organic ferromagnets, and systems with reduced dimensions. The methodology follows a chain: synthesis – analysis – structure – magnetoactivity – thermoactivity – modification – theoretical analysis – understanding of phenomena – optimization – application. The research was performed by using elemental and X-ray structure analysis, IR, UV/VIS, ESR, NMR and MS spectroscopies, magnetometry, susceptometry, conductometry, calorimetry, photomagnetism, theoretical approaches, and quantum-chemical calculations. The studies were conducted in a temperature range of 2 – 400 K and also in sub-kelvin and above-room region if necessary. By combining synthetic, analytical and detection techniques, know-how is achieved for the development of new magnetic materials with high added value that are applicable in display and storage techniques, in photonics and spintronics. The development of theory facilitates the description as well as the understanding of the properties of the materials from the point of view of functionality leading to the proposed optimization for possible technical applications.

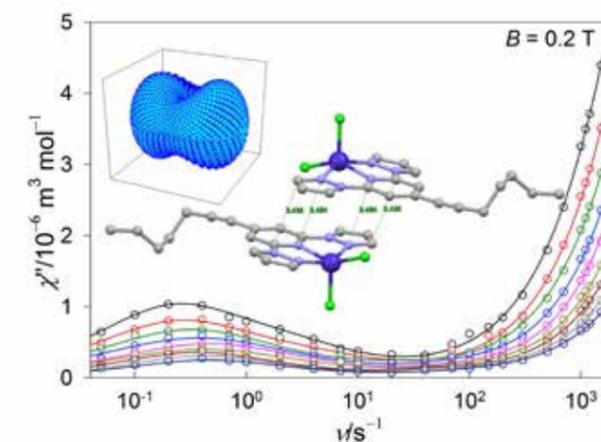
Aim of the project

The aim of the project was to conduct basic research of nanomagnetism that involves the synthesis and characterization of nanoobjects showing magnetoactivity. The studied objects are polynuclear complexes of transition metals (Mn, Fe, Co, Ni), systems of reduced dimension, magnetic chains and supramolecular aggregates involving modified organic magnets that show molecular magnetism, enhanced magnetic anisotropy, spin crossover and magnetocaloric effects.

Benefits for practice

-The project dealt with basic research in the synthesis, analysis, characterization and applications of coordination compounds as new materials, mainly single molecule magnets. Its results can be applied to the development of nano-electronic and spintronic devices, as elements of memory and display units.

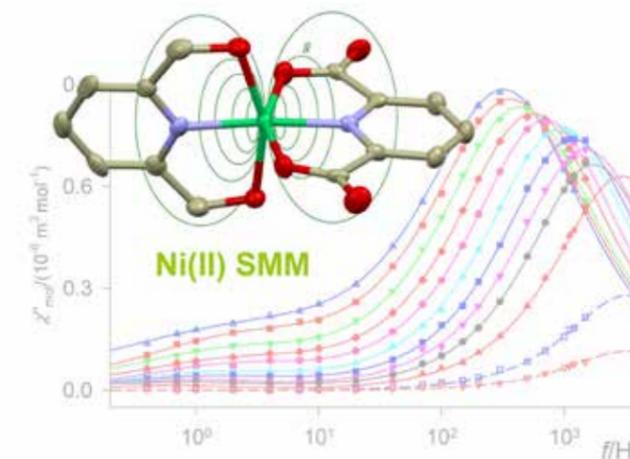
- 12 PhD theses were defended during the project period.
- 84 research papers were published in international journals.



Slow magnetic relaxation in the first mononuclear complex of Ni(II).

Most important publications

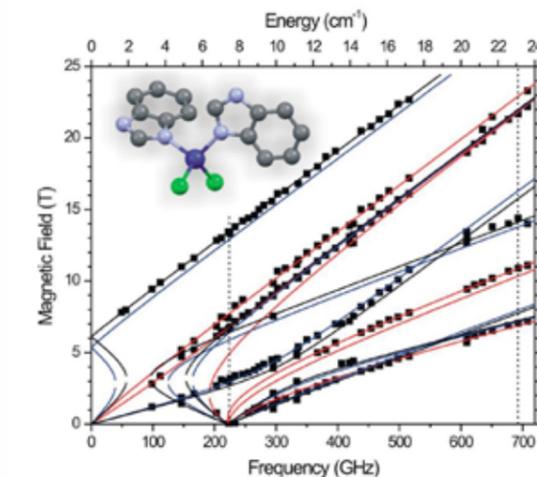
- R. Boča: *A Handbook of Magnetochemical Formulae*. Elsevier, Amsterdam, 2012, 1010 pp. Monograph
- M. Idešicová, J. Titiš, J. Krzystek, R. Boča: *Inorganic Chemistry* 52 (2013) 9409–9417. Zero-Field Splitting in Tetracoordinate Co(II) Complexes: a Structural, Magnetic, High-Frequency and -Field EPR, and Theoretical Study.
- C. Rajnák, J. Titiš, R. Boča, O. Fuhr, M. Ruben: *Inorganic Chemistry* 53 (2014) 8200–8202. Single-molecule magnetism in a mononuclear pentacoordinate Co(II) complex supported by an antenna ligand.
- R. Boča, J. Mikovič, J. Titiš: *Inorganic Chemistry* 53 (2014) 2367–2369. Simple Mononuclear Cobalt(II) Complex: A Single-Molecule Magnet Showing Two Slow Relaxation Processes.
- J. Miklovič, D. Valigura, R. Boča, J. Titiš: *Dalton Transaction* 44 (2015) 12484–12487. Mononuclear Ni(II) Complex: A Field Induced Single-Molecule Magnet Showing Two Slow Relaxation Processes.



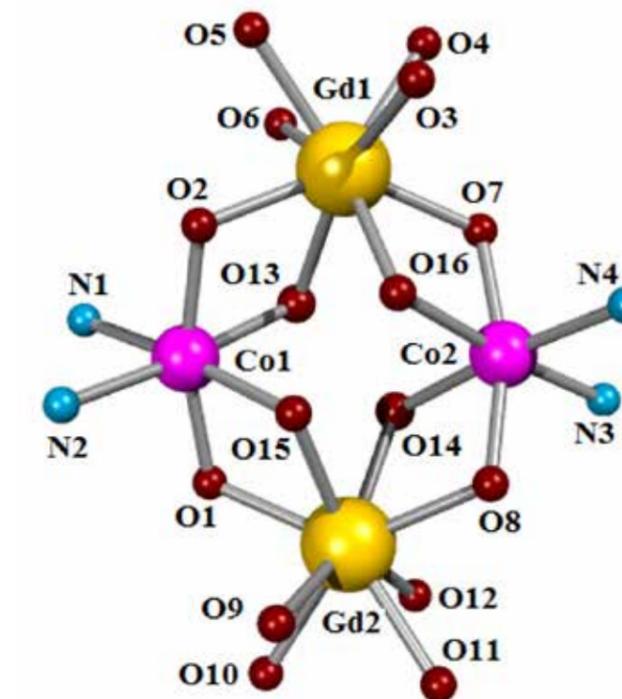
Slow magnetic relaxation in a pentacoordinate Co(II) complex.

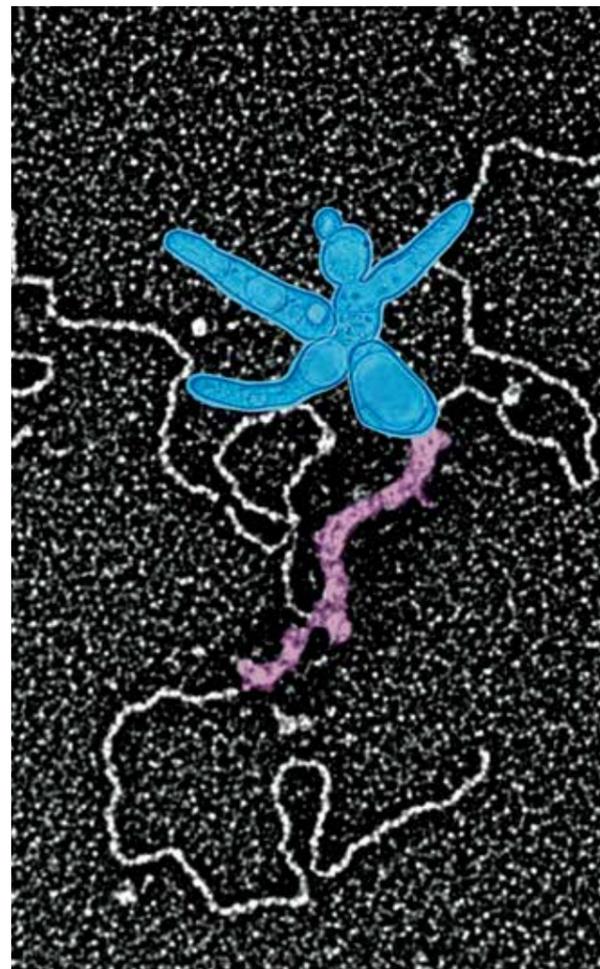
Results

A series of new coordination compounds based upon the central atoms Mn(II), Mn(III), Fe(II), Fe(III), Co(II), Ni(II), Cu(II) and Dy(III) were synthesized. These objects were characterized by their composition, crystal and molecular structure, and molecular spectra. In addition, the magnetic functions taken in DC and AC mode were interpreted. A number of Fe(II) and Fe(III) compounds show a thermally induced spin crossover with various critical temperatures; photomagnetic phenomena (LIESST, LITH) were also studied. Some compounds of Co(II), Ni(II) and Dy(III) behave as single molecule magnets (SMM) with single, two, or three slow relaxation processes. This behaviour is supported by substantial magnetic anisotropy that was studied in detail for mononuclear Co(II) and Ni(II) complexes resulting in the formulation of magnetostructural D-correlations. Classical magnetostructural J-correlations were also investigated.



High-frequency/high-field electron magnetic resonance.





Tay1 protein bound to telomeres of the yeast *Yarrowia lipolytica*. Tay1 (pronounced as Taiwan) is a TBP, whose biochemical properties were compared with its mammalian counterparts TRF1 and TRF2 (Višacká *et al.* (2012) *The Journal of Biological Chemistry* 287: 32206-32215). Three linear DNA molecules are shown carrying telomeric repeats of *Y. lipolytica* (a group of blue cells) that are joined by Tay1 (an array of pink particles).

COMPARATIVE AND FUNCTIONAL ANALYSIS OF NUCLEAR TELOMERES

Principal investigator: prof. RNDr. Lubomír Tomáška, DrSc.
 Applicant organisation: Comenius University in Bratislava, Faculty of Natural Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 133 800 EUR
 Project ID: APVV-0035-11

Subject of research

Telomeres are nucleo-protein structures at the ends of linear DNA molecules whose main function is to mediate their replication and prevent their degradation. Defects in telomere functions often result in genomic instability accompanying various pathological cellular states including tumorigenesis. We have performed comparative and functional analyses of telomeres in yeasts in order to identify evolutionary trajectories leading to a diversity of molecular strategies employed in telomere maintenance.

Aim of the project

The main aim of our project was to employ conventional and nonconventional yeast species and to identify novel mechanisms involved in telomere maintenance. We searched for universal as well as species-specific mechanisms of stabilization of the ends of linear DNA molecules by comparing the biochemical properties of telomere components in yeasts with their mammalian counterparts. In addition to telomeres, we investigated DNA-protein interactions in the mitochondria of several yeast species and sought to identify their function in communication between the nucleus and mitochondria of eukaryotic cells.

Results

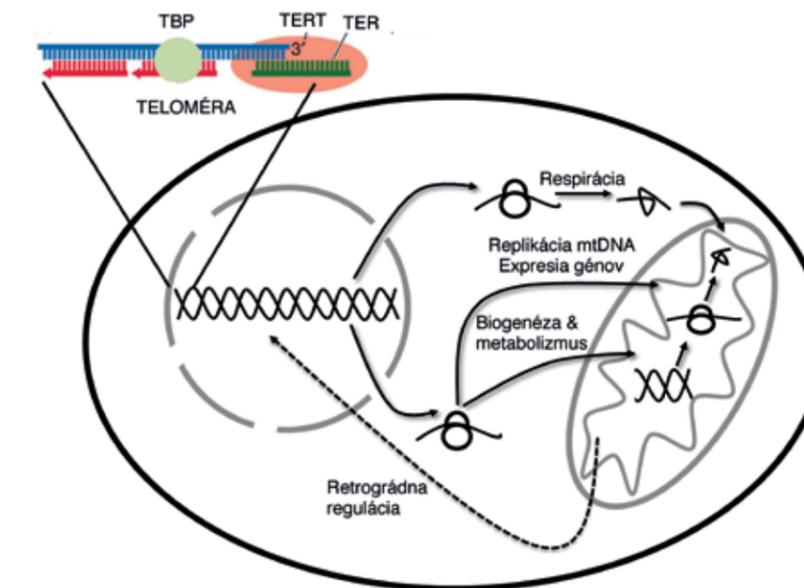
The comparative analysis of biochemical properties of yeast and mammalian telomere-binding proteins (TBP) demonstrated that their evolution was not accompa-

nied by a maximization of their affinities to telomeric sequences, but an optimization of their DNA-binding characteristics enabling the flexibility needed for the dynamic character of telomeres. A key enzyme for the replication of terminal structures of DNA is telomerase, which was recently shown to also function outside telomeres. Our research involved the preparation of a unique experimental system for studying the mitochondrial functions of the catalytic sub-unit of mammalian telomerase (mTERT) *in vivo* in cells of *Saccharomyces cerevisiae*. We demonstrated that the heterologous expression of mTERT protects yeast cells against oxidative stress. We also identified novel genomic sequences specifying telomerase RNA (TER) in several species of the genus *Yarrowia* and identified new conserved secondary structures. We also studied the consequences of the deletion of a gene encoding mitochondrial HMG box (mHMG) protein in a strictly aerobic yeast species *Yarrowia lipolytica* and found that the mutant cells exhibit a dramatically decreased number of copies of mitochondrial DNA (mtDNA). We discovered that this defect is compensated for on a (post) translational level and thus the cells are able to avoid the proteotoxic stress caused by an imbalance between protein sub-units of the respiratory chain encoded by nuclear and mtDNA respectively. Based on our analysis of the biochemical properties of yeast mHMG proteins, we revised the model of compaction of mtDNA into mitochondrial nucleoids. Our model is based on the preferential binding of mHMG proteins to recombination structures occurring during replica-

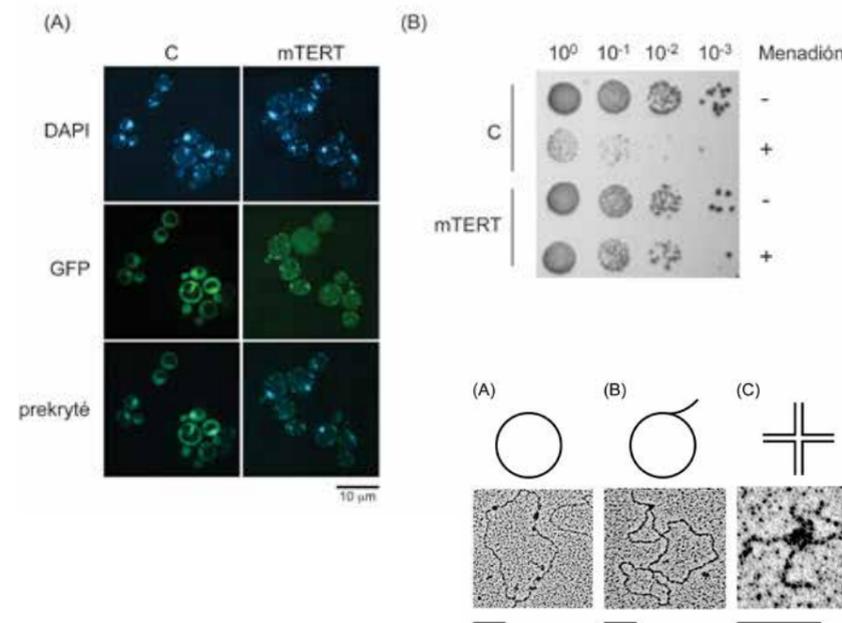
tion and/or recombination. Our results were published in 13 peer-reviewed papers. During the project, 5 PhD. and 13 MSc. students successfully defended their theses. In addition, we carried out experiments in collaboration with leading foreign laboratories providing unique technology for the investigation of DNA-protein interactions (Jack D. Griffith, University of North Carolina, Chapel Hill, USA; Ctirad Hofr, Masaryk University, Brno, Czech Republic; Isamu Miyakawa, Yamaguchi University, Japan).

Benefits for practice

Our results have potential biomedical implications. For example, (1) the identification of conserved regions in telomerase RNA can lead to a better understanding of telomerase biogenesis and properties; (2) the heterologous system for the study of mitochondrial functions of mammalian catalytic subunit of telomerase in *Saccharomyces cerevisiae* represents a unique „living test-tube“, enabling studies of extratelomeric functions of telomerase; (3) the characterization of biochemical properties of TBPs from yeasts and their comparison with their mammalian counterparts is important for understanding universal and species-specific features of telomeres; and (4) yeast mutants lacking functional mHMG protein enable the investigation of molecular mechanisms involved in the regulation of the balance of protein subunits of the respiratory chain that may be defective in some pathological states of mammalian cells.



Nucleus and mitochondria of the eukaryotic cell are two interconnected genetic systems. Nuclear DNA is represented by a population of linear DNA molecules (only one is depicted) containing special nucleo-protein structures (telomeres) at its ends. Telomeres are replicated by an enzyme telomerase composed of a protein catalytic subunit (TERT) and an RNA molecule (TER) serving as a template. The chromosomal ends are stabilized by DNA-binding proteins (telomere-binding proteins, TBP; green oval). Mitochondria DNA (mtDNA) is represented by a population of molecules compacted into a nucleo-protein structure called mitochondrial nucleoid (not shown). Arrows indicate some of the communication pathways between the organelles.



The catalytic sub-unit of mammalian telomerase (mTERT) is localized in *S. cerevisiae* mitochondria and protects the cells against oxidative stress. (A) mTERT in a fusion with green fluorescent protein (GFP) co-localizes with mitochondria in cells stained with a DNA-binding fluorescent dye DAPI. (B) Compared with the control (“C”), the cells of *S. cerevisiae* producing mTERT are more resistant to oxidative stress induced by menadione (Šimoničová *et al.* (2015) *Current Genetics* 61: 517-527).

Mitochondrial HMG-box proteins exhibit an affinity to recombination structures. The biochemical and electron-microscopic analysis of yeast mHMG proteins showed that compared to an intact double-stranded DNA (A) they exhibit a preference for recombination structures such as replication forks (B) and Holliday junctions (C) (Bakkaiová *et al.* (2016) *Bioscience Reports* 36: e00288). The bars under the electron micrographs correspond to 50 nm.

ANTITUMOUR EFFECT OF BIOLOGICALLY ACTIVE LIGANDS OF NUCLEAR RETINOID X RECEPTOR HETERODIMERS IN TISSUE CARCINOMA CELL LINE

Principal investigator: Ing. Július Brtko, DrSc.
 Applicant organisation: Institute of Experimental Endocrinology, Slovak Academy of Sciences
 Participating organizations: Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences
 Cancer Research Institute, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 198 528 EUR
 Project ID: APVV-0160-11

Subject of research

Nuclear retinoic acid receptors are transcription factors inducible by retinoic acid or synthetic retinoids that play an irreplaceable role in the human organism. Their presence in the organism together with their cognate biologically active ligands is essential for many important functions, e.g., in cell growth and cell differentiation they play an important role in embryonic development, reproduction and apoptosis. They take part in bone and blood cells development and are essential for the normal functioning of the immune system. Dysfunction of nuclear receptor signalling leads to cell proliferation defects and reproductive and metabolic diseases such as cancer, infertility, obesity and diabetes.

Aim of the project

The objective of the project was to investigate the molecular and functional aspects of the heterodimers of nuclear retinoid/retinoid X receptors in tumour cell lines in order to study the synergic effects of triorganotin compounds on the activation of retinoid receptors in the presence of their cognate ligands, as well as to find the effect of various retinoid X receptor ligands on tumour cell proliferation, apoptosis, differentiation, migration and modification of P-gp mediated multidrug resistance of tumour cells.

Results

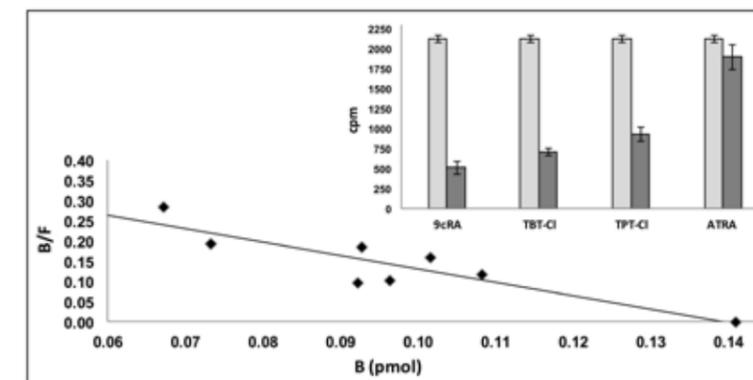
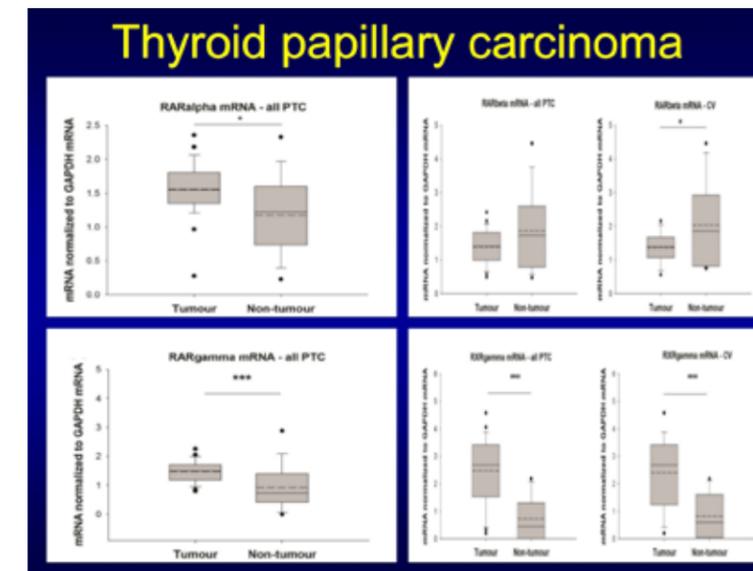
Novel diagnostic method (“radioligand binding assay”) for the quantitative determination of nuclear retinoid X receptors in tissues with possible application in clinical oncology, which enables the prediction of the applicability of the treatment of thyroid cancer, breast cancer or kidney cancer patients with retinoid X receptor ligands. A wide range of analyses belonging to molecular endocrinology and oncology on the expression of all nuclear retinoid or retinoid receptors subtypes as well as selected nuclear receptors linked with considerable genes in thyroid cancer, breast cancer and kidney cancer tissues was performed. Novel and original data on the expression of particular subtypes of retinoid and retinoid X receptors in tissues of thyroid papillary carcinoma, breast and kidney cancer in groups of patients of various ages and both genders was acquired. We performed *in vitro* experiments with biologically active compounds - ligands of transcription factors inducible by retinoids or retinoids with the aim to find and confirm their role in human breast cancer tumour cells proliferation, apoptosis and migration. Novel and original data on the biological properties of triorganotin compounds acting through nuclear retinoid X receptors on breast cancer cell proliferation, apoptosis and migration were acquired. Findings on

whether selected triorganotin compounds are capable of modifying P-gp mediated multidrug resistance at transport and expression levels was obtained. We demonstrated that retinoic acid isomers (1 µmol/l) cause significant changes in several specific biomarkers of breast cancer appearance as well as the appearance of other proteins that might play a role as novel specific biomarkers of breast cancer.

Benefits for practice

Novel biological properties and effects of biologically active nuclear retinoid and retinoid X ligands that might function as selective agonists of corresponding nuclear receptors with their possible exploitation in clinical oncology were identified.

Expression of nuclear retinoid receptor subtypes and retinoid X receptor subtype (RXR gamma) in human thyroid papillary carcinoma.

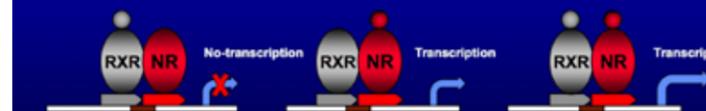


Scatchard analysis representing interaction of 9-cis retinoic acid (9cRA) with nuclear retinoid X receptors (RXR). Tributyltin chloride and triphenyltin chloride compete for 9-cRA binding sites at RXR molecule.

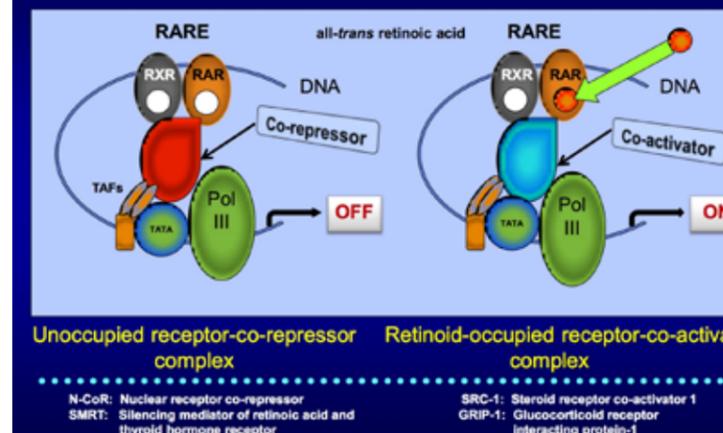
Conditional heterodimers

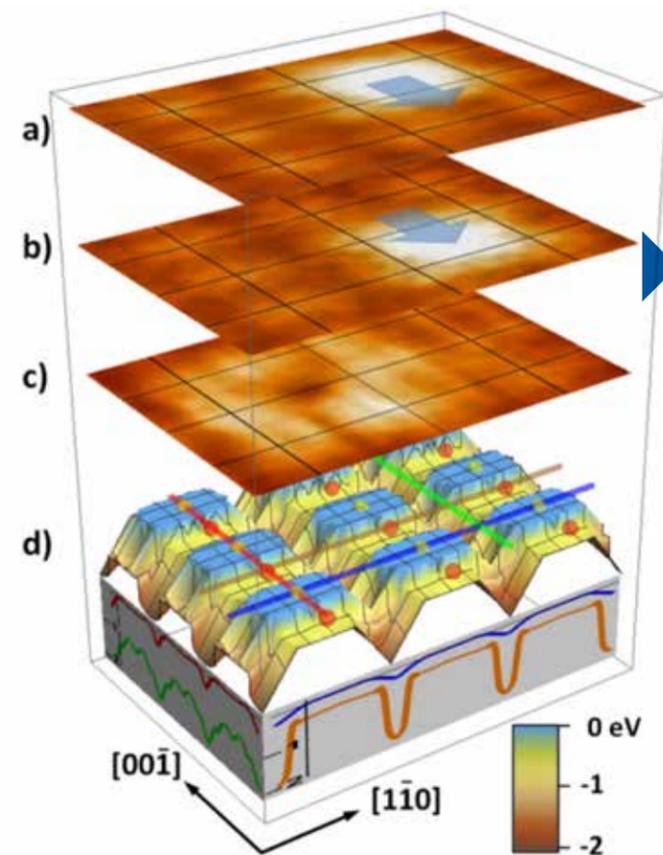
RXR/RAR, RXR/TR

They are unresponsive to retinoids, but these (RXR) agonists superactivate transcription by synergizing with partner agonists



Interaction between the Nuclear Retinoid Receptor and Components of the Transcription Machinery





Experimental images (a–c) of the atom lateral, from a to b, and delocalization (c), manipulations placed on top of the DFT calculated adiabatic PES of the Co atom in the [Ar]d8 state on the $p(2\times 1)\text{Cu}(110):\text{O}$ surface. The circular character of the image of the Co atom in the delocalized state is clearly seen in c.

NANOTIP – TIP INDUCED SPM PROCESSES: IMAGING AND NANOMANIPULATION

Principal investigator: prof. Ing. Ivan Štich, DrSc.
 Applicant organisation: Institute of Physics, Slovak Academy of Sciences
 Participating organisation: Faculty of electrotechnics and informatics, Slovak University of Technology (only the first year)
 Term of solution: July 2012 – December 2015
 Budget from agency: 197 524 EUR
 Project ID: APVV-0207-11

Subject of research

The NANOTIP project focused on computer modelling of imaging and nanomanipulation using SPM techniques, i.e., primarily on noncontact atomic force microscopy (NCAFM) and scanning tunnelling microscopy (STM). A smaller part of the project also targeted nanotribology.

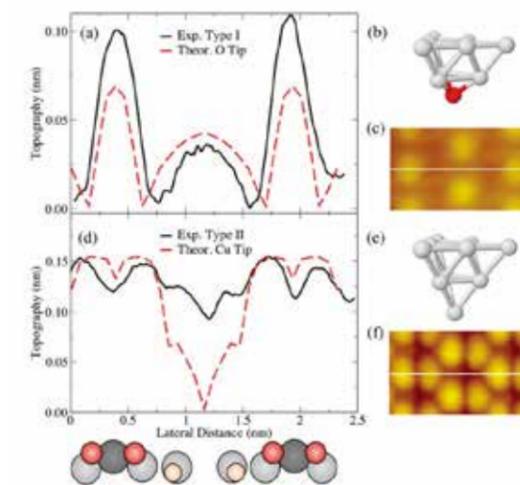
Results

The most impressive results were achieved in NCAFM at low temperatures in UHV conditions. This part of the project was conducted in collaboration with the experimental group of Prof. Sugawara at the Institute of Applied Physics, Osaka University, Japan. Our contribution primarily involved the simulation of NCAFM experiments using density functional theory (DFT) techniques. The best results were achieved in imaging and nanomanipulation on oxidized copper surfaces $\text{Cu}(110)$ ($p(2\times 1)\text{Cu}(110):\text{O}$ and $c(6\times 2)\text{Cu}(110):\text{O}$). In particular, we demonstrated that the $c(6\times 2)\text{Cu}(110):\text{O}$ surface can effectively be used for chemical tip fingerprinting. In other words, in every moment during imaging/manipulation we know the chemical tip termination and if not satisfied, the desired termination can be enforced using a protocol that we developed. This is of paramount importance for both imaging and atomic-scale manipulation.

Using NCAFM microscope we also performed and provided an atomic-scale understanding of two nanomanipulations on the $p(2\times 1)\text{Cu}(110):\text{O}$ surface: 1) vertical manipulation of Cu (ad)atoms and, 2) lateral manipula-

tion of magnetic Co atoms. In 1) we not only demonstrated the ability to manipulate, in a controlled way, the Cu adatoms and “write” with them on the surface; we also demonstrated the ability of their atomic-scale understanding. We developed a 4-state model which, using a combination of DFT methods for the calculation of the barriers separating these states and the modified kinetic Monte Carlo method, enabled us to calculate the total probabilities of Cu atom extraction/deposition. The calculated probabilities were found in very high agreement with the experiments. This combination of methods made it possible for the first time to explicitly include the very slow tip motion ($\approx \text{kHz}$ oscillations) in the model. The method we developed is entirely general and can be used for other manipulation simulations as well. Perhaps most surprising was the finding that both the deposition/extraction of Cu atoms leaves the apex unchanged, i.e., the manipulated atom must diffuse along the conical tip body.

In 2) we studied the *delocalization manipulation* of Co atoms leaving the Co atom in a magnetically modified state delocalized over several surface unit cells over a macroscopic time of the order of dozens of minutes. We demonstrated that the existence of the delocalized state is a result of two factors: a) an extremely flat potential energy surface due to the local spin change of the manipulated Co atom by the oscillating tip and b) the localizing potential generated by Friedel oscillations of the charge density of the substrate screening the other Co atoms. In other words, the manipulation is a 2-stage manipulation, where first a Co nanostructure is formed by a series of lateral manipulations generating long-range Friedel oscillations which, in turn, en-



force the delocalization pattern on the manipulated Co atom. The ability of the mechanical control of spin may have importance in spintronics. The following high-impact publications are deemed the main results of this research:

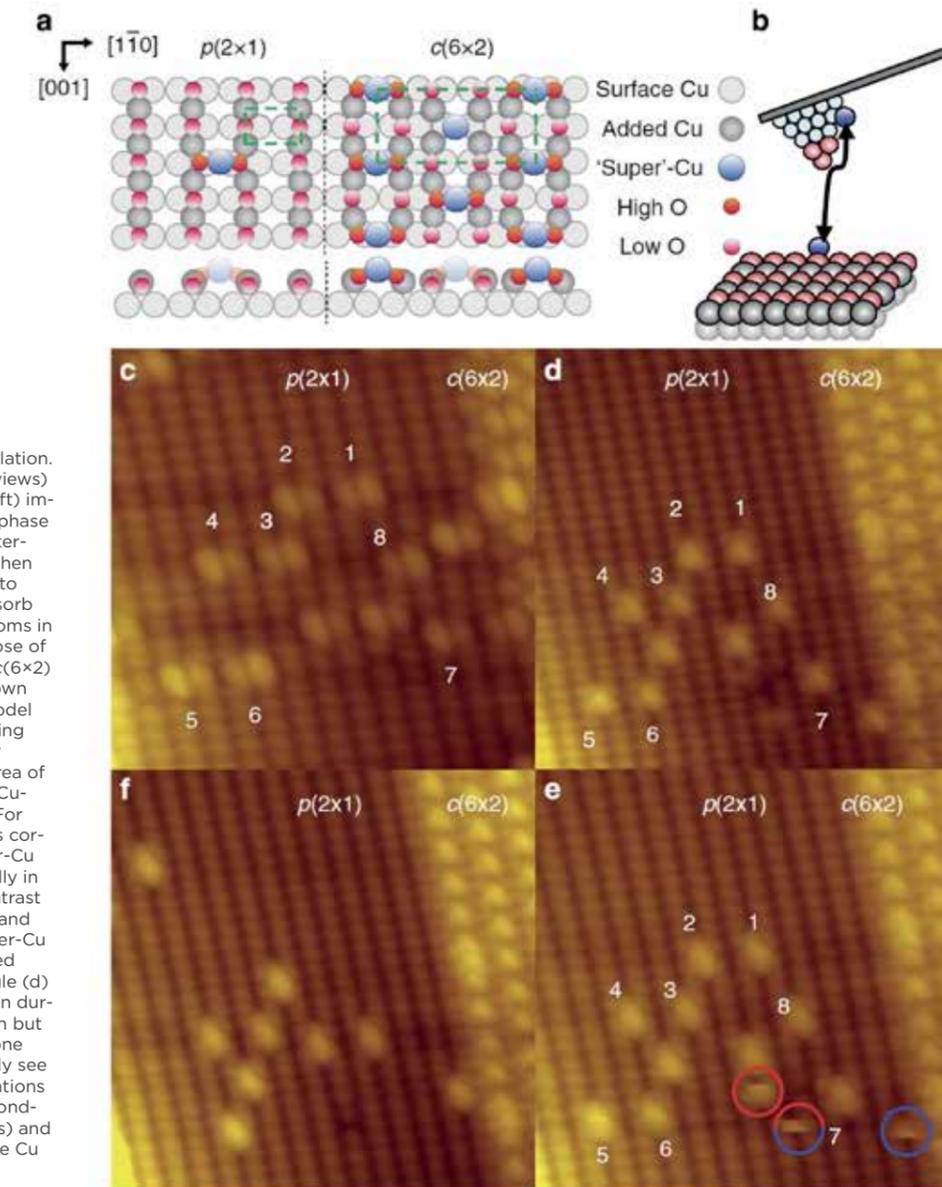
BAMIDELE, J. – KINOSHITA, Y. – TURANSKÝ, R. – LEE, S. H. – NAITOH, Y. – LI, Y. J. – SUGAWARA, Y. – ŠTICH, I. – KANTOROVICH, L.: Chemical tip fingerprinting in scanning probe microscopy of an oxidized Cu(110) surface. In: *Phys. Rev. B* 86, 155422 (2012), (IF 2012: 3.7)

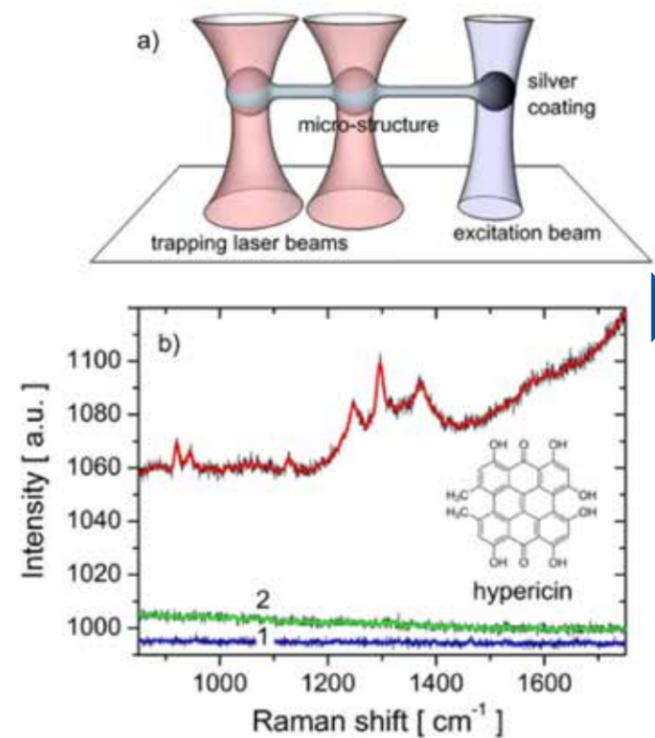
BAMIDELE, J. – LEE, S. H. – KINOSHITA, Y. – TURANSKÝ, R. – NAITOH, Y. – LI, Y. J. – SUGAWARA, Y. – ŠTICH, I. – KANTOROVICH, L.: Vertical atomic manipulation with dynamic atomic-force microscopy without tip Change via a multi-step mechanism. In: *Nature Commun.* 5, 4476 (2014), (IF 2014: 11.5)

Kinoshita, Y. – Turanský, R. – Brndiar, J. – Naitoh, Y. – Li, Y. J. – Kantorovich, L. – Sugawara, Y. – Štich, I.: Promoting atoms into delocalized long-living magnetically modified state using Atomic Force Microscopy. In: *Nano Letters* (2016), doi: 10.1021/acs.nanolett.6b03203, (IF 2016: 13.8).

Experimental (black solid curves) and theoretical (red dashed curves) scan lines of the $\text{Cu}(110)$ $c(6\times 2)$ surface. (a) Scan lines with experimental “type I” tip and the theoretical O terminated tip; (b) the corresponding tip model and (c) the experimental topography image. (d) Scan lines with experimental “type II” tip and the theoretical Cu terminated tip; (e) the corresponding tip model and (f) the experimental topography image.

NC-AFM imaging and manipulation. (a) Ball model (top and side views) of the $p(2\times 1)$ phase (on the left) immediately next to the $c(6\times 2)$ phase (on the right). Note that at intermediate oxygen exposures, when both phases are formed next to each other, Cu atoms also adsorb on the $p(2\times 1)$ surface as adatoms in geometries very similar to those of the “super”-Cu atoms of the $c(6\times 2)$ surface (one such atom is shown on the left). (b) Schematic model of vertical manipulations leaving the tip apex chemical identity unchanged. (c–f) The same area of the surface as imaged by (c) Cu- and (d–f) O-terminated tips. For ease of comparison, the spots corresponding to the same super-Cu atoms are numbered identically in c–e. Notice that the same contrast is found on the $c(6\times 2)$ island and the $p(2\times 1)$ terrace for the super-Cu atoms in c,d; they are observed either as double (c) or as single (d) spots. Images (d–f) were taken during the same experimental run but not necessarily immediately one after the other. One can clearly see a number of vertical manipulations on the $p(2\times 1)$ terrace corresponding to extractions (blue circles) and depositions (red circles) of the Cu adatoms during imaging.





Micro-structures trapped in optical tweezer. Trapping laser beams are red and excitation beam laser is blue. b) Surface enhanced Raman spectrum of hypericin (red).

TOWARDS INCREASED SENSITIVITY OF CANCER DETECTION AND SELECTIVITY OF CANCER TREATMENT: BIOPHOTONIC NANOTECHNOLOGY APPLICATIONS (NANOTECHPDT)

Principal investigator:
Applicant organisation:
Participating organisations:

prof. RNDr. Pavol Miškovský, DrSc.
Pavol Jozef Safarik University in Kosice
International Laser Center, Bratislava; Polymer Institute of Slovak Academy of Sciences; Institute of Animal Biochemistry and Physiology of Slovak Academy of Sciences
July 2012 – December 2015
171 159 EUR
APVV-0242-11

Term of solution:
Budget from agency:
Project ID:

Subject of research

NanoTechPDT was a multidisciplinary project based on a combination of modern technology and disciplines (biophotonics, molecular biophysics, polymer chemistry, cell biology and bioinformatics) whose main goal was to improve understanding of the mechanisms and increase the efficiency of the diagnosis and treatment of tumour mediated photoactive drugs (PDT).

Aims of the project

Increasing the sensitivity and efficacy of cancer diagnostics and treatment was defined as the main aim of the NanoTEchPDT. Specific aims were described as: 1. Development of non-invasive technology for the effective detection of cancer tissue, 2. Construction of a nano-delivery system based on LDL for targeted drug delivery, 3. Description of cell death pathways induced by PDT, 4. Increase of PDT efficacy *in vivo*.

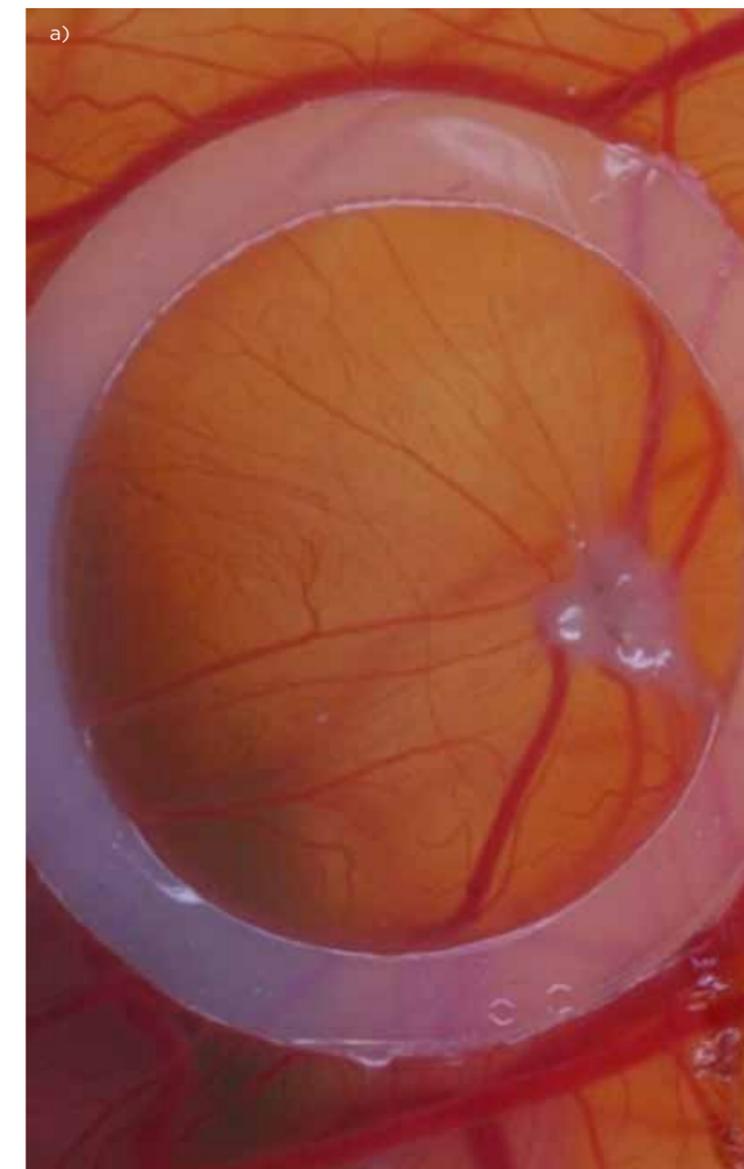
Results

1. We were able to design an experimental protocol for measuring the time-resolved autofluorescence of endogenous fluorophores and for monitoring the metabolic status of cancer cells in 2D and 3D cell cultures and implementing algorithms to optimize and adapt linear un-mixing image data obtained by time- and spectrally-resolved fluorescence.

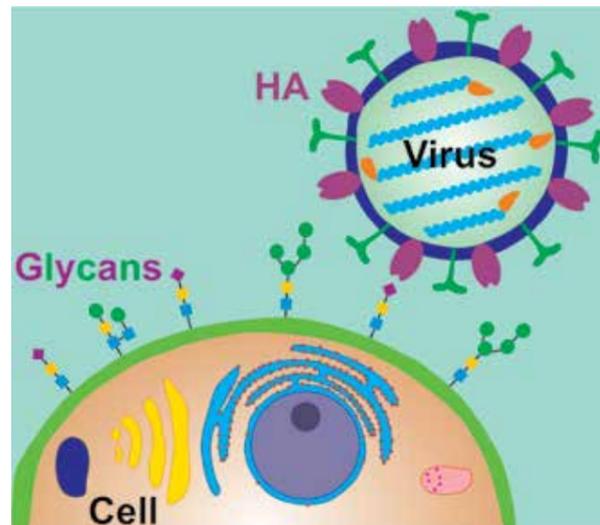
2. We prepared a synthetic LDL particle and large unilamellar vesicles, which can be used as future delivery systems for the targeted delivery of drugs to the tumour tissue.
3. Through the optimization of the detection of drug molecules by optical tweezers, we demonstrated that large vesicles resulting in the formation of large aggregates of drug molecules can significantly protect the delivery system from oxidation and damage.
4. In the environment of an experimental model (CAM), complex LDL/pts very well visualized tumour tissue. The CAM model simulates the proliferation of the tumour and the stage of CAM tissue micro-invasion.

Benefits for practice

An important NanoTechPDT contribution applicable in practice is to improve the detection of modifications of cell metabolism associated with the presence of cancerous changes in the cells. Our new algorithms and computer analyses of autofluorescence data are used in clinical research in the early detection of lesions in the oral cavity. Features of the complex LDL / pts *in vivo* allow the optimization of diagnostics and are promising for the treatment of certain types of cancer by using PDT.



TE1 tumor in reflectance (a) and fluorescence (b) 6 hours after local application of LDL/Hyp 1:200 complex.



Interaction between a virus and a glycan of a host cell applicable in diagnostics of viruses.



Incorporation of bacterial cells of *Gluconobacter oxydans* with graphene oxide.

PREPARATION OF NANOSTRUCTURED INTERFACES, THEIR INTEGRATION WITH BIOELEMENTS AND SUBSEQUENT USE

Principal investigator:
Applicant organisation:
Participating organisations:

Ing. Ján Tkáč, DrSc.
Institute of Chemistry, Slovak Academy of Sciences
Institute of Molecular Physiology and Genetics, Slovak Academy of Sciences,
Polymer Institute, Slovak Academy of Sciences, Institute of Experimental
Physics, Pavol Jozef Šafárik University in Košice, Faculty of Medicine,
Comenius University
July 2012 – December 2015
194 562 EUR
APVV-0282-11

Term of solution:
Budget from agency:
Project ID:

Subject of research

The integration of nanotechnology for the construction of: 1. biobatteries (biofuel cells) to produce green electricity (e.g., from sugars); 2. lectin and glycan biosensors which could be used in the diagnosis of various diseases, including prostate cancer.

Objectives of the project

- 1) Preparation and characterization of modified surfaces at nanoscale and using nanomaterials (metal nanoparticles, carbon nanotubes, and soot, graphene);
- 2) The integration of these surfaces with bioelements and the characterization of the resulting operational parameters of constructed devices

Results

We were able to prepare highly sensitive lectin biosensors for the analysis of the sera of healthy people as well as people with rheumatoid arthritis and systemic sclerosis. Lectin biosensors were employed for the analysis of intact cells of mouse leukaemia lines, as well. Some of these biosensors are still among the most sensitive biosensors used for the analysis of the glycoproteins described in the literature, with a limit

of detection (LOD) down to aM (10-18 M), and their performance was validated with other bioanalytical techniques. This low detection limit means that we can determine glycoproteins at a concentration a million times lower compared to the concentration of proteins present in the blood, which is very important in the early diagnosis of diseases. The use of lectin biosensors in the diagnosis of prostate cancer by determining changes in the glycan composition of the prostate cancer biomarker - prostate-specific antigen seems to be very promising.

A glycan biosensor constructed with the control of the immobilization process at nanoscale is among the most sensitive glycan biosensors described in the literature (LOD of aM level) and it was applied for the detection of different types of influenza viruses such as H3N2, H7N7, which may be potentially dangerous for humans. The construction of biobatteries entailed the preparation of different nanocomposites by using a binder such as a polylactide biopolymer, and chitosan (enzyme biobatteries), or without it (microbial bioanodes). A wide variety of carbon nanoparticles, such as carbon nanotubes, but also platelet carbon nanoparticles, were applied for the preparation of microbial bioanodes. Recently we started to use one of the most promising nanomaterials - graphene, whose discovery resulted

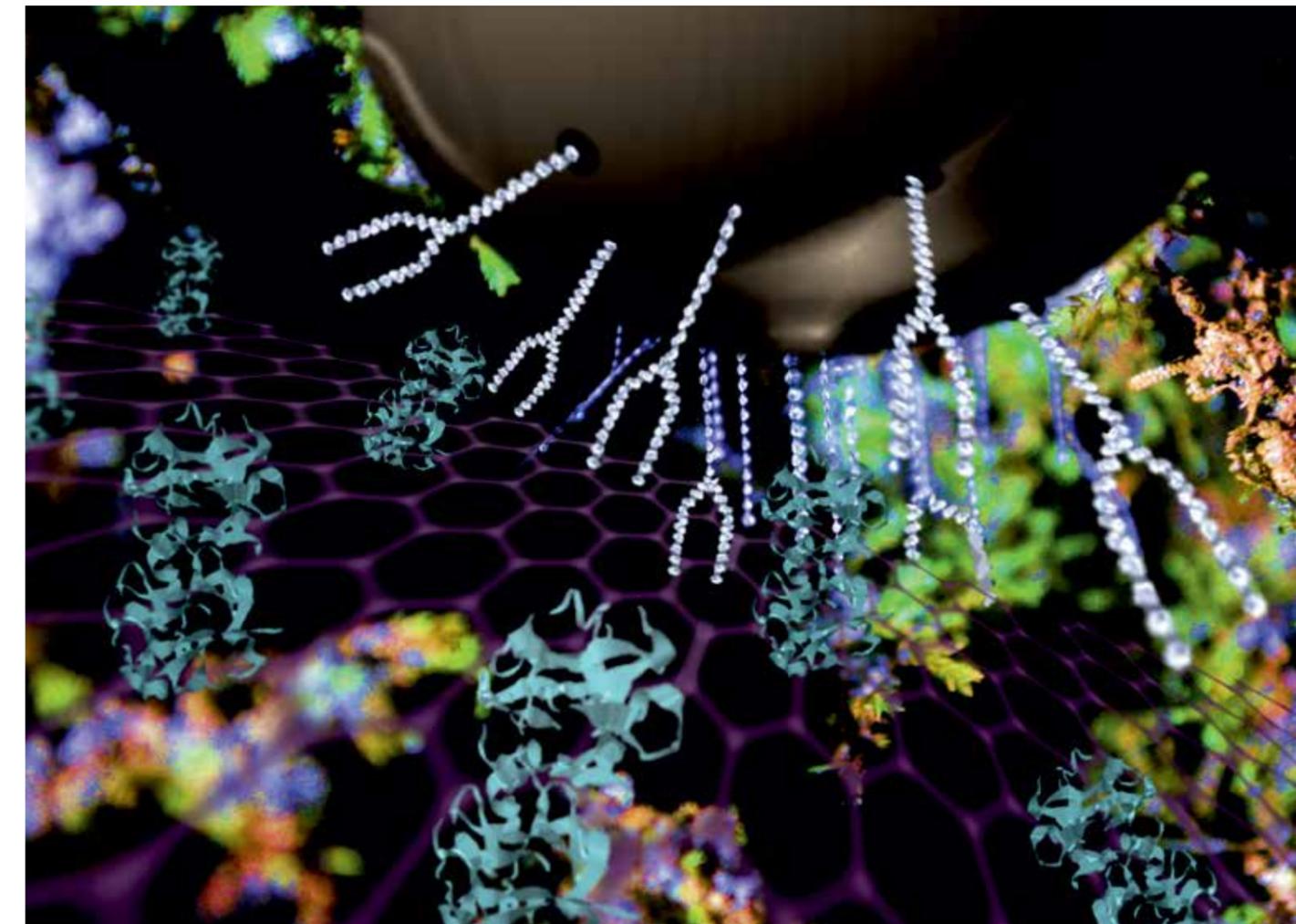
in the awarding of the Nobel Prize for Physics in 2010. Graphene has unique characteristics usable in various scientific fields, including the preparation of biobatteries and biosensors. The latest results of the integration of the enzyme bilirubin oxidase with graphene oxide (GO) are very promising because of the cost-effective preparation of GO-based biocathodes, which have the potential to be applied for highly efficient, inexpensive and miniaturised biofuel cells.

Overall, the results obtained from the project were published in 32 articles and one book chapter. Quite a few experimental articles have been published in prestigious journals such as Analytical Chemistry, Langmuir, Chemical Communications, Analyst, while review articles have been published in journals such as Microchimica Acta, Analytical Methods, and in the most prestigious journal focused on publishing review articles Chemical Reviews with IF = 46.568. Moreover, the issue of Chemical Reviews containing our article has a cover image designed by us. The articles published from the project were cited more than 100 times during the term of the project.

Benefits for practice

Lectin and glycan biosensors are also planned to be used for the detection of leukaemia (chronic lymphocytic), breast cancer, as well as various virus particles such as influenza viruses of different types, tick-borne encephalitis virus, and other types of viruses. The goal of such studies at the final stage is to develop novel methodology and/or a prototype of a handheld device that would assist in the diagnosis of prostate cancer and the other above-mentioned diseases, and for the identification of the risk of diseases spread by different virus particles.

We were able to prepare biobatteries with the aid of nanotechnology from cost-effective and renewable sources capable of producing a power density of 50 $\mu\text{W cm}^{-2}$ at an operating potential of 300 mV with the possibility of using such devices for the power supply of appliances with low power consuming appliances in the near future.



Analysis of glycoproteins by a lectin biosensor based on graphene oxide.



flax flower - radio-contaminated area



flax - radio-contaminated area

UNDERSTANDING OF PLANT ADAPTATION IN THE RADIOACTIVE CHERNOBYL AREA

Principal investigator: Mgr. Martin Hajduch, DrSc.
 Applicant organisation: Institute of Plant Genetics and Biotechnology, Slovak Academy of Sciences
 Participating organisations: Institute of Virology, Slovak Academy of Sciences, Animal Production Research Center, Faculty of Agrifood Resources – Slovak University of Agriculture, Institute of Chemistry, Slovak Academy of Sciences, Institute of Chemistry, Center of excellence for white-green biotechnology

Term of solution: July 2012 – December 2015
 Budget from agency: 114 640 EUR
 Project ID: APVV-0740-11

Subject of research

To understand the molecular basis of plant adaptation in the radio-contaminated Chernobyl area.

Objectives of the project

Objective 1: Elucidation of protein post-translational modification in plant adaptation in the radioactive Chernobyl area
 Objective 2: Screening of crops grown in the Chernobyl area for changes in protein and DNA levels
 Objective 3: Elucidation of flax and canola oil from the radioactive Chernobyl area for biofuel production

Results

The project was aimed at achieving an understanding of the molecular basis of plant adaptation in the radio-contaminated Chernobyl area. For this purpose, we used genomic and proteomic approaches. Genomic experiments were based on the analyses of retro-transposons and global DNA methylation. Proteomic approaches were included in the analyses of developing seeds using protein two-dimensional electrophoresis and tandem mass spectrometry. We also analysed protein post-translational modifications (phosphorylation and glycosylation). An interesting outcome of this project was the discovery that the radio-contaminated environment altered oil levels in mature soybean and flax seeds. In this regard, we analysed the genetic stability of genes encoding fatty acid desaturase, an key enzyme of fatty acid biosynthesis.

For the implementation of this project we developed a novel experimental design for radio-contaminated areas that minimizes the risk of pseudoreplication in these heavily controlled areas. Based on the results, we proposed a working model for plant adaptation toward radio-contaminated environments. This working model showed adaptation changes that are specific for individual plant species. However, it also detected common changes in adapting plants such as alterations in fatty acid biosynthesis or a mobilization of seed storage proteins.

For friendly dissemination of these results we established web-database that is available at www.chernobylproteomics.sav.sk. We use this database to show the project results in an easy-to-use manner after publication in scientific journals.

Benefits for practice

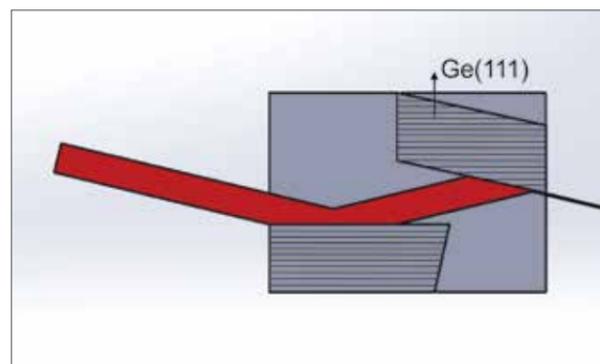
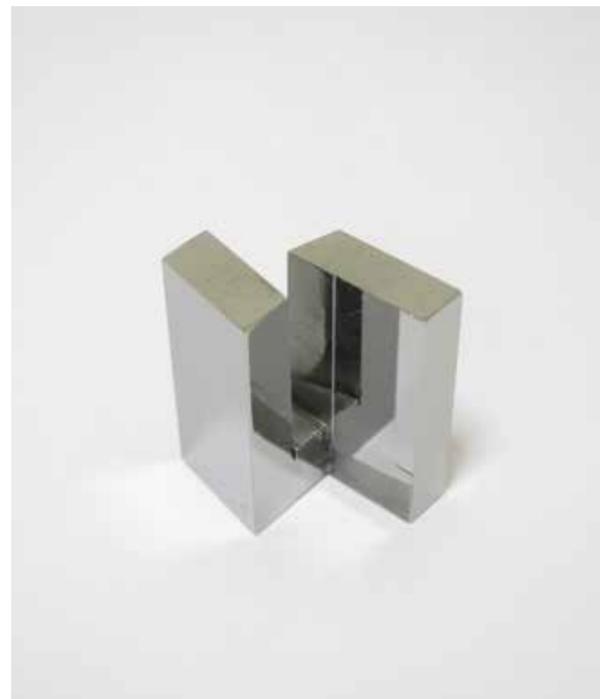
The results of this project include basic research in the field of plant adaptation in a radio-contaminated environment and they provide the foundation for the development of agricultural practices in radio-contaminated areas. However, the principal investigator strongly hopes that humanity will never need to use these results, due to the fact that it would mean that there is a need to grow plants for agricultural purposes in radio-contaminated areas. Such need could only arise after a global catastrophe that contaminated large areas with radioactivity.



soybean - radio-contaminated area

▼
TECHNICAL
SCIENCES





Principle of V-shaped X-ray monochromator for X-ray beam compression/expansion and realization.

CRYSTAL ELEMENTS OF X-RAY OPTICS FOR BEAM COMPRESSION AND EXPANSION

Principal investigator: Ing. Matej Jergel, DrSc.
 Applicant organisation: Institute of Physics, Slovak Academy of Sciences
 Participating institution: Institute of Electrical Engineering, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 200 000 EUR
 Project ID: APVV-0308-11

Subject of research

The development of nanotechnologies and studies of nanostructures by X-ray scattering techniques call for new solutions of laboratory X-ray sources and consequently new X-ray optics for shaping X-ray beams. The research was aimed at effective X-ray beam compression and expansion for the needs of X-ray metrology and X-ray imaging as well as the development of a new deterministic technology of nanomachining of active surfaces of X-ray optics elements based on single-point diamond turning (SPDT) technology. The research results were achieved and tested in collaboration with the beneficiaries of the project results, Integra TDS s.r.o. of Piešťany, and Technodiamant Almere B.V. of the Netherlands.

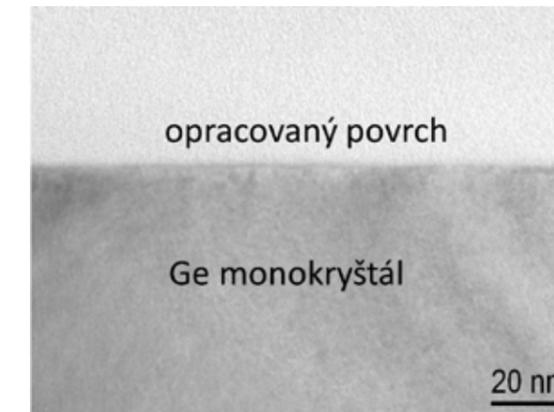
Aim of the project

The project aims were the research and development of new X-ray optics elements for X-ray beam shaping based on strongly asymmetric diffraction, new nanomachining technology necessary for achieving these elements and piloting them in X-ray metrology and X-ray imaging.

Results

Relying on the dynamic theory of X-ray diffraction, V-shaped germanium channel-cut X-ray monochromators for extreme X-ray beam compression/expansion with factors of 15 and 21 and with an original

compensation of the refraction effect were designed and prepared. Measurements in the compression mode revealed output intensity that was 1 order of magnitude higher compared to classic parallel channel-cut monochromators combined with slit collimation. This has a direct application to X-ray diffraction measurements at medium resolution and for the small-angle X-ray scattering (SAXS) technique. By employing the ray-tracing method, the application of X-ray compressors in a real experimental setup was simulated, and relying on these results, a pilot measurement setup lab-GISAXS with microfocus X-ray source μS^* and two-dimensional detector Pilatus 100K was designed and created. The SAXS measurements showed resolution in reciprocal space comparable to that achieved at synchrotron beamlines and several times higher than that offered by commercial laboratory X-ray setups. Measurements in the expansion mode revealed spatial resolution on the micrometre scale which allows the X-ray microscopy of biological objects in their natural environment. Simultaneously, SPDT technology was being developed and gradually implemented into monochromator preparation. Analyses of active surfaces by Raman confocal microscopy, stylus profilometry, AFM, TEM, and grazing-incidence X-ray diffraction exhibited surface planarity of the order of 10^{-5} on the lengths of millimetres at a local roughness of 0.2 nanometres, no dislocations being observed under the surface. Classic techniques of active surface finishing (lapping, chemomechanical or chemical polishing) do not allow the simultaneous achievement of such values. Due to the



The cross-section transmission electron microscopy image of germanium surface treated by SPDT technique shows no dislocations.

diamond tip scanning movement, surface roughness has the shape of a grating that is projected into a periodic deformation of the lattice parameter close to the surface. This phenomenon is the subject of study in a current APVV project.

The project team had 4 PhD students, 2 of whom defended their theses during the project run, and 1 bachelor student who defended his diploma work. The project results were published in 12 papers in journals registered in the Current Contents database and 10 papers in reviewed scientific journals.

Benefits for practice

V-shaped X-ray monochromators developed within the project allow for the performance of high-resolution SAXS measurements, to date confined exclusively to synchrotrons, also in the laboratory. This substantially extends the employment of SAXS as a diagnostic tool in the development of nanotechnology and nanostructures and for real-time studies of processes on the nanoscale. The X-ray monochromators used as beam expanders allow laboratory-based X-ray imaging. Integra TDS s.r.o. of Piešťany, a beneficiary of the project results, will boost production by new products with high added value which will ensure the further development of the company with a positive impact on employment. It is a highly innovative company with its own know-how. The development of such companies requires a highly qualified staff and lays the groundwork for the development of scholarship in the region while supporting economic growth.



X-ray measurement setup lab-GISAXS with integrated X-ray beam compressor.



Preparation of the measurement of fast neutrons produced by DT nuclear reaction at the Van de Graaff accelerator at CTU in Prague. The SiC detector with a HDPE conversion layer (on green holder) is placed in front of the tritium target bombarded by accelerated deuterons from the accelerator.

NEW SEMICONDUCTOR DETECTORS OF NEUTRONS

Principal investigator: Assoc. prof. Andrea Šagátová, PhD.
 Applicant organisation: Slovak University of Technology in Bratislava, Faculty of Electrical Engineering and Information Technology
 Participating organisation: Institute of Electrical Engineering, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 229 965 EUR
 Project ID: APVV-0321-11

Subject of research

The project focused on semiconductor detectors of neutrons which can find application in neutron imaging, space research, particle physics, radiation safety or material research and nuclear power engineering.

Aim of the project

The aim of the project was to develop a new type of semiconductor detector based on perspective SiC material. It should have higher detection efficiency of fast or thermal neutrons thanks to an appropriate neutron conversion layer. During the design of neutron conversion layers, the newest version of the Monte Carlo code, the MCNPX (Monte Carlo N-Particle eXtended), was used. Using the results of simulations, the scientific team estimated the optimal thickness of appropriate conversion layers, which were prepared, applied on the SiC detector surface and experimentally tested with neutrons. The twenty-years of experience of the team with semiconductor detectors based on GaAs were utilized during the solving of the project. Silicon carbide (SiC) is one of the most promising and attractive materials of recent science. The newest studies show that SiC material is suitable for the detection of alpha particles, beta particles, gamma rays and X-rays, ions or neutrons. This material has high radiation hardness and high thermal stability, which made it one of the possible materials for fusion reactors. During the project solving, the properties of the SiC neutron detectors were improved by the application of an

ideally thick neutron conversion layer based on HDPE (High Density PolyEthylene) for the detection of fast neutrons and on 6LiF for the registration of thermal neutrons. The detection efficiency of fast neutrons was increased by a layer up to 5-times in comparison with the detector without a conversion layer. The detection of thermal neutrons with a usual semiconductor detector or SiC detector is impossible. By applying 6LiF conversion layers of various thicknesses on the surface of the investigated SiC detector, the ideal thickness of the layer was experimentally determined to 25 μm , which was in perfect accordance with simulation results in the MCNPX code.

Results

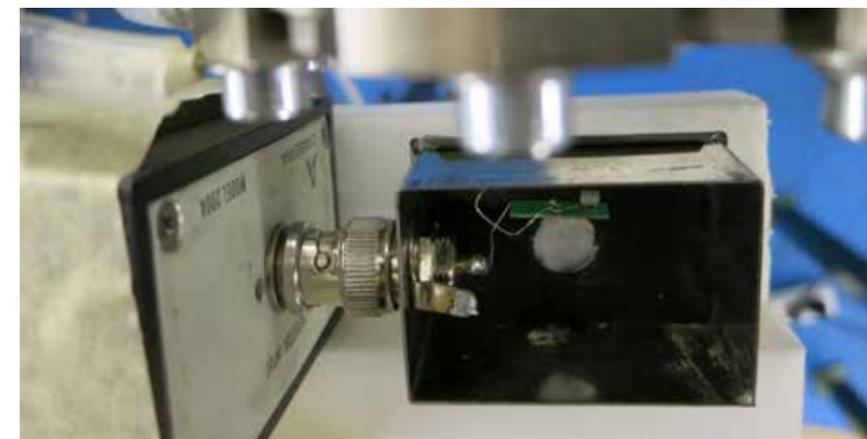
As a result of the project, there are two types of SiC detectors, one optimal for the registration of fast neutrons and the second for thermal neutron registration. Both types were tested within the framework of electro-physical and detection properties and compared to the properties of a SiC detector without a conversion layer as well as GaAs detectors with and without identical conversion layers.

Benefits for practice

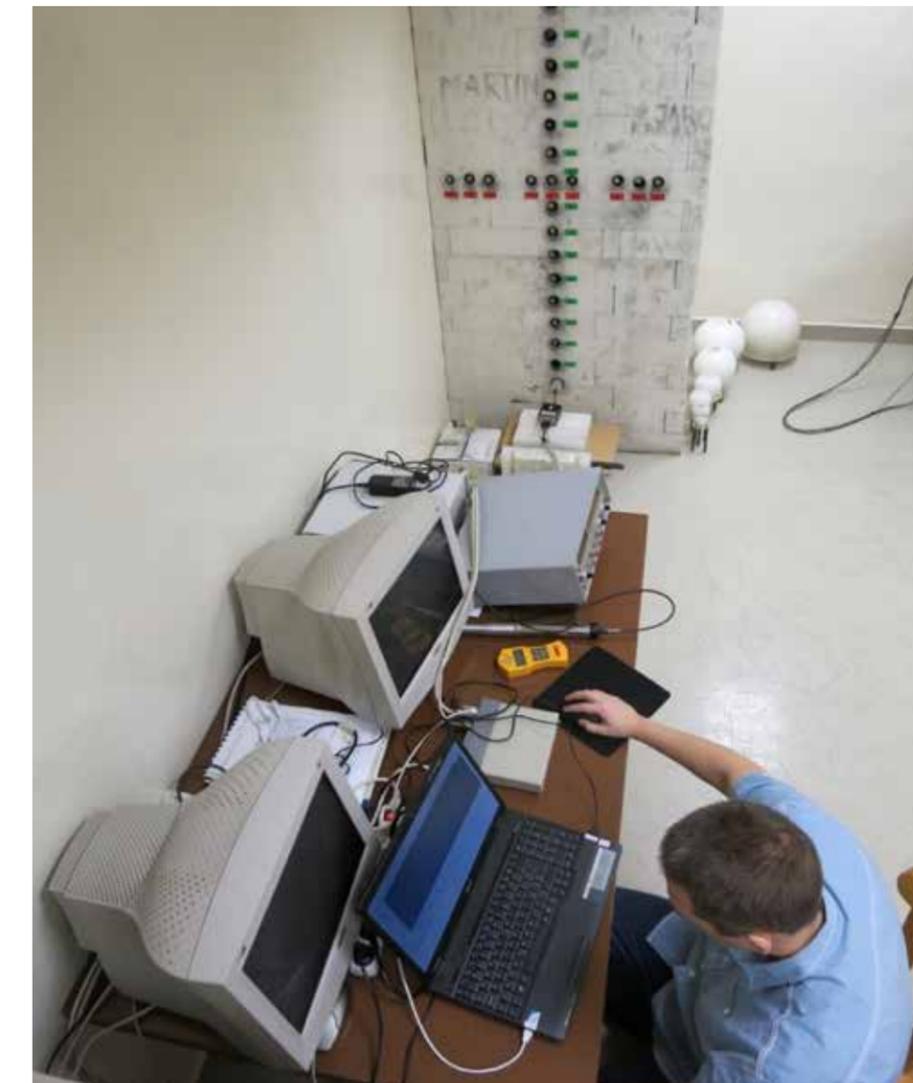
The results were presented at international and domestic conferences and have been published in 12 scientific papers published in CC journals as well as in 42 articles published in other scientific journals and conference proceedings.



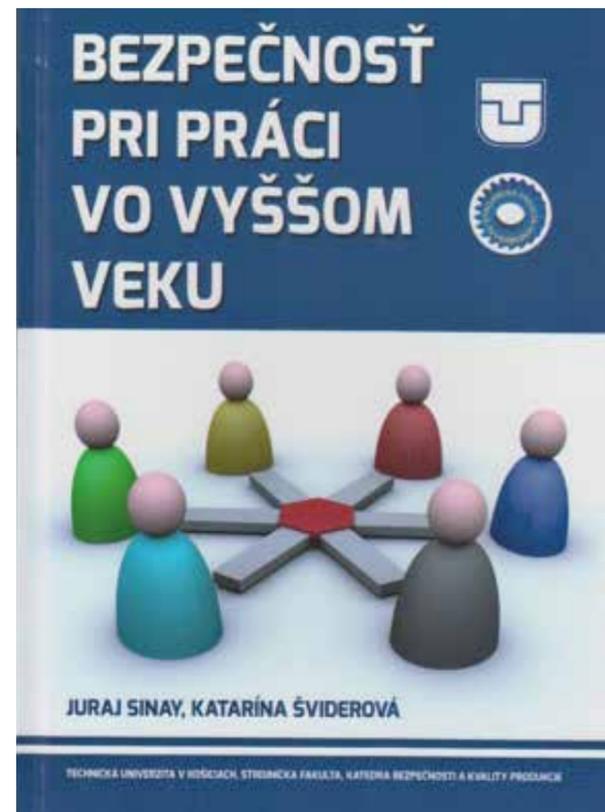
SiC detector with a diameter of 8 mm and an applied 6LiF conversion layer connected to the testing spectrometric chain for thermal neutron detection.



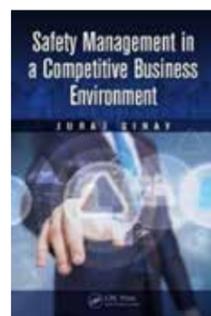
SiC detector (on green holder) with 1.5 mm diameter and conversion layer based on HDPE connected to the preamplifier of the spectrometric chain for testing the detector by monoenergetic fast neutrons from DT nuclear reaction.



Measuring the thermal neutrons produced by stopping fast neutrons from the $^{239}\text{PuBe}$ neutron source at FEEIT SUT in Bratislava. The SiC detector with a 6LiF conversion layer is placed directly in the shielding structure of the neutron source.



National monograph – Occupational safety at an older age.



Foreign monograph – Safety management in a competitive business environment.

RESEARCH INTO NEW AND NEWLY EMERGING RISKS OF INDUSTRIAL TECHNOLOGIES WITHIN INTEGRATED SAFETY AS A PRECONDITION FOR THE MANAGEMENT OF SUSTAINABLE DEVELOPMENT.

Principal investigator: Dr.h.c. mult. prof. Ing. Juraj Sinay, DrSc.
 Applicant organisation: Faculty of Mechanical Engineering, Technical University of Košice
 Term of solution: July 2012 – December 2015
 Budget from agency: 247 100 EUR
 Project ID: APVV-0337-11

Subject of research
 New and newly emerging risks

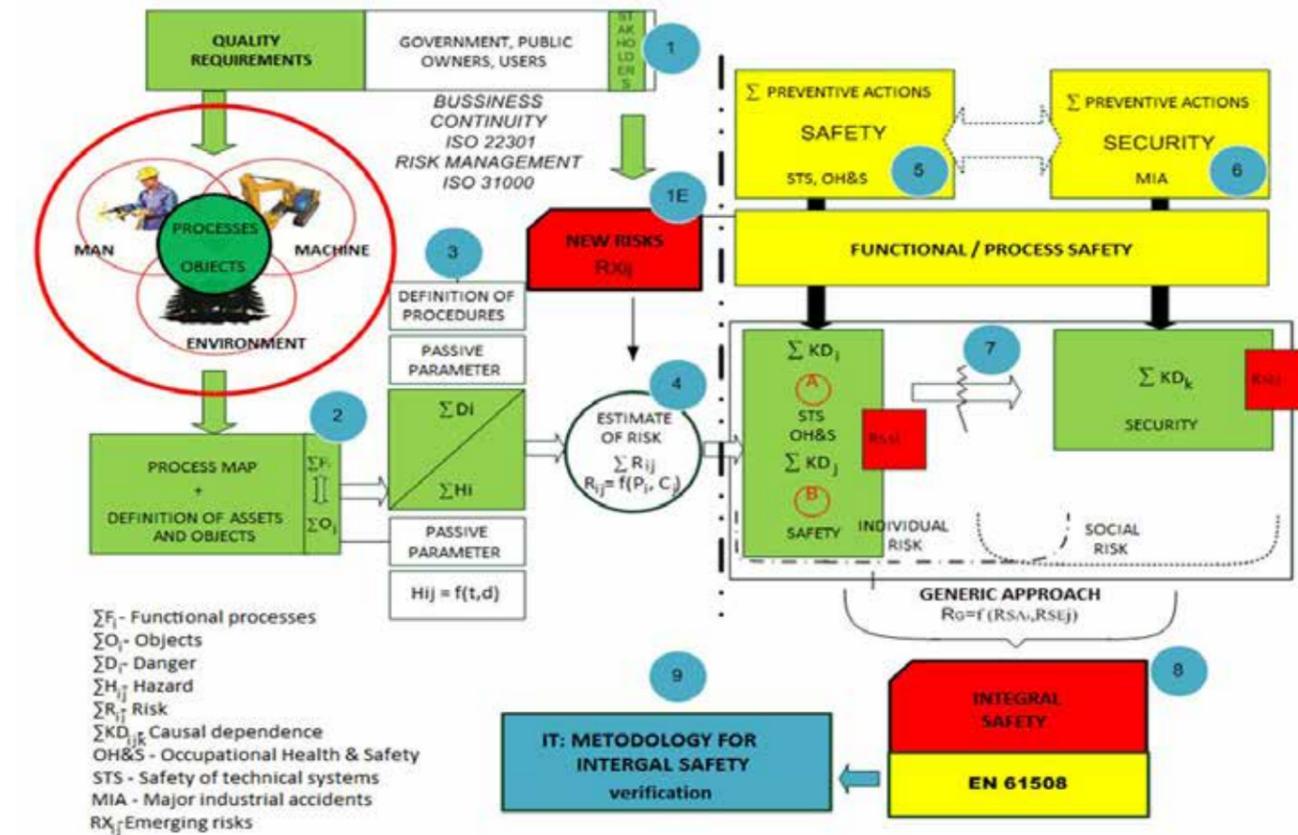
Aims of the project
 A model based on integrated risk analysis was developed to support the management of the sustainable development of industrial technologies of mechanical engineering products. The model integrates risk management methods of new technology and products in particular phases of their life cycle. The goal is to define the particular phases of causal dependence upon the occurrence of negative phenomena in order to effectively apply prevention methods in the form of effective interruption.

Results
 New applicable characteristics and tools for a group of new and newly-arising risks were defined within the framework of the selected industrial technologies in the context of a generic relationship between the risks concerning Safety + Security. For this purpose, a risk assessment generic model – GRAM was developed. The algorithms for the risk-management were modified as part of integrated security with regard to the first phase of causality – danger and hazard, as well as with regard to the initiation phase. The KPI method was applied in the GRAM model for choosing the relevant input parameters. The first application was tested on an example of the risk management of noise in the new technology so that methods could be effectively

used in the process of constructing machinery and mechanical systems and integration them into the technological process. Other deliverables are methods of verification of the GRAM model for each of the selected strategic industrial technology types (e.g., technology for hydrogen powered cars, renewable sources of energy, fire-fighting processes). In cooperation with the Department of Computers and Informatics, of the Faculty of Electrical Engineering and Informatics, of the Technical University of Košice; a software package was developed for practical GRAM applications for risk-management in the construction and operation of hydrogen powered cars.

Benefits for practice
 Development of generic risk assessment GRAM model and its application in selected industrial technology with the ultimate goal of substantially minimizing risks and thereby increasing economic efficiency of production. Distribution of partial results for their application in practice in a foreign monograph - Safety management in a competitive business environment / Juraj Sinay - 1. vyd - Danvers : Taylor & Francis Group - 2014. - 184 p. - ISBN 978-1-4822-0385-1 [SINAY, Juraj (100%)] and the monograph - Bezpečnosť pri práci vo vyššom veku / Juraj Sinay, Katarína Švídorová - 1. vyd - Košice : TU - 2013. - 112 s. - ISBN 978-80-553-1444-0. [SINAY, Juraj (50%) - ŠVIDEROVÁ, Katarína (50%)] published in the Slovak Republic.

Scheme GRAM.



Measuring equipment and evaluation software.



MONOLITHIC INTEGRATION OF DEPLETION-AND ENHANCEMENT-MODE INAlN/GaN HFET TRANSISTORS

Principal investigator:
Applicant organisation:
Participating organisation:
Term of solution:
Budget from agency:
Project ID:

prof. Ing. Alexander Šatka, PhD.
Slovak University of Technology in Bratislava, Faculty of Electrical Engineering and Information Technology
Institute of Electrical Engineering, Slovak Academy of Sciences
July 2012 – October 2015
250 000 EUR
APVV-0367-11

Subject of research

The subject of the research was comprised of structures of depletion-and enhancement-mode InAlN/GaN HFET transistors, the design of such structures aimed at their monolithic integration and their optimization using numerical simulation methods combined with the development of electrical characterization methods, diagnostics and electrical model parameters extraction, as well as the design and technology of their monolithic integration into basic logic cells.

Objective of the project

The main goal of the project was to gather new knowledge about the properties of InAlN/GaN HFET transistor structures for depletion and enhancement modes and the research of the methods and technology of their monolithic integration for the preparation of basic logic cells.

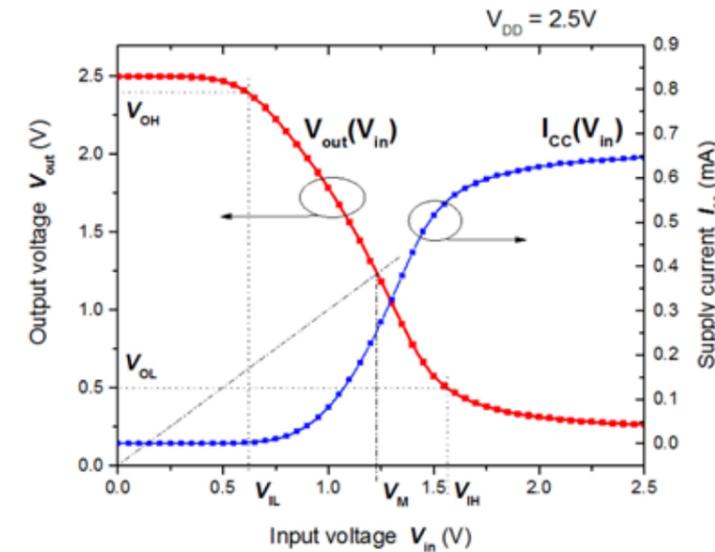
Results

New knowledge about electro-physical properties of InAlN/GaN depletion-and enhancement-mode D- and E-HFET transistors was been gained and the methods and technology of their preparation and monolithic integration into basic electronic logic cells (inverter, NAND, NOR) were explored. Specifically: InAlN/GaN

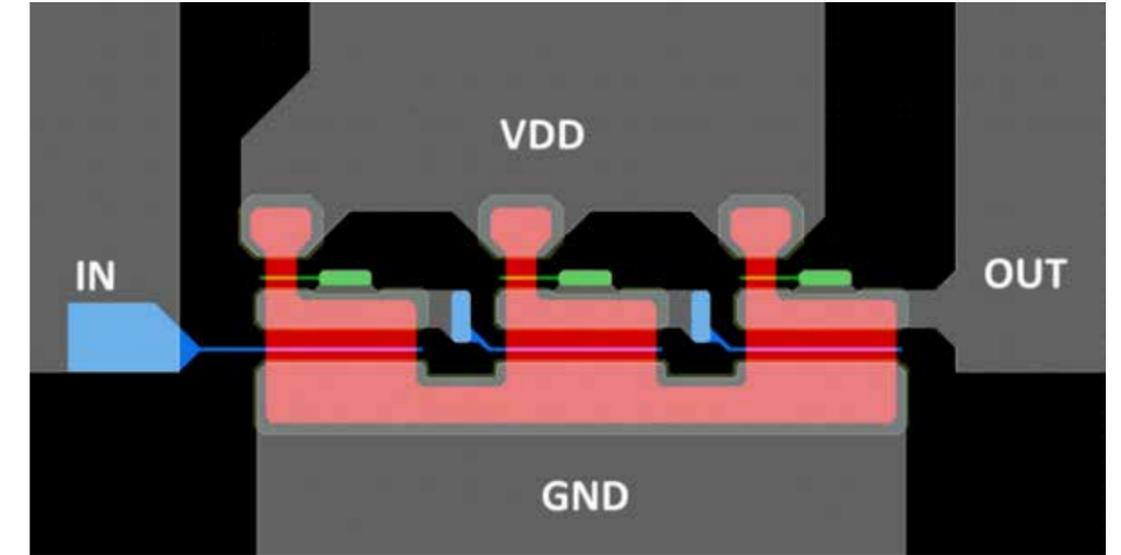
E- and D-HFET transistors compatible with technology available were designed and developed. New knowledge about the (GaN)/InN heterostructures for very fast transistors with 2-DEG in the InN was achieved. InAlN/GaN E-/D-HFET transistors were prepared on the same chip. Electro-physical calibrated models of InAlN/GaN transistors were developed. Numerical simulations revealed the effects of traps in InAlN/GaN structures on large signal characteristics of E-HEMT transistors. An electro-physical model of a dual-gate InAlN/GaN HEMT transistor was developed to optimize its electrical characteristics. New information about GaN HFET structures and devices was gathered by characterization and diagnostic methods using static and/or pulse electrical, optical and electron excitations. A calibrated equivalent circuit electrothermal model of InAlN/GaN HEMT transistors was created and the methodology of heterogeneous simulations of electro-thermal processes was studied. A new concept of the monolithic integration of InAlN/GaN E-/D-HFET transistors was proposed. Methods of the circuit simulations and design in HSPICE and Synopsys were used to design prototypes of monolithic inverter, NAND and NOR logic gates, and ring oscillator in DCFL logic. Fully functional InAlN/GaN E-/D-HFET monolithic integrated inverters, NOR and NAND gates for use in DCFL logic were prepared.

Benefits for practice

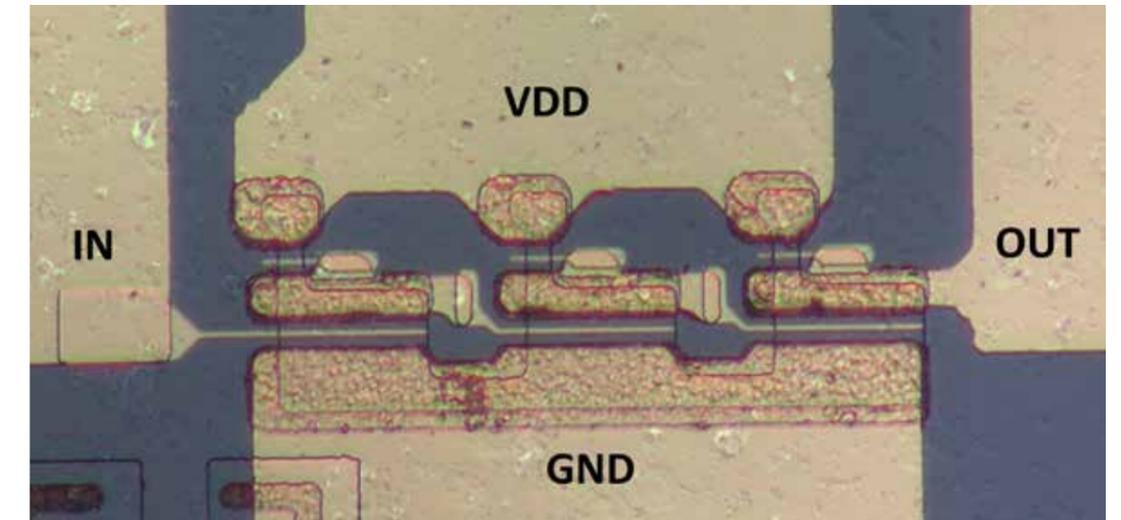
The new knowledge achieved within the project has been published in 64 publications (12 CC journals). They contributed to the development of the problematic of the design and preparation of GaN integrated circuits in Slovakia and the widening of the international cooperation of FEI STU and IEE SAS with renowned research centres in the EU, resulting in three new international projects (two of them in the ECSEL programme) and several local projects. Equally importantly, the knowledge and experience gathered within the project are implemented in education curricula for the education of young researchers and masters in electronics with very high knowledge and skills in emerging GaN electronic devices and their application in advanced electronic circuits.



Transfer and supply characteristics of the prepared one-stage InAlN/GaN E-/D-HFET inverter at VDD = 2.5V supply voltage.



Topology design of the three-stage InAlN/GaN E-/D-HFET inverter.



Top-view of the three-stage InAlN/GaN E-/D-HFET inverter.

STUDY OF SYSTEMS AND CONTROLLERS OF FRACTIONAL, VARIABLE, AND DISTRIBUTED ORDER: METHODS, ALGORITHMS, AND TOOLS FOR MODELLING, SIMULATION, ANALYSIS AND SYNTHESIS

Principal investigator: prof. RNDr. Igor Podlubný, DrSc.
 Applicant organisation: Technical University of Košice
 Participating organisation: University of Prešov
 Term of solution: July 2012 – December 2015
 Funding from agency: 249 910 EUR
 Project ID: APVV-0482-11

Subject of research

The theory of the differentiation and integration of arbitrary real order (integer and non-integer) and its applications to the modelling and control of objects, systems and processes.

Objectives of the project

The project was aimed at the development of methods for the modelling, simulation and analysis of dynamic systems and processes described by models of non-integer order, the development of the theory of controllers of non-integer order, the creation of necessary new hardware and software tools, and pilot applications in laboratory conditions.

Results

The most important results of this project include improved methods for the numerical solution of fractional-order differential equations; the extension of the matrix approach to solving fractional-order differential equations for cases of non-equidistant discretization, distributed-order systems and variable-order systems; the new method called “method of large steps”, which opens the way to the development of methods with a variable step length of discretization; experimental work on the modelling of dynamical systems and

processes of fractional order; the new method for the identification of the parameters of such systems, which is based on using the Mittag-Leffler function; the development of an adaptive fractional-order controller; methods for fractional-order signal processing; the development of laboratory equipment for the digitization of large area prints; the preparation of a catalogue of the library of old prints and pilot works on their digitization; the creation of 11 software products. Publications included 2 monographs (one of them with Springer), articles in journals indexed in Current Contents / Web of Science; 12 articles in other refereed journals abroad; 2 articles in refereed national journals; 33 papers in proceedings of international conferences; and 19 papers in proceedings of national conferences. The project also resulted in the following awards: Scientist of the Year in Slovakia; two Prizes of the Literary Fund of the Slovak Republic; two medals of the Union of Scientific and Technical Societies of Slovakia; the “Riemann-Liouville Award – Best Paper in Applications” at ICFDA’2014; long-term positions of the published articles among the „Top 25 Hottest Articles“ (Elsevier); invited lectures and addresses at important international conferences.

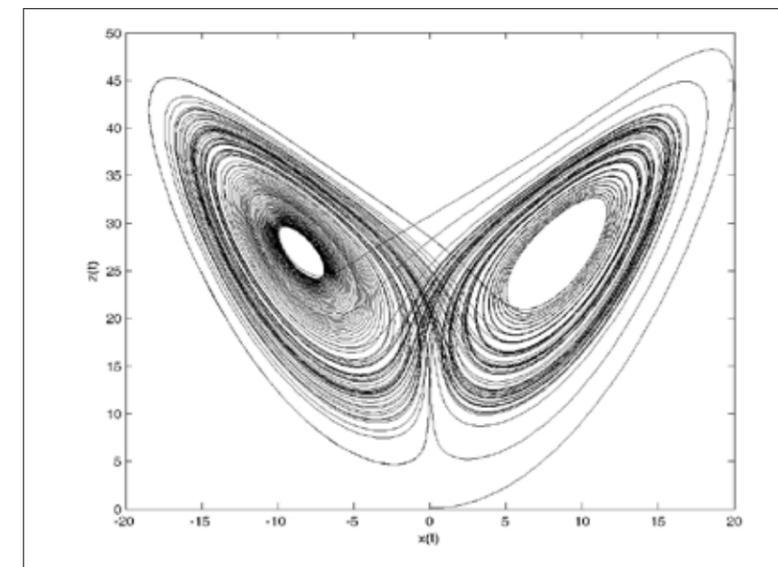
Contribution to practice

For the first time, it was demonstrated that electrical circuits of a ladder-like structure containing passive elements (resistors and capacitors) are systems of variable fractional order, and a method and software were developed for identifying the parameters of such systems. Methods and tools for the analysis of distributed-order systems were also developed. These results open the way to the creation of better and more accurate models of those real objects and processes, for which the classical integer-order methods do not provide the necessary level of adequacy.

Furthermore, a laboratory prototype of equipment for the digitization of large-size documents was developed, and in collaboration with the participating research organisation, a catalogue of old prints was created, along with the performance of pilot work on their digitization.

In total, 11 software products were developed and published at MATLAB Central File Exchange. The MATLAB toolbox “Matrix approach to the discretization of ODEs and PDEs of arbitrary real order” has become especially popular and widely used, and was featured among the 10 selected user-contributed toolboxes when MathWorks, Inc., the maker of MATLAB, introduced the recent R2016a version of their product.

Lorenz attractor of fractional-order.



The day of September 30, 1695, is considered as the birthday of the fractional-order calculus.

Fractional Calculus birthday: September 30, 1695

... from integer to non-integer ...



$$x^n = \underbrace{x \cdot x \cdot \dots \cdot x}_n$$

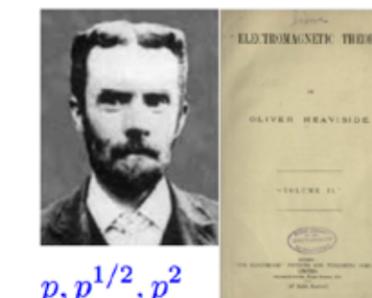
$$x^n = e^{n \ln x}$$

$$n! = 1 \cdot 2 \cdot 3 \cdot \dots \cdot (n-1) \cdot n,$$

$$\Gamma(x) = \int_0^\infty e^{-t} t^{x-1} dt, \quad x > 0,$$

$$\Gamma(n+1) = 1 \cdot 2 \cdot 3 \cdot \dots \cdot n = n!$$

Generalization of the type “from integer to noninteger” is omnipresent.

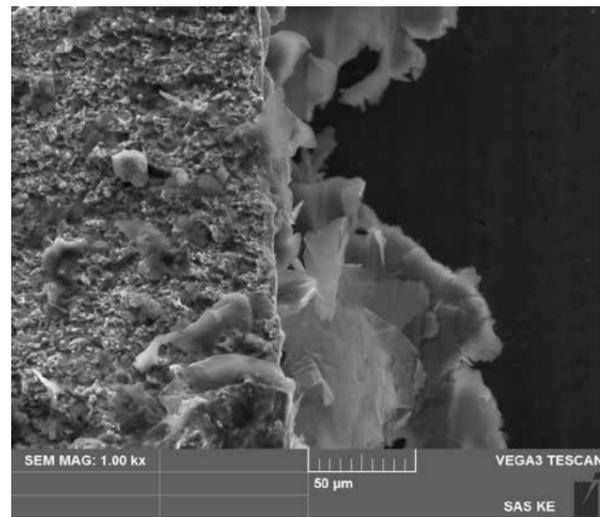


Oliver Heaviside, “Electromagnetic Theory”, vol. 2

$$p, p^{1/2}, p^2$$

“There is a universe of mathematics lying in between the complex differentiations and integrations.”
 “... fractional ones ... are just as real as the others”.

Oliver Heaviside used fractional-order operators.



Punch with stuck particles of processed aluminium alloy sheet.



Drawing punches with PVD coatings and the number of produced units.

APPLICATION OF PROGRESSIVE TOOL COATINGS FOR INCREASING THE EFFECTIVENESS AND PRODUCTIVITY OF FORMING SHEETS MADE OF MODERN MATERIALS

Principal investigator: prof. Ing. Emil Spišák, CSc.
 Applicant organisation: Technical University of Košice, Faculty of Mechanical Engineering
 Participating organisation: Institute of Materials Research, Slovak Academy of Sciences, Košice
 Term of solution: July 2012 – June 2015
 Budget from agency: 249 537 EUR
 Project ID: APVV-0682-11

Subject of research

The subject of the research was the study of a coating-material system for tools and the experimental verification of the relation among the process of friction, the wear and type of applied coating and the parameters of its preparation. The research of the active parts of tools focused on the coating-material system of the tool in the initial state, after the application of the conventional Ti-Al-N coatings and after the application of new composite TiN, TiCN and TiAlN coatings after mechanical load and the simulation of operating conditions.

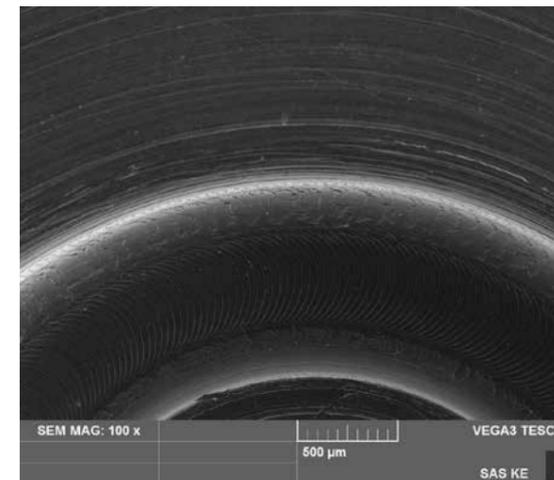
Objectives of the project

The project objectives were based on a systematic and comprehensive approach to solving the problems of forming technology in terms of tribological processes, including research of the relation of a tribological pair of tool – materials in connection with the applied coatings. Meeting the goals of the project led to recommendations for the transfer of knowledge, which assisted in the selection of a suitable coating system for various combinations of surface-treated sheets and sheets based on aluminium alloys and their surface morphology, as well as the increase of tool life, the surface quality of formed parts and working productivity.

Results

The quantitative parameters of morphology of contact surfaces of the tools with deposited PVD coatings and processed sheets were determined within the ex-

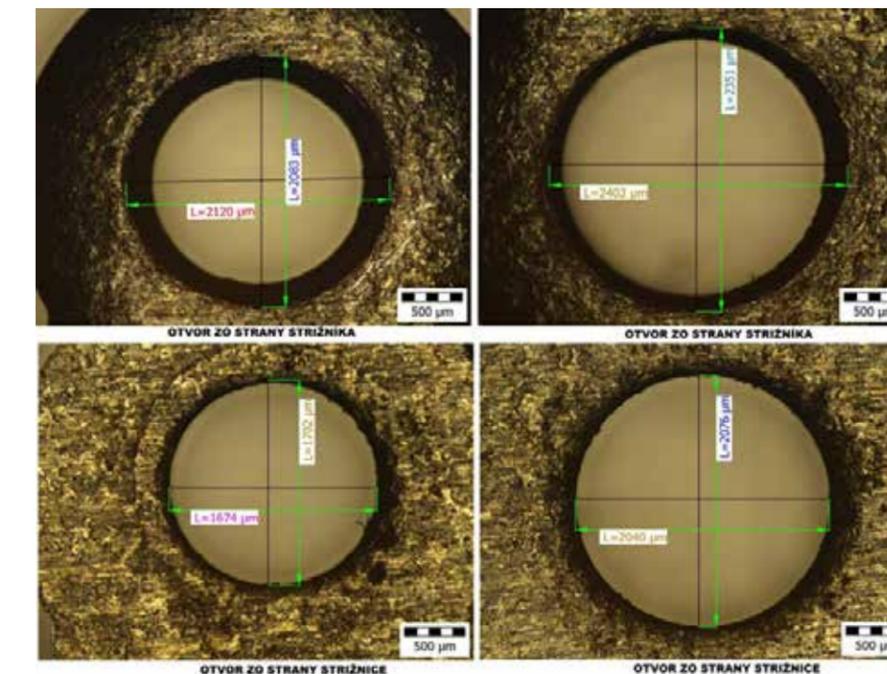
perimental measurements. The chemical composition of PVD coatings on the testing samples deposited together with a particular group of tools was measured by the GD-OES method. The coefficient of friction, wear and surface microgeometry changes of the drawn part and coating tool in the production of drawn parts were determined. The analytical models of friction and their verification as well as the fractal analysis of wear during metal forming were proposed. The results of friction were verified by a cupping test of formability. Raman spectroscopy was utilized for observing the structural changes of TiCN, CrN and ZrN coatings after an adhesive wear test of coatings. The limit deformation of galvanized and tinned steel sheets and sheets from aluminium alloys in various friction conditions were also determined. The influence of the friction coefficient and blank holder force on the spring-back effect in bending U-shape was observed. The lifetime testing and wear of the coated forming tools were conducted under production conditions. The procedure of the non-destructive testing of tool surfaces by the application of replicas on the base of a short curing, two-component flexible silicon rubber was determined and verified. The specific worn parts of tools were analysed by the SEM method. The wear of broaching tools was localized on the ogival part of the tool. TiCN MP, CrN and ZrN coatings were evaluated by SEM as well. Coating analyses were also carried out on the tools for mechanical joining. The surface morphology of all PVD coatings after deposition was verified by the SEM method, confocal microscopy and the replica method.



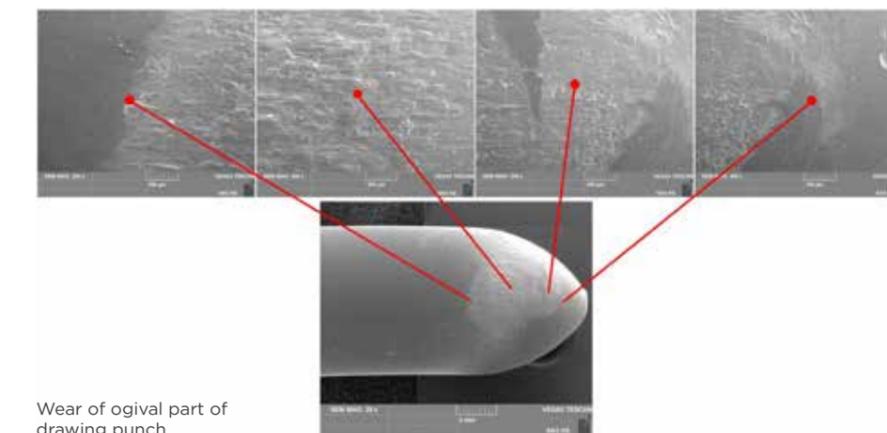
Wear of punch with CrN coating.

Benefits for practice

The results were applied in real production conditions for shearing tools and forming tools. The results can be applied in the proposal of optimal forming technology and the mechanical joining of thin steel sheets of various grades (galvanized steels, tin-coated steels and aluminium alloys sheets). The proposed coatings deposited on suitable materials increase the durability and lifetime of forming tools and decrease the friction in the forming process, which leads to the increased production of these tools from 20 to 100% (in some tools under compression stresses even up to 300%). Verified procedures in obtaining surface microgeometry from the tool with the replicas allow the identification of real tool wear directly in operating conditions, without the need for tool disassembly. The proposed analytical models of friction and their verification allow the optimisation of the proposed forming processes by lubricating to increase the forming tool lifetime. The determination of limit strains of the sheets allows for the optimal utilization of sheet properties and are used as input data for simulation software for sheet metal forming.



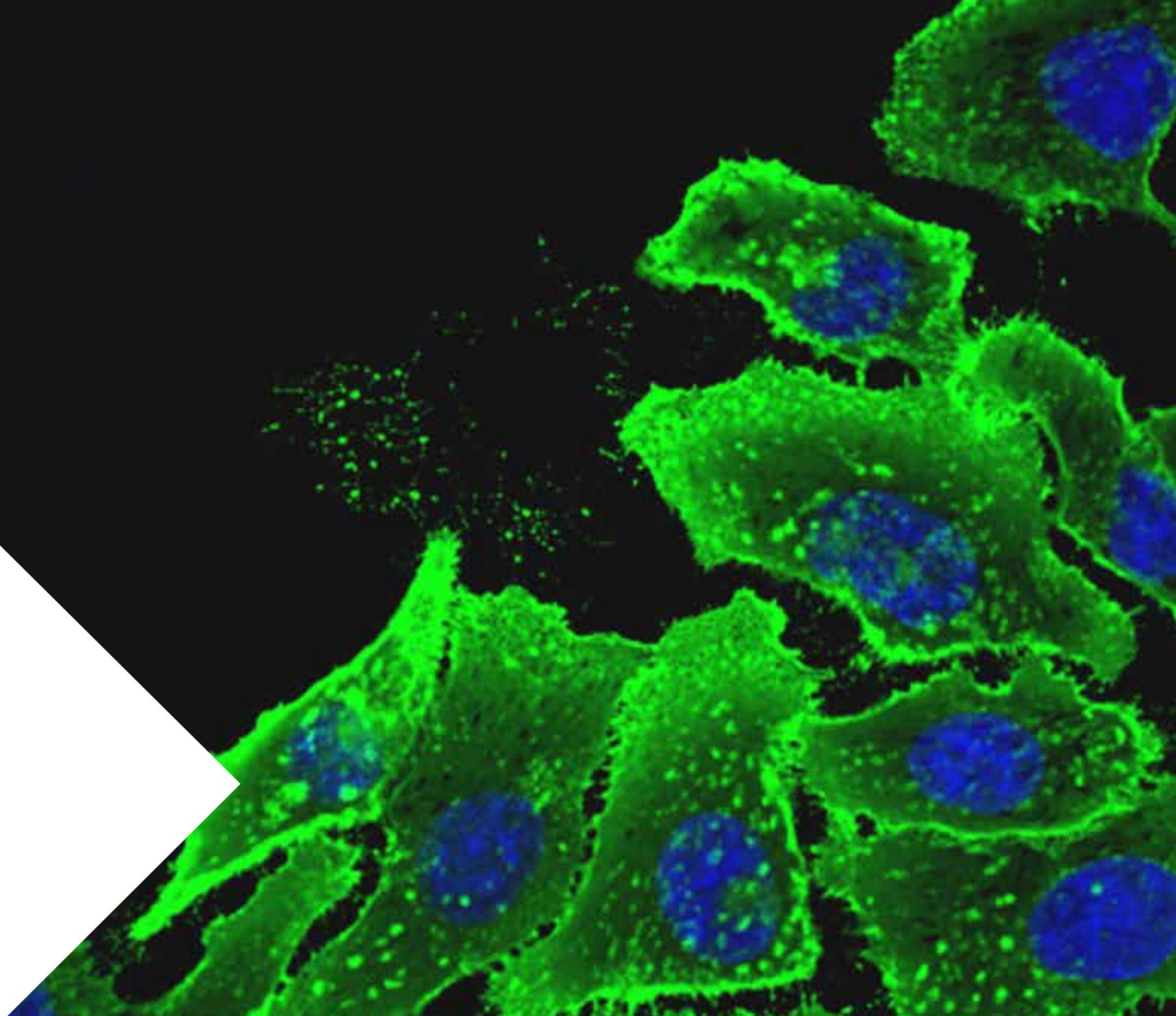
Accuracy analysis of the cuttings after processing with coated cutting punches.

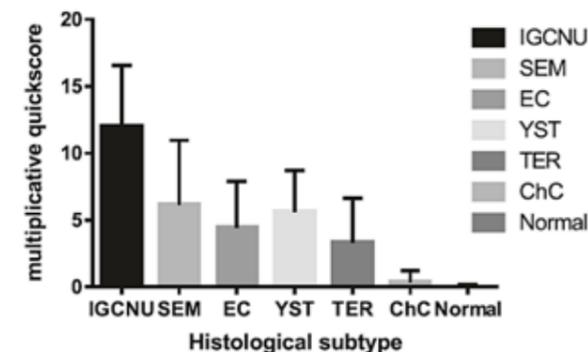


Wear of ogival part of drawing punch.

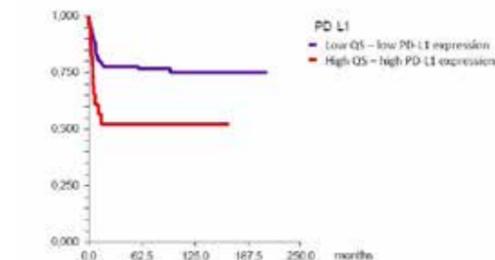


MEDICAL SCIENCES

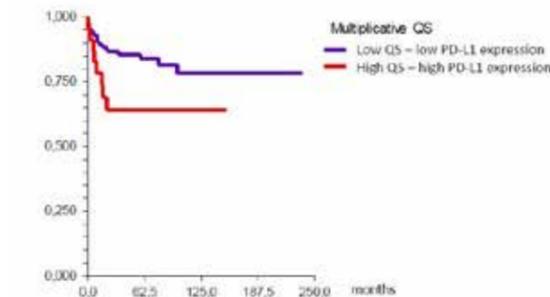




The expression of fibrillin 1 (FBN1) in various histological subtypes of testicular germ cell tumors.



Progression-free survival of patients with testicular germ cell tumors according to expression of PD-L1 in the primary tumor. Patients with low expression of PD-L1 have significantly better progression-free survival compared to patients with high expression of PD-L1.



Overall survival of patients with testicular germ cell tumors according to expression of PD-L1 in the primary tumor. Patients with low expression of PD-L1 have a significantly better survival compared to patients with high expression of PD-L1.

IDENTIFICATION OF BIOMARKERS ASSOCIATED WITH TREATMENT RESISTANCE IN TESTICULAR GERM CELL TUMOURS

Principal investigator:
Applicant organisation:
Participating organisations:

doc. MUDr. Michal Mego, PhD.
Comenius University, Faculty of Medicine
Cancer Research Institute, Slovak Academy of Sciences, Laboratory of Biomedical Microbiology and Immunology; University of Veterinary Medicine and Pharmacy, Department of Urology, Slovak Medical University; St. Elisabeth Cancer Institute
July 2012 – December 2015
170 000 EUR
APVV-0016-11

Term of solution:
Budget from agency:
Project ID:

Subject of research

Testicular germ cell tumours

Objectives of the project

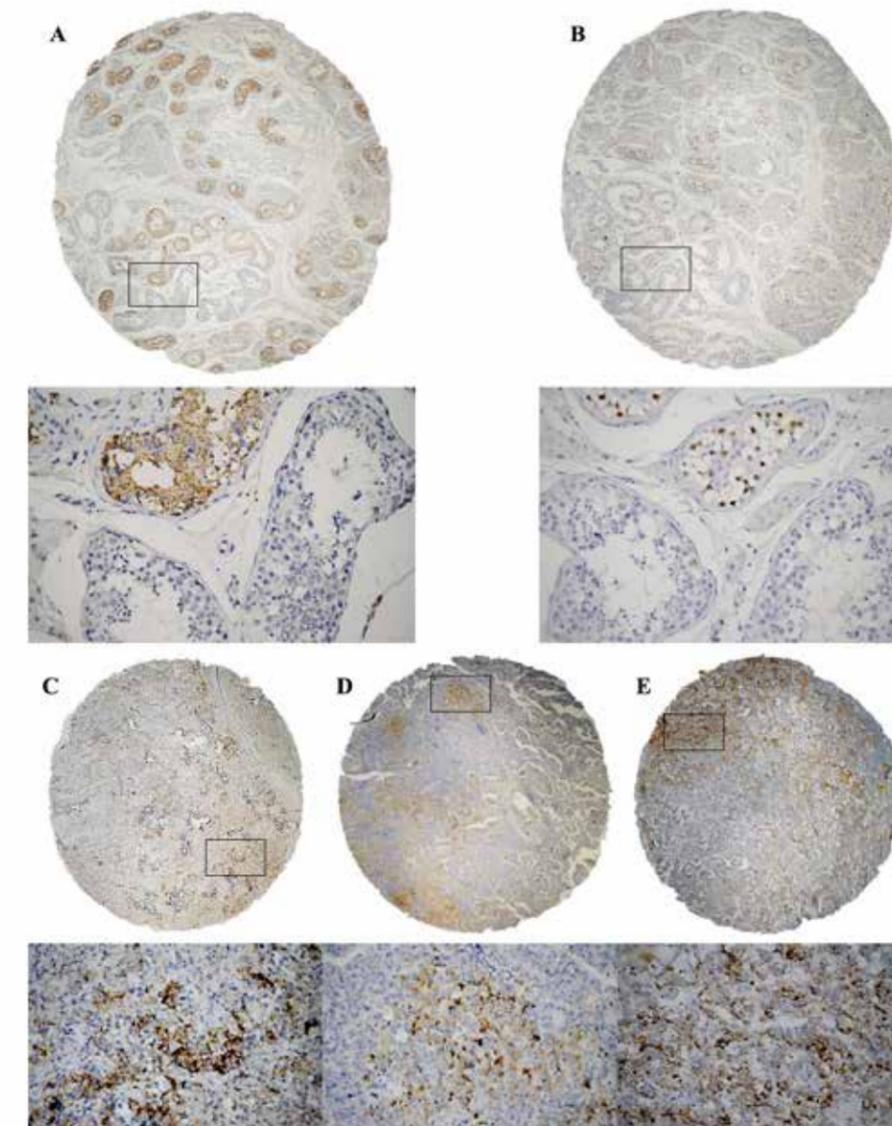
1. To identify biomarkers associated with the failure of standard treatment (etoposide, bleomycin and cisplatin) in TGCTs
2. To establish tissue bank and cell primocultures from TGCTs
3. To assess the association between DNA repair capacity and response to chemotherapy in TGCTs

Results

Testicular germ cell tumours (TGCTs) are extremely chemosensitive tumours with increasing incidence in Slovakia, being the most common cancer in young men. Despite the high cure rate, a small percentage of patients fail to reach sustained remission, and thus succumb to the disease. The goal of this project was to identify biomarkers linked to treatment failure, the establishment of a tissue bank of testicular tumours, as well as to search for an association between DNA damage and its repair on one hand and resistance to the treatment on the other. We identified several new

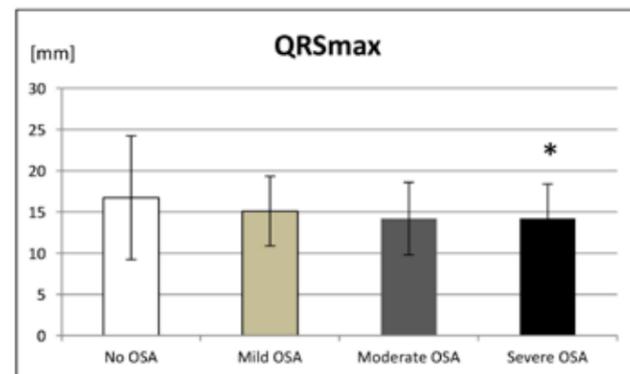
biomarkers associated with chemoresistance, clinico-pathological characteristics, toxicity of chemotherapy and prognosis of patients. The most important of them are carbonic anhydrase CAIX, cytokine profile, protein FBN1, and especially PD-L1 and PARP proteins, which potentially constitute new therapeutic targets for TGCTs. A direct result of the project in terms of clinical practice is the commencement of clinical phase II in order to use PARP inhibitors in the treatment of refractory TGCTs, as well as start-up work on the initiation of an additional Phase II trial aimed at inhibiting PD-L1 in refractory TGCTs. The FBN1 protein was identified as a new marker of intratubular germ-cell neoplasia with potential use in histopathological diagnosis. Creating a tissue bank of TGCTs also creates the possibility of future rapid validation of candidate biomarkers in TGCTs. Identified changes in the efficiency of DNA repair in refractory TGCTs can contribute to a better understanding of the mechanisms of resistance to their subsequent use in the design of new clinical trials based on the use of inhibitors of specific DNA repair proteins / enzymes. The resulting cooperation between the clinical and experimental research laboratories of the project is promising for the continuation of research TGCTs in the future.

Immunohistochemical detection of fibrillin-1 (FBN-1) and OCT3/4 expression in testicular tissues. (A) Intratubular germ cell neoplasia, unclassified type (IGCNU) showed constant and strong cytoplasmic granular FBN-1 positivity (brown colour) with negativity in normal seminiferous tubules with spermiogenesis; (B) OCT3/4 expression in the same sample as in (A) with strong nuclear positivity in IGCNU (brown colour) and negativity in normal tubules. (C) Seminoma with focal strong cytoplasmic FBN-1 positivity; (D) Embryonal carcinoma with focal moderate to strong cytoplasmic FBN-1 positivity; (E) Yolk sac tumour with focal strong cytoplasmic FBN-1 positivity. Original magnification ×40/x400



Benefits for practice

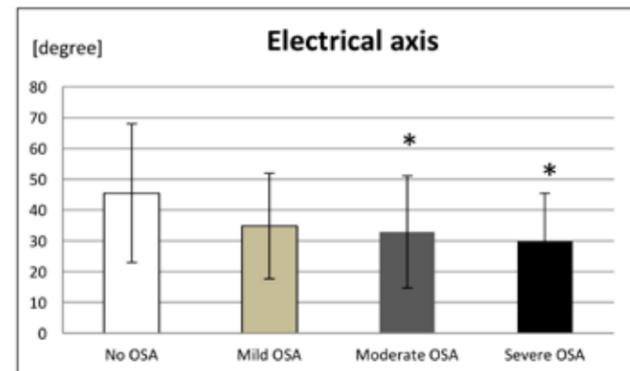
The PARP protein was identified as a potential new therapeutic target in refractory TGCTs, and on the basis of these results, a phase II clinical trial was initiated in order to verify the effectiveness of gemcitabine, carboplatin and PARP inhibitor veliparib in refractory TGCTs. FBN1 expression analysis showed that it is a new and hitherto blank slate marker of intratubular germinal neoplasia (IGCNU), which can be used in IGCNU diagnosis, again the results of research with application in clinical practice. PD-L1 was identified as a novel prognostic factor in patients with TGCTs, and represents a potential new therapeutic target. Based on this result, a phase II clinical trial was initiated to verify the effectiveness of PD-L1 inhibition in refractory TGCTs. The finding that TGCT refractoriness is likely associated with the increased activity of DNA repair nucleases opens up new therapeutic possibilities for the use of DNA repair inhibitors in the treatment of such patients. Experimental data generated by the project represent the basis for further research in this field.



EFFECTS OF HYPOXIA ON MOLECULAR PATHWAYS RELATED TO INCREASED CARDIOVASCULAR RISK IN PATIENTS WITH SLEEP APNEA AND THEIR REVERSAL BY THERAPY

Principal investigator:
Applicant organisation:
Participating organisation:
Term of solution:
Budget from agency:
Project ID:

prof. MUDr. Ružena Tkáčová, DrSc.
Pavol Jozef Safarik University in Kosice
International Laser Center, Bratislava
July 2012 – December 2015
160 000 EUR
APVV-0134-11



Subject of research

Obstructive sleep apnoea (OSA) is associated with metabolic syndrome, arterial hypertension and increased cardiovascular risk. Clinical studies also suggest the presence of atherogenic dyslipidemia and impairment of endothelial-dependent vasodilation in patients with OSA. Nevertheless, many questions regarding the OSA-related mechanisms responsible for these adverse clinical outcomes remain unanswered.

Aims of the project

Our aims were to analyse a) the effects of the interactions of the selected single nucleotide polymorphisms and chronic intermittent hypoxia on lipid metabolism in genetic association studies; b) relationships between the severity of nocturnal hypoxaemia in patients with OSA and various phenotypic features of increased cardiovascular risk in clinical cohort studies; and c) molecular mechanisms related to hypoxic activation of inflammatory and apoptotic pathways in adipose tissue in OSA, and *in vitro*.

Results

1) Genetic association studies

1.1 Among OSA patients with the high-risk ε4 APOE genotype, those with the most severe nocturnal hypoxia had significantly higher triglyceride and lower

HDL cholesterol levels compared with nonhypoxic ε4 subjects. Therefore, OSA has an adverse effect on lipid parameters over and above the effects carried by the APOE genotype. Our next study indicated that both the ε4 APOE genotype and the metabolic syndrome are independently related to smaller LDL size in patients with OSA.

1.2 Diabetic patients homozygous for the A-allele of SLC47A1 had a twofold higher reduction in HbA1c in response to metformin treatment compared to patients carrying the G-allele. In addition, CAPN10 gene polymorphism was related to the therapeutic response to metformin.

2) Analysis of the relationships between the severity of nocturnal hypoxaemia in OSA and various phenotypical features of increased cardiovascular risk

2.1 Patients with OSA displayed a combination of changes in QRS complex morphology, a leftward shift of EA, low QRS voltage and fQRS, suggestive of depolarization sequence deterioration that might be indicative of considerable electrical remodelling (Fig. 1).

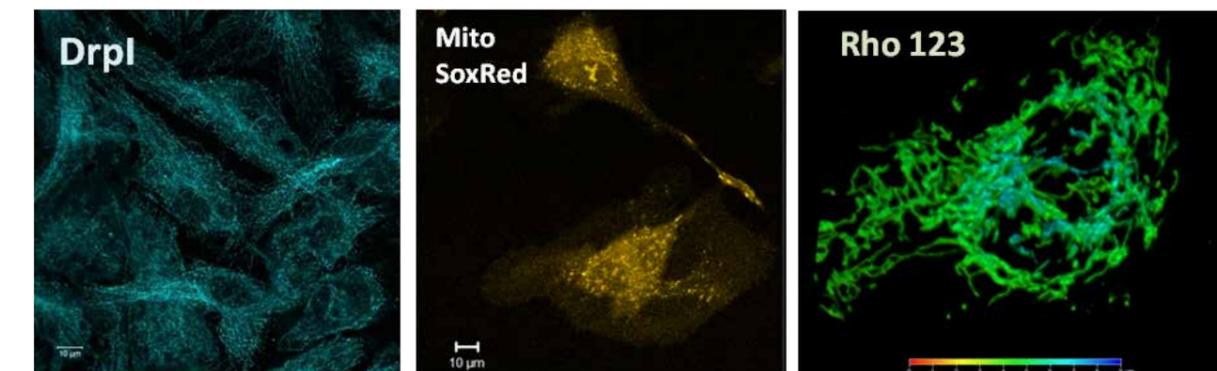
2.2 Patients with moderate-to-severe OSA had increased resting energy expenditure (REE) paralleled by impaired insulin sensitivity. The severity of nocturnal intermittent hypoxia reflected by oxygen desaturation index was an independent predictor of REE/fat free mass and HOMA-IR.

2.3 Compared to subjects with no OSA, patients with

Values of the maximum QRS spatial vector magnitude (QRSmax) and the electrical axis (EA) in patients with different severity of obstructive sleep apnoea (OSA).

* p < 0.05 as compared to the no OSA group

HCAEC cells: the distribution of Drp1 (fission/fusion) regulatory protein, detection of oxidative stress in mitochondria by MitoSoxRed, and mitochondria mass detected by Rhodamine 123.



severe OSA had significantly higher carotid intimo-medial thickness and increased arterial stiffness. Both parameters reflect subclinical atherosclerosis and are associated with OSA severity and hypoxia.

2.4 Osteoporosis of the hip is associated with increased circulatory levels of osteoprotegerin in patients with chronic obstructive pulmonary disease. Osteoprotegerin might serve as a biomarker of this comorbidity related to respiratory diseases.

2.5 Underweight patients with chronic obstructive pulmonary disease had increased REE, reduced serum and adipose tissue leptin and increased adiponectin, suggesting the role of adipokines in energy imbalance in cachexia related to respiratory diseases.

3) Analysis of molecular mechanisms related to the activation of inflammatory and apoptotic pathways

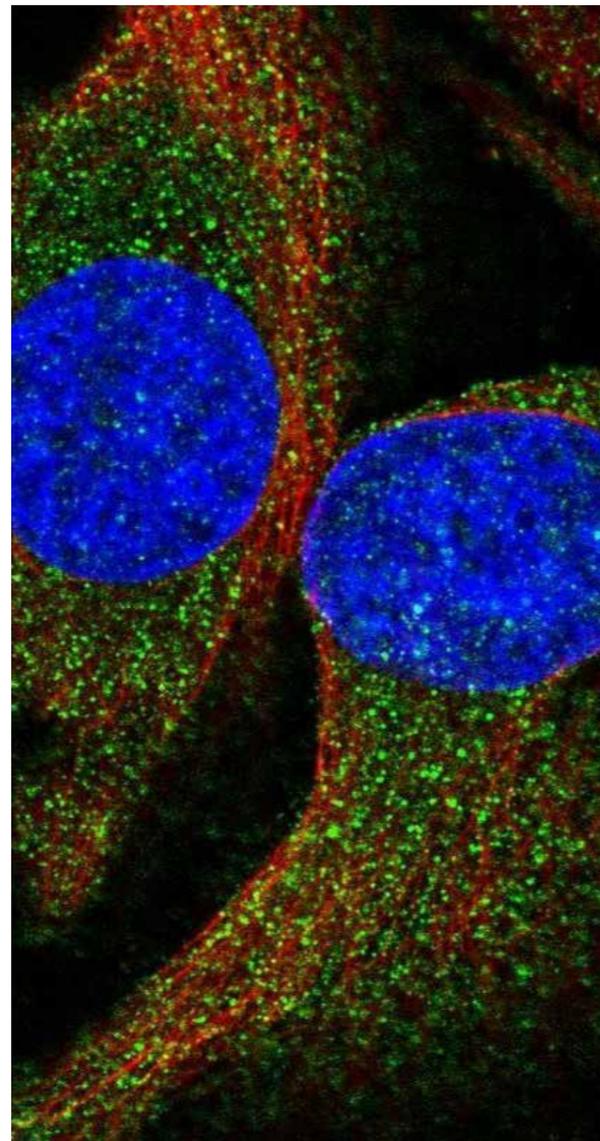
3.1 Patients with OSA had reduced adipose tissue expressions of CD40, MKK4 and JNK compared to patients without OSA; nevertheless, NFκB1, NFκB2 and TNFα mRNA were not related to OSA. Thus serum sTNF-RII levels were related to chronic intermittent hypoxia, they were not linked to increased adipose tissue inflammation.

3.2 In *in vitro* studies we presented a model that can predict the multimerization of G-quadruplexes – structures that are an essential component of regulatory mechanisms involved in the expression of the respective genes including HIF1α, VEGF, c-KIT a Bcl-2.

3.3 We identified the distribution of Drp1 (fission/fusion) regulatory protein in mitochondria in *in vitro* studies in human endothelial cell lines (Fig. 2). Using ABT263, a BH3 mimetic molecule inhibiting Bcl2, we showed that Hyp binds to Bcl2 in the hydrophobic site for BH3 mimetic molecules.

Benefits for practice

The project's findings contribute to the stratification of patients with sleep-disordered breathing and high cardiovascular risk, and therefore to the optimisation of diagnostic and therapeutic interventions. We expect that these results will also contribute to improved preventive strategies and to the improved prognosis of such patients.



Anti-VASP (vasodilator-stimulated phosphoprotein) antibody.

POSSIBILITIES OF STENT RESTENOSIS AND THROMBOSIS PREDICTION IN PATIENTS WITH ACUTE CORONARY SYNDROME UNDERGOING PERCUTANEOUS CORONARY INTERVENTION

Principal investigator: prof. MUDr. Peter Kubisz, DrSc.
 Applicant organisation: Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin
 Term of solution: July 2012 - December 2015
 Budget from agency: 112 000 EUR
 Project ID: APVV- 0222-11

Subject of research

The project was focused on the laboratory monitoring of platelet reactivity in patients with acute myocardial infarction treated with dual antiplatelet therapy in the following combination: acetylsalicylic acid and ADP receptor (type P2Y12) antagonist (clopidogrel, prasugrel, tikagrelor), undergoing percutaneous coronary intervention (PCI) with coronary stent implantation. The objective was chosen due to the need for the elucidation of repeated thrombotic episodes after successful PCI described in the literature. The variability in platelet response to antiplatelet drugs was the supposed cause of this phenomenon.

Aims of the project

The aims of the project were to reveal the prevalence of the insufficient response to P2Y12 antagonists, to identify predictive markers of coronary stent thrombosis and restenosis in patients with MI after PCI and to contribute to the creation of a laboratory monitoring algorithm through the laboratory monitoring of platelet functions.

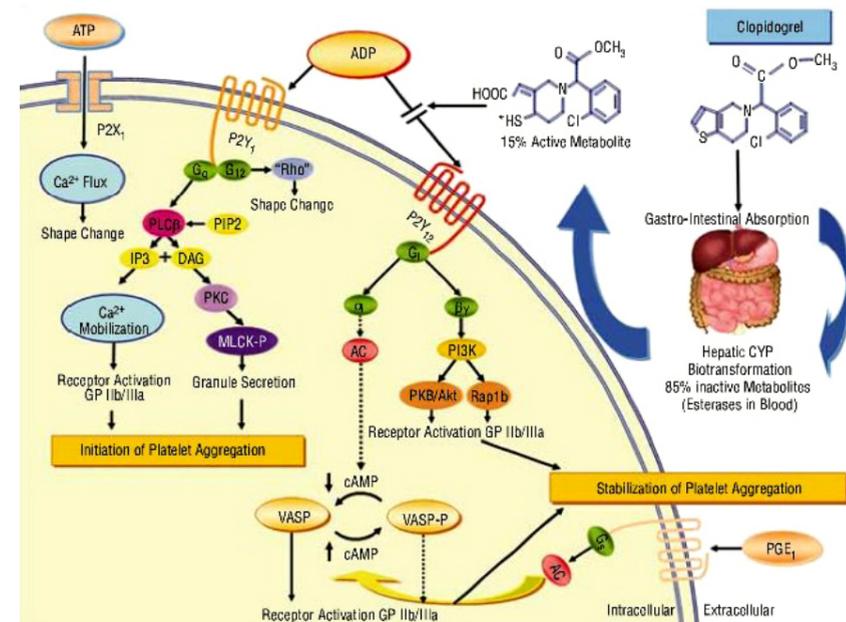
Results

102 patients with acute MI (67 STEMI, 35 non-STEMI), undergoing PCI, treated at the Clinic of Internal Medicine I, JFM CU and UHM were included in this study. Light transmission aggregometry with specific induction and VASP phosphorylation flow cytometric

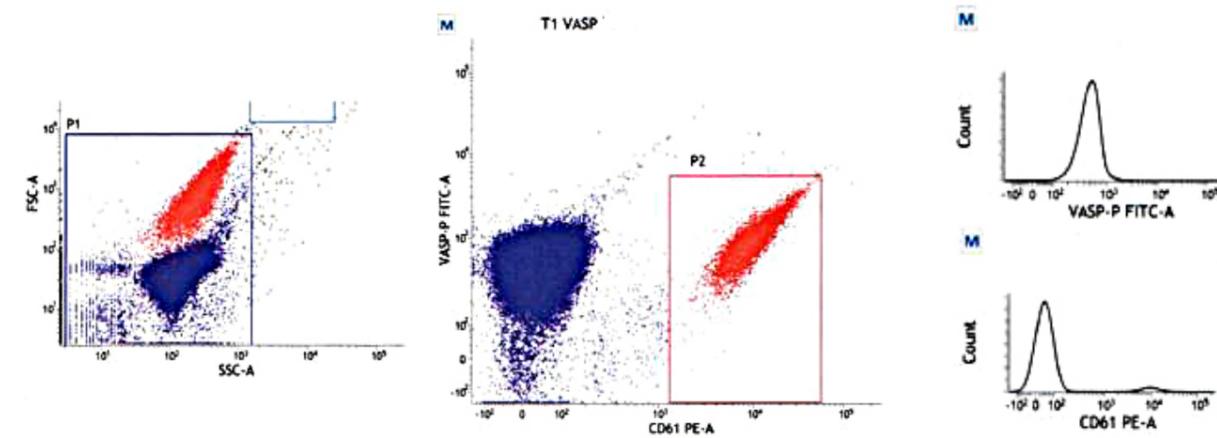
analysis in the monitoring of antiplatelet treatment effectiveness in the clinical practice proved to be very useful. Significantly stronger platelet inhibition in treatment with the new P2Y12 antagonist (prasugrel) compared to the conventional clopidogrel using both mentioned methods during the acute phase as well as during secondary thromboprophylaxis was confirmed. Although the primary supposition of the significant impact of diabetes mellitus type 2 on platelet reactivity was not confirmed in our study, the higher long-term mortality of diabetics with acute coronary syndrome was found. The project's results were published in 10 scientific papers in journals with impact factor.

Benefits for practice

This project confirmed that the laboratory monitoring of on-treatment platelet reactivity succeeds in the identification of patients with insufficient response. The optimisation of treatment based on laboratory monitoring and the improvement of the patient's prognosis is a good perspective for the future. On the other hand, extremely strong platelet inhibition during treatment with new P2Y12 antagonists can be associated with the risk of bleeding complications. To date, routine laboratory monitoring is not included in the current ACS management guidelines; however, based on our data, its implementation in clinical practice should be considered.



Platelet receptor P2Y12.



VASP flow cytometry results.



Coronography of the patient with acute coronary syndrome.

PROTON RADIATION-INDUCED CARDIOVASCULAR TOXICITY (PATHOPHYSIOLOGY AND PREVENTION)

Principal investigator: prof. MUDr. Ján Slezák, Ph.D., DSc., FIACS
 Applicant organisation: Institute for Heart Research, Slovak Academy of Sciences
 Participating organisation: Slovak Medical University
 Term of solution: July 2012 – December 2015
 Budget from agency: 170 000 EUR
 Project ID: APVV-0241-11

Subject of research

Cardiovascular diseases and cancer are the leading causes of death in the modern industrialized world. The treatment of cancer patients often requires radiation therapy. However, even with the most sophisticated radiological techniques, the exposure of normal healthy tissue adjacent to the tumour is sometimes unavoidable. In the case of chest irradiation, it can affect the heart, blood vessels and lungs with adverse side effects and symptoms that occur as a pathological entity known as “radiation-induced heart disease” (RIHD). RIHD is a major source of morbidity and mortality. RIHD pathogenesis is still largely unknown and effective therapy is not available. Finding ways to avoid these problems was the subject of this research.

Objectives of the project

- to examine the effect of ionizing radiation on the functioning of the cardiovascular system in normal and pathological conditions
- to characterize the adverse effects of radiation on the cardiovascular system
- based on results, to find the best options to prevent potential adverse effects of ionizing radiation
- to implement the results into practice, to disseminate them through lectures, workshops, seminars and conferences between scientists, teachers and clinicians, and thus to improve the quality of life of oncology patients.

Results

The exposure of the heart and blood vessels to radiation leads to a chronic increase in reactive oxygen species and nitrogen oxide, which act as an intracellular signal to change cell function, induce chronic inflammation, heart dysfunction and failure. Our research showed that this process can be modulated by therapy to affect processes taking place in the damaged tissue.

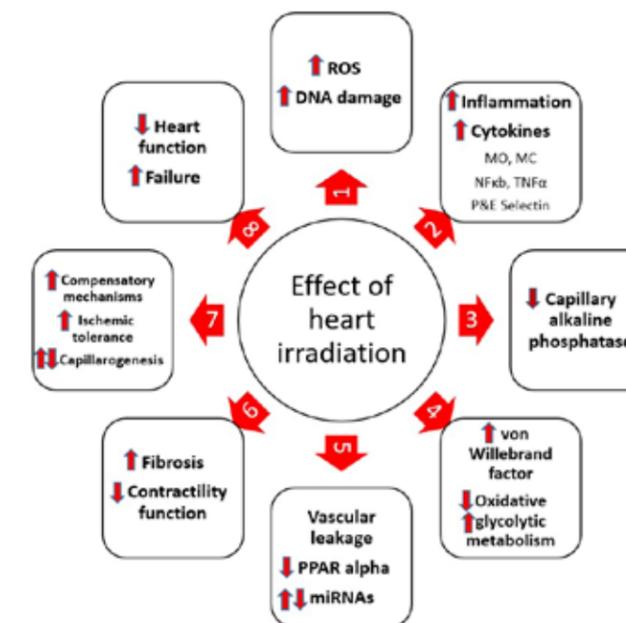
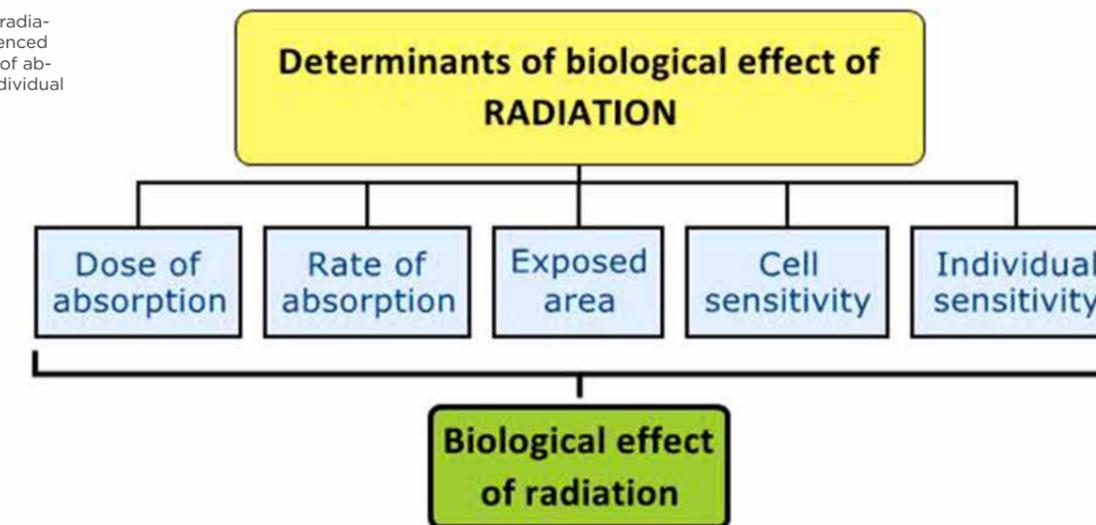
Overview

- Characterization of the mechanisms of radiation injury to the cardiovascular system
- Characterization of radiation-induced heart disease
- Identification of the pathophysiological processes, factors and markers of RIHD related to heart function after irradiation
- Identification of morphological, cellular and subcellular characteristics of the heart after irradiation
- Selection of substances involved in molecular mechanisms of protection against radiation damage (Aspirin, Atorvastatin, Sildenafil, Tadalafil, Enbrel)
- From the pathophysiological results, the increased resistance against myocardial ischemia in the irradiated heart after 6 weeks was notable and indicated a certain level of radiation-induced preconditioning.
- Testing the effectiveness of the drugs action revealed a positive protective effect of aspirin (anti-inflammatory and antithrombotic action) and statins (indirect NO donor). The manipulation of PPAR and the miRNA, administration of anti-TNF, inhibition of NFkB and phosphodiesterase 5 also seems to be effective.

Benefits for practice

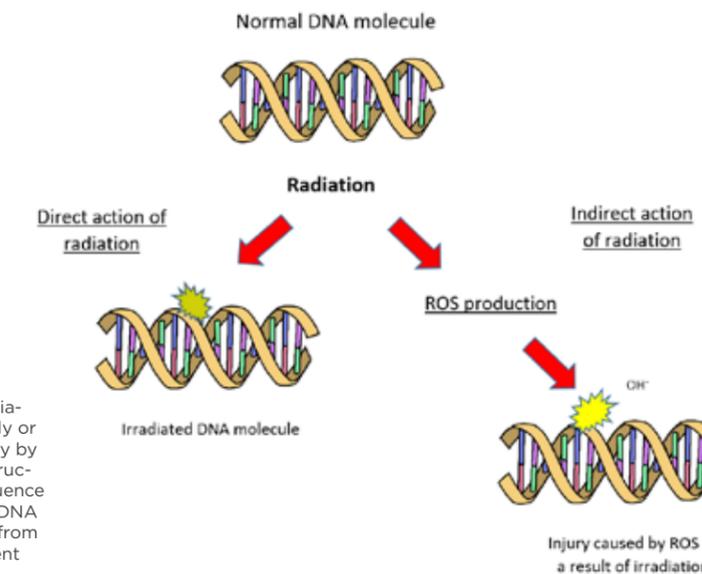
- Protection of normal tissues from injury induced by radiation may increase the therapeutic benefit of radiation therapy.
- Treatment that specifically interferes with the mechanism of radiation injury, namely anti-inflammatory and fibrinolytic drugs and some others (aspirin, statins, NO donors compounds with antioxidant properties, PPAR ligands, manipulation the mi-RNA, anti -TNF, NFkB inhibitors, phosphodiesterase inhibitors 5) has a protective effect against RIHD.
- In the initial phase after irradiation (6 weeks), a cascade of adaptive processes temporarily activates and compensates for the adverse effects of radiation and maintains the functioning of the heart.
- The priority is the demonstration that the modulation of the characteristics of cytokines and miRNA expression can upregulate the proteins involved in the protection of the heart and limit the extent of injury. The most effective procedure should be specified before the clinical use of the outcomes.

The determinants of the biological effects of radiation. The biological effect of radiation is influenced by many factors, including the dose and rate of absorption, exposed area, cell sensitivity and individual sensitivity.



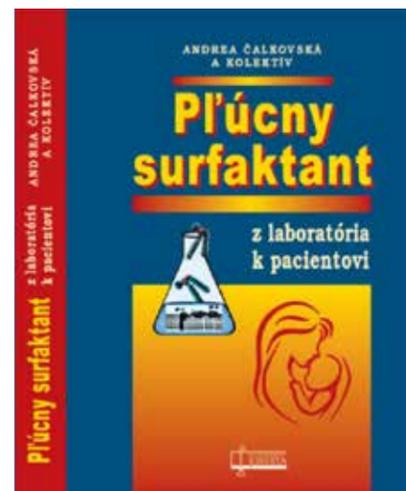
Effect of radiation on the heart. Changes in an irradiated heart were observed at molecular and structural levels. Radiation of the heart induces increased levels of ROS leading to DNA damage, increased levels of inflammatory cells, macrophages, monocytes and cytokines, NF B and TNF levels. Furthermore, the alkaline phosphatase level of capillaries decreases. In the early stages, the compensatory mechanisms to maintain normal heart function are activated. Later, increased fibrosis and decreased heart function lead to heart failure.

Mechanisms of DNA damage after irradiation. Radiation can damage DNA directly or indirectly. Radiation affects DNA directly by breaking chemical bonds in the DNA structure leading to the change of DNA sequence and mutations. In the second case, the DNA molecule is affected by ROS produced from the disruption of water molecules present in cells.





Testing of surfactant properties was carried out by using a unique pulsating bubble surfactometer, which imitates inspiration and expiration during the respiratory cycle.



Some of the results obtained with the support of the project were published in a scientific monograph: *Pulmonary surfactant - from the laboratory to the patient.*

INACTIVATION OF ENDOGENOUS SURFACTANT: MOLECULAR, TISSUE AND FUNCTIONAL ASPECTS OF INJURY TO THE RESPIRATORY SYSTEM

Principal investigator: prof. MUDr. Andrea Čalkovská, DrSc.
 Applicant organisation: Comenius University in Bratislava, Jessenius Faculty of Medicine in Martin
 Term of solution: July 2012 – December 2015
 Budget from agency: 170 000 EUR
 Project ID: APVV-0435-11

Subject and aims of research

We analysed surfactant inactivation in certain pathological conditions (e.g., meconium aspiration syndrome MAS, lipopolysaccharide LPS-induced fever) and the possibility of reversing these conditions by an exogenous surfactant and other pharmacological treatment, as well as the question of whether surfactant inactivation can be included in the increased contractility of smooth airway muscle and thus included in the pathogenesis of asthma among others.

The main aim of the first phase was to prove the hypothesis that the combination of an exogenous surfactant with agents inhibiting certain signal pathways will have a more pronounced effect on pulmonary function improvement and MAS accompanying inflammation processes than monotherapy with a surfactant, with attention paid to molecular mechanisms of the particular combined treatment. The functional and molecular responses of different treatments were also investigated.

The aim of the second phase was to evaluate the changes in the endogenous pulmonary surfactant in a rat model of LPS-induced fever.

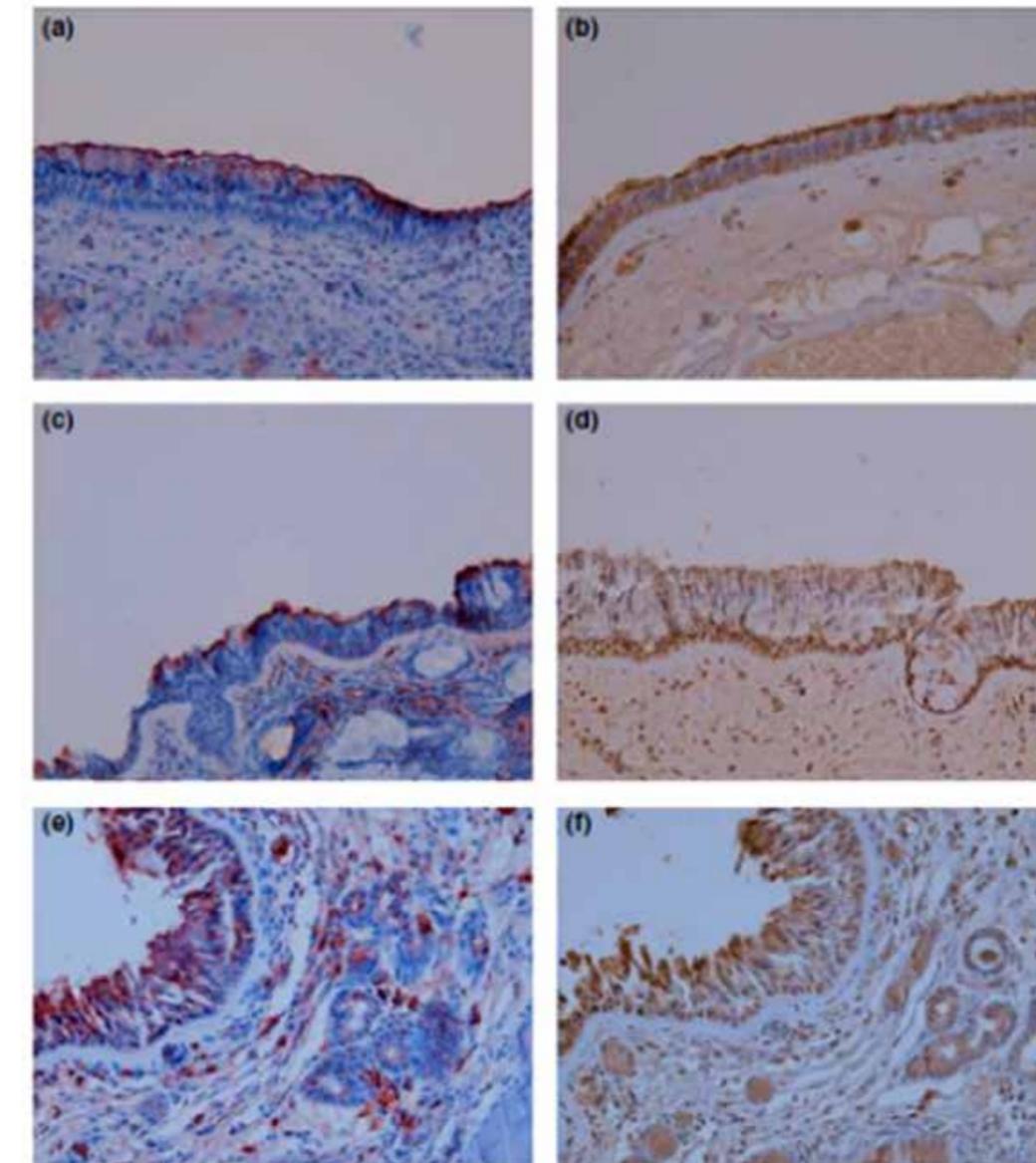
The aim of the third phase was to investigate the physiological role of the surfactant in the airways, to prove the hypothesis that a surfactant has a relaxing effect on the airway smooth muscle (of trachea and bronchi), and to provide indirect evidence that surfactant inactivation may play a role in conditions with increased contractility. Another aim was to evaluate potential

differences in the activity of preparations of exogenous surfactants that differ in their composition and thus also in their physiological and pharmacological activities.

Results

The project proved the inflammatory aspect of meconium aspiration syndrome, and the hypothesis that a combination of anti-inflammatory treatment (glucocorticoids, N-acetylcysteine, a soluble nitric oxide donor SNAP, superoxide dismutase, an inhibitor of NF-kappa B and the anti-IL-8) with surfactant instillation has a more positive effect on the respiratory parameters and the markers of inflammation and oxidative stress than a surfactant as monotherapy. LPS-induced fever leads to changes in all surfactant-specific proteins. Changes in proteins related to local immune mechanisms (SP-A, SP-D) are probably evoked by the general inflammatory response of the body after exogenous pyrogen administration. Changes in proteins related to surface activity (SP-B and SP-C) might reflect the effort to stabilize the lungs during breathing pattern alterations in thermal challenge. The results also showed that surfactants play an important role in the airways by relaxing the bronchial smooth muscle. All surfactant proteins, including SP-B and SP-C, have key immunological functions in the upper airways. In addition to publications in international peer-reviewed journals, some results became part of the monograph

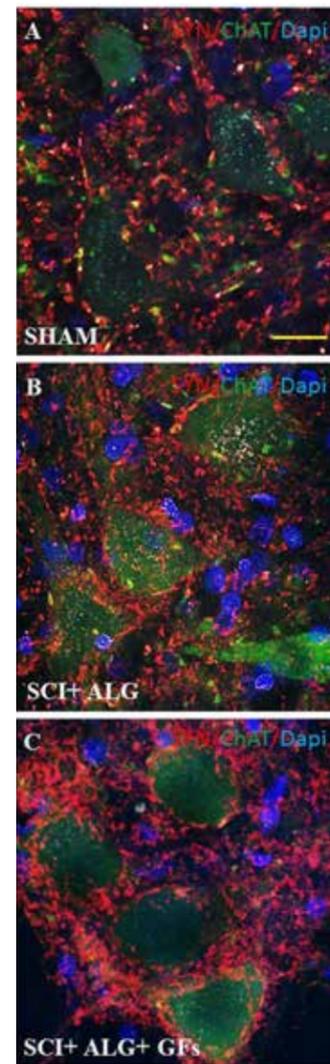
Immunostaining for surfactant proteins A and D in nasal mucosa in patients with chronic rhinosinusitis with nasal polyps (a, b), with chronic rhinosinusitis without nasal polyps (c, d) and in control group with pathogenic bacteria (e, f). magnification x40 (from Uhliarova et al., *Clin Otolaryngol* 2016)



awarded by the Slovak Pediatric Society and Slovak Literary Fund. They were presented at three invited lectures. Several diploma students and 7 PhD students, two of whom successfully defended their dissertations, participated in the project. The project improved cooperation between the Department of Physiology with other Slovak and foreign institutions. There have been five popularization events, one training course and one symposium at the International Congress organized.

Benefits for practice

The project addresses the issue of basic research in the field of pulmonary surfactants and has brought many original findings, but its immediate practical application was not expected. The benefits for clinical medical practice could be the results related to the treatment of meconium aspiration syndrome. Here, it was confirmed that inflammation is an important part of the pathogenesis of MAS, and thus combined treatment with an exogenous surfactant and anti-inflammatory substances was more effective than monotherapy with a surfactant. The results also confirm the role of surfactants in the physiology of the upper and lower respiratory airways. It means that exogenous surfactant preparations could be used in the future in the treatment of airway diseases, and not only in diseases affecting lung parenchyma.



Distribution of synaptophysin positive vesicles (red) in the area of ChAT positive motoneurons (green) of the ventral horns.

MODIFIED BIOMATERIALS AND CELL THERAPY FOR PROMOTING REGENERATION OF INJURED SPINAL CORD

Principal investigator: MVDr. Daša Čížková, DrSc.
 Applicant organisation: Institute of Neurobiology, Slovak Academy of Sciences
 Participating organisations: Laboratoire Protéomique, INSERM U1192- Université Lille 1, (non- financed APVV) France
 Regenerative Medicine and Stem Cell (RMSC) Research Center Avram and Stella Goldstein-Goren, Department of Biotechnology Engineering Ben-Gurion University of the Negev, Beer Sheva, Israel
 Term of solution: July 2012 – December 2015
 Budget from agency: 160 000 EUR
 Project ID: APVV-0472-11

Subject of research

The subject of this research was the use of a special biodegradable implant developed on an alginate basis with the controlled release of key trophic factors and bioactive substances in the treatment of traumatic spinal cord injury in a rat.

Aim of the project

This project focused on 1. The preparation of “smart” alginate biomaterial which is capable of the long-term binding and release of epidermal growth factor (EGF) and a basic fibroblast growth factor 2 (bFGF); 2. The analysis of the proliferation and differentiation of 3D biomaterials colonized by neural progenitor cells (NPC) *in vitro*; and 3. The monitoring of the neuroprotective effect of injected biomaterial used for bridging the central lesion after experimental spinal cord injury (SCI) in a rat. The correlation of the results obtained from behavioural tests and histology with molecular level analyses enabled us to assess the effectiveness of the selected therapy and to clarify the mechanisms underlying the efficacy of trophic factors and biomaterials, so that they can be applied in the treatment of SCI.

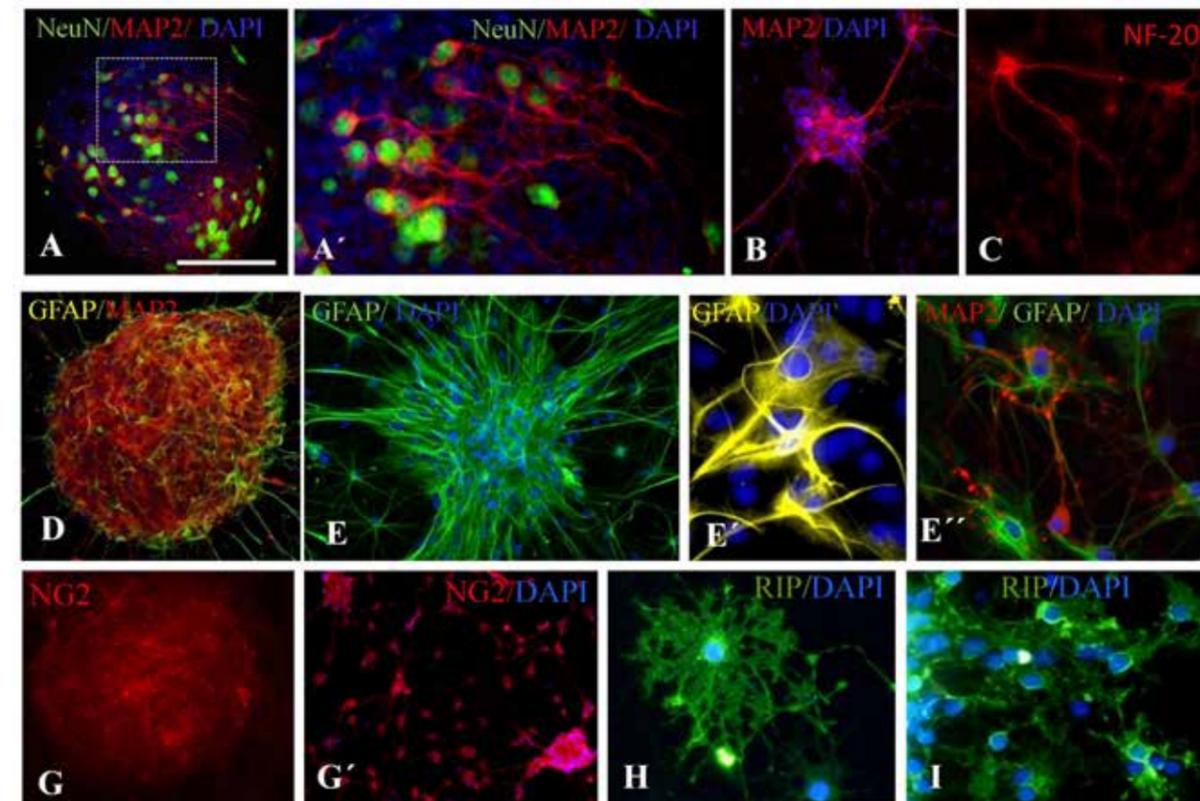
Results

Our experimental studies confirmed the neurogenic activity of biomaterial prepared on the basis of alginate sulphate, which is capable of binding and then progressively releasing bFGF and EGF. We demonstrated that in the course of 21 days such enriched biomaterial progressively releases a sufficient amount of bioactive molecules which are important for the neuronal differentiation of stem and progenitor cells. We confirmed that alginate-based 3D

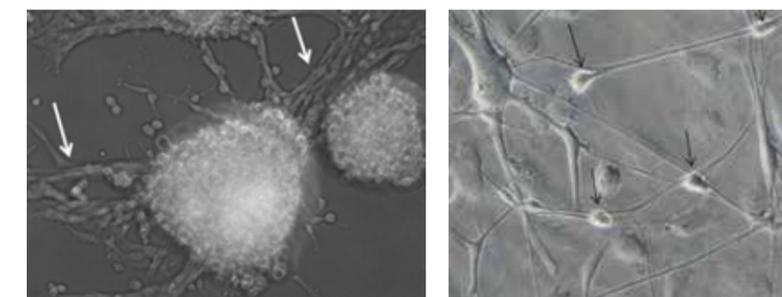
biomaterial providing a complex of bioactive molecules creates the optimum environment for the long-term survival and ultimate differentiation of co-cultivated neural progenitors *in vitro*, and is therefore suitable biomaterial for transplantation studies. We subsequently implanted 3D biomaterial in a rat with SCI. Our results confirmed that the increased biological availability of the key factors EGF and bFGF from the alginate transplanted in the central lesion led to the marked stimulation of neuroregenerative processes. We observed an increased amount of preserved spinal cord tissue with increased numbers of surviving neurons and synaptic vesicles above and below the central lesion, as well as the presence of corticospinal fibres and blood vessels at the lesion site. Inflammation processes mediated by activated microglia were partially suppressed, although the astrocyte response was similar to that in rats after injury but without biomaterial therapy. These results indicate the possibility of the therapeutic application of active alginate implants with a complex of bioactive molecules for the treatment of SCI.

Benefits for practice

Work on this project has produced nine publications in foreign current contents journals (IF 3-5), and more than 20 publications in foreign peer-reviewed or non-reviewed scientific journals or conference proceedings or abstracts. The project results have also been presented at scientific meetings in Slovakia and abroad. Continuity in the project has produced an application for a US patent and continuing research into biomaterials in correlation with CNS damage and malfunction. Our efforts have led to the granting of APVV and EU projects.

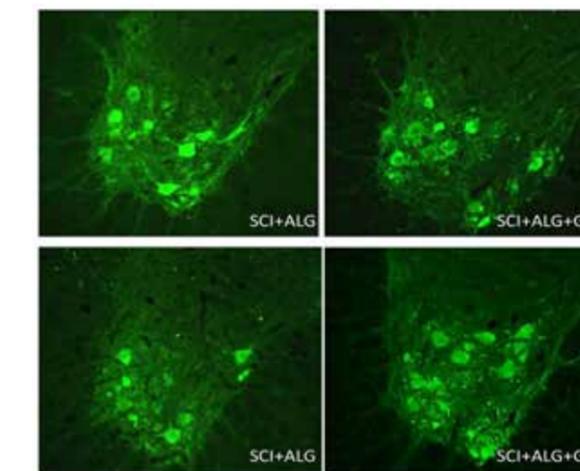


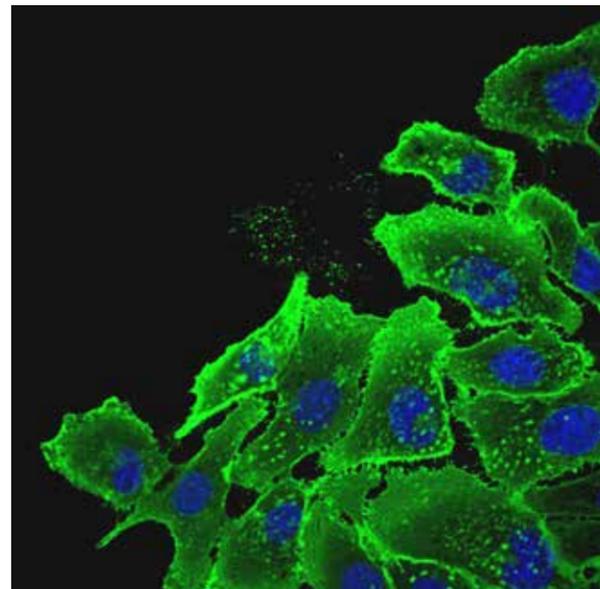
Immunocytochemical analyses of NPC differentiation in 2D cultivation mode. Occasional clusters of neurons expressing MAP2 (red) and NeuN (green), GFAP-positive (D,E), NG2 positive (G,G') glia visible in neurospheres (A, A') on days 7-10. Final differentiation of MAP2 and NF-200-positive neurons (B, C), GFAP-positive astrocytes (E') and RIP-positive oligodendrocytes (H, I) on day 21.



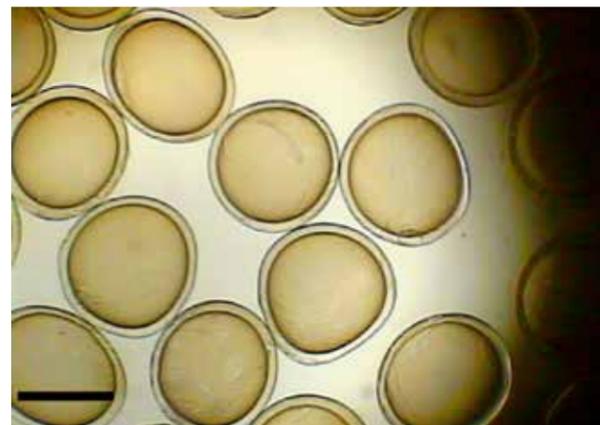
Release patterns of (A) bFGF and (B) EGF from the affinity-binding alginate scaffold; the scaffold was seeded with NPCs (dashed lines) or without NPCs (solid lines). Representative phase-contrast images of neurospheres or confluent single-cell population, cultured in alginate scaffold on day 10 or 21.

Transverse sections revealing ChAT positive motoneurons located rostrally and caudally to the lesion site in SCI+SAL, and SCI+ALG+GFs experimental groups.





Immunofluorescence staining of living cells that express CA IX biomarkers on the cell surface.



Optical microscopy image of microcapsules containing the encapsulated CA IX-specific antibody. The scale bar corresponds to 0.5 mm.

CARBONIC ANHYDRASE IX AS A FUNCTIONAL COMPONENT OF CANCER PROGRESSION: THE ROLE IN EPITHELIAL-MESENCHYMAL TRANSITION AND INTERCELLULAR SIGNALING

Principal investigator: prof. RNDr. Silvia Pastoreková, DrSc.
 Participating organisation: Institute of Virology, Biomedical Research Center, Slovak Academy of Sciences
 Participating organisation: Polymer Institute, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 210 000 EUR
 Project ID: APVV-0658-11

Subject of research

The project focused on the investigation of molecular mechanisms utilized by cancer cells to adapt to stresses in the microenvironment of tumour tissues and to acquire metastatic propensity. Our interest was centred on the enzyme carbonic anhydrase IX (CA IX) that was identified and characterized with our major contribution. CA IX is a clinically relevant biomarker of aggressive tumours and a promising molecular target for anticancer therapy. It is present particularly in hypoxic (i.e., insufficiently oxygenated) tumours and is a key component of the molecular machinery which regulates pH and supports the survival of cancer cells in acidosis generated by oncogenic metabolism.

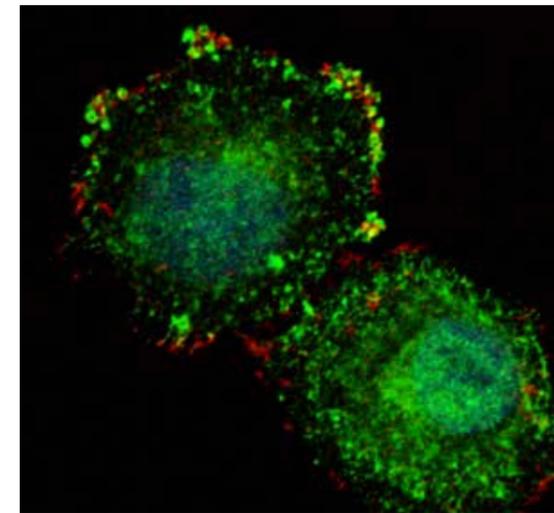
Aim of the project

The project was aimed at the elucidation of the signalling role of the hypoxia-induced CA IX in the epithelial-mesenchymal transition (which is an integral part of the metastatic cascade) and cell-to-cell communication, and at the development of an innovative anti-cancer strategy based on microparticles with the controlled release of the CA IX-selective anticancer compounds.

Results

(a) We demonstrated that CA IX contributes to the regulation of epithelial-mesenchymal transition through

the control of focal adhesion during migration/invasion, and that this function requires a catalytic domain. At the same time, through a proteoglycan-like domain, CA IX regulates adhesion and the spread of tumour cells to solid support. (b) We found that these CA IX functions depend on correct post-translational modifications including glycosylation and phosphorylation and on the proper cleavage of the extracellular domain of this transmembrane protein (ectodomain). (c) We showed that the CA IX ectodomain represents a paracrine signal modulating tumour phenotypes and intracellular pathways via the activation of transcription factors linked with stemness and secretome modulation. (d) CA IX-mediated adhesion can be inhibited by an M75 monoclonal antibody binding to the N-terminal part of the molecule, whereas a VII/20 antibody specific for the catalytic domain can inhibit migration/invasion. (e) We prepared microcapsules of continuously releasing antibodies specific for CA IX predominantly in acidic conditions typical for tumour tissues. The antibodies retain binding and internalization properties and are therefore potentially applicable to anti-tumour immunotherapy. (f) We demonstrated that CA IX supports the expression of glycolytic enzymes and regulates the metabolism of tumour cells exposed to hypoxia. (g) Acidosis decreases the shedding of the CA IX ectodomain from the surface of tumour cells and thereby presumably supports the survival of cells in stressful conditions.

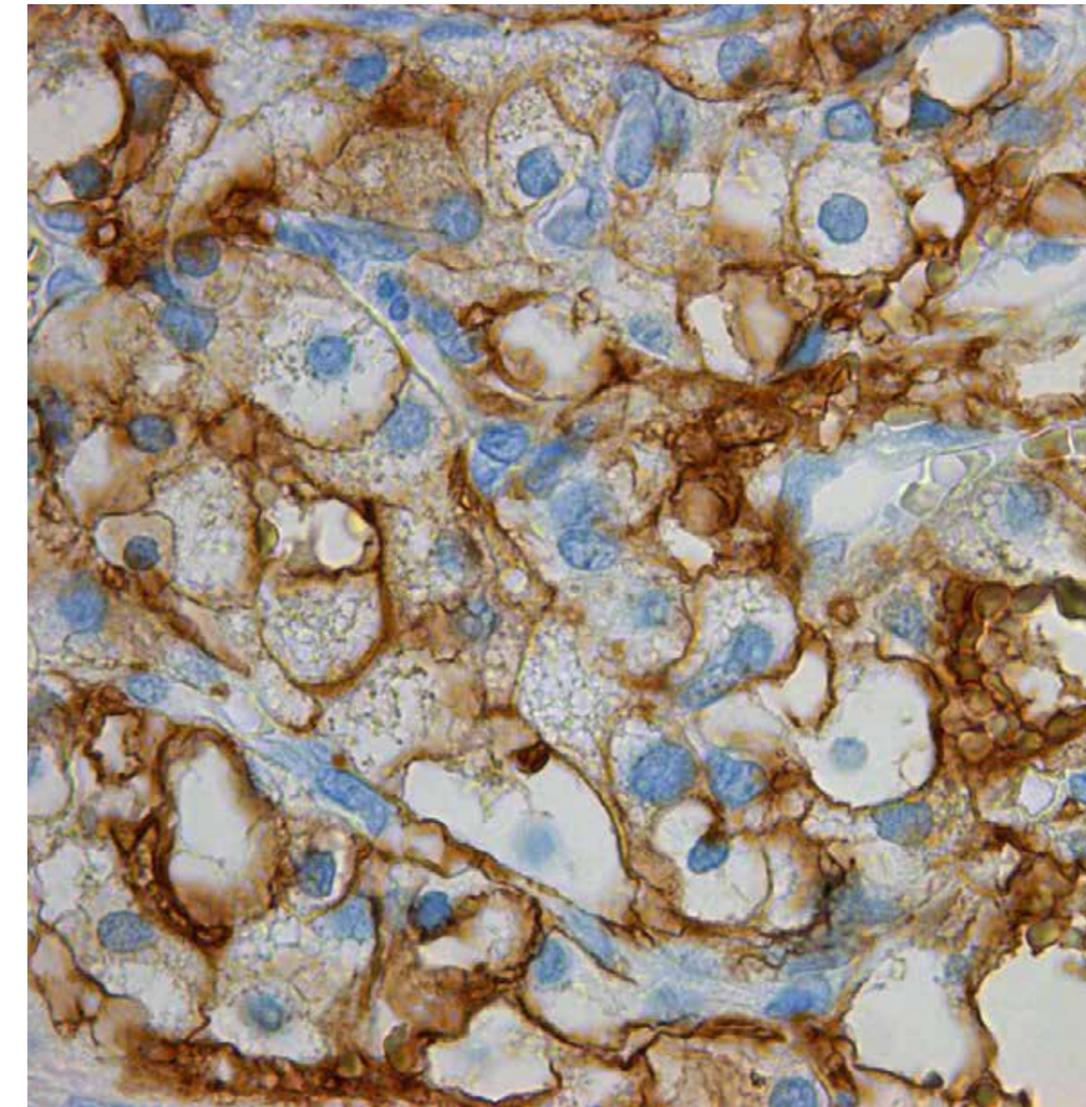


Immunofluorescence analysis of the localization of CA IX during the initial spreading of cancer cells. CA IX (green) staining signal overlaps with the paxillin (red) signal, a typical component of focal adhesion contacts.

The project results were published in 8 papers in renowned international journals and in two chapters in books edited and published abroad, and to date they have been cited more than 100 times. The paper published in *Seminars in Cancer Biology* was designated by Web of Science as a highly cited paper and placed in the top 1% of its academic field (based on data from Essential Science Indicators on July 2016). The results were also presented at international scientific meetings via posters, oral presentations and eight invited lectures. The research team included six researchers up to 35 years of age. The investigations are proceeding within the continuing APVV project aimed at understanding the role of CA IX in resistance to anticancer therapy.

Benefits for practice

Because hypoxia and acidosis in a tumour microenvironment support aggressive properties of cancer cells and reduce their sensitivity to therapy, the elucidation of the role of CA IX as a mediator of adaptive responses to these stresses and as a factor contributing to metastatic propensity brought new knowledge with potential applications in the development of rational diagnostic approaches and innovative anticancer strategies.



Immunohistochemical detection of CA IX in the tissue section of clear cell renal cell carcinoma visible as a brown staining signal produced by specific monoclonal antibody binding to CA IX.



AGRICULTURAL SCIENCES





Soil quality depends on its structure.

INTEGRATED SYSTEM OF EVALUATION OF THE AGRICULTURAL SOIL QUALITY AND POTENTIAL OF THE SIMPLIFIED WAYS OF THEIR CULTIVATION

Principal investigator: prof. Ing. Jozef Vilček, PhD.
 Applicant organisation: National Agricultural and Food Centre, Soil Science and Conservation Research Institute Bratislava
 Participating organisation: University of Prešov, Faculty of Humanities and Natural Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 210 830 EUR
 Project ID: APVV-0131-11

Subject of research

The research focused on the categorization of agricultural soils according to quality, which was defined and expressed by a *quality index*, whose production parameters also included environmental functions and processes occurring in the soils. Soil quality index is part of an information data bank on Slovak soils, including map products in digital form. The subject of the research also included the creation of a database on soil suitability for carrying out minimum agrotechnical measures which enable the application of alternative or differentiated systems in tillage using graphic interpretation.

Aims of the project

The main objective was to elaborate a system of categorizing agricultural soils in Slovakia according to quality evaluation (quality index), which besides the production parameters considers the soil's potential to fulfil its environmental functions as well as the processes that threaten its stability. The partial aim was to categorize the suitability of agricultural soil for the application of differentiated agrotechnical measures (ploughless, minimal technology).

Results

A. Integrated system of evaluation of agricultural soil quality
 While solving project tasks, partial indexes of production potential (the first digit in the final three-digit

code), non-production potential (the second digit in the final three-digit code) and endangerment potential of agricultural soils in Slovakia (the third digit in the final three-digit code) were elaborated and characterized with the help of chosen parameters. The final *integrated quality index* was formed in a GIS setting by the intersection of the above mentioned partial indexes, whereby the equivalency demand was maintained, i.e., all evaluated parameters were equal. The result is expressed in the layers of spatial differentiation of areal units:

- three-digit code (index) characterizing the particular unit from the production potential, non-production (environmental) and potential endangerment point of view. For example, a 132 code represents very highly productive soils, with medium environmental potential and low endangerment potential.

- final - integrated quality index. This was formed as an average of values from the three-digit index, maintaining the rule of their equality. Integrated indexes were categorized as follows: very high quality soils – index 1, high quality soils – index 2, medium quality soils – index 3, less quality soils – index 4, low quality soils – index 5.

The research of agricultural soil quality showed that in Slovakia there is a low occurrence of very high quality soils (0.98 %), but also low quality soils (0.30 %). Almost each soil potentially (more or less) fulfils production or non-production functions on a good level. From our point of view, 30.27 % of the soil in Slovakia is of high quality, 3.92 % of the soil is of medium quality and 30.53 % of the soil is of less quality.



Detection of soils properties using soilplots.

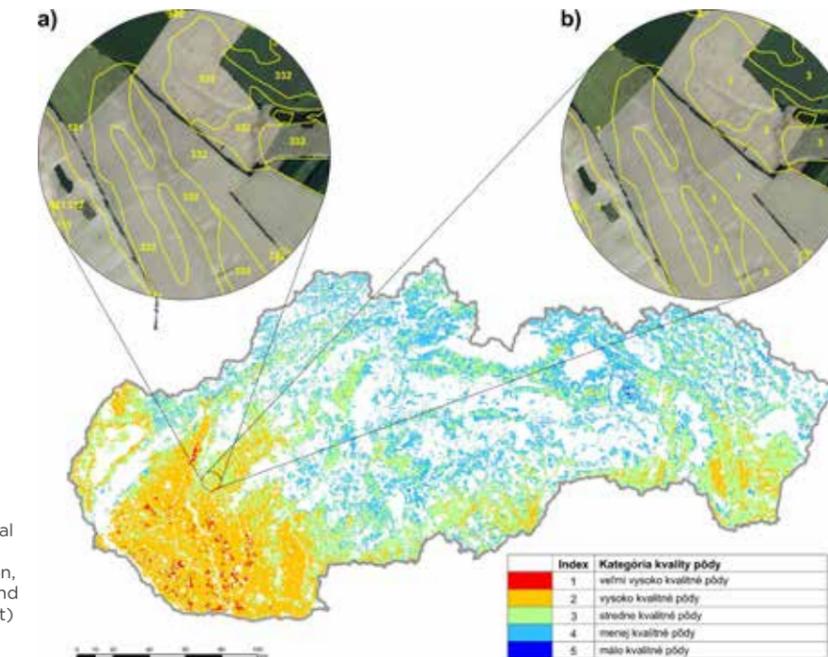


Soil profile.

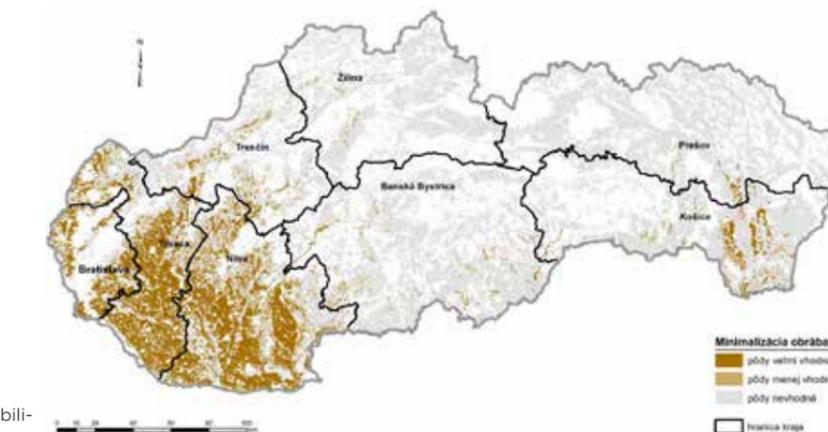
B. Categorization of agricultural soil ability for the application of minimised agrotechnical measures
 Minimised cultivation and ploughless tillage technology may only be employed under particular soil conditions. Approximately 25.3% of agricultural land in Slovakia (20.4% very suitable and 4.9% less suitable) is available for the application of minimised cultivation, while 74.7% of agricultural land is not suitable for this approach. Only 19.8% of soils (17.8% very suitable and 2.0% less suitable) are suitable for the ploughless technology of soil preparation before sowing, while 80.2% of soils are not suitable for this method. The best conditions for these approaches are found in lowland areas and lower altitude basins. We do not recommend employing these methods in higher altitude regions. The input parameters were the climatic conditions of the locality as well as the steepness, depth, stoniness and texture of the soil.

Benefits for practice

The results of the project enable access to information on the quality of the agricultural soils and their suitability for the application of minimised cultivation. The localities can be identified via GIS applications (maps, databases) both for farmers and for land use planning and the project sphere. The results can be used in the application of progressive methods of soil cultivation and for the planning and optimisation of agricultural landscape utilization.



Identification of the agricultural land quality using
 a) three-digit code (production, non-production potential and the potential endangerment)
 b) integrated quality index



Identification of the soils suitability to minimise cultivation



Plot tended by heavy thinning from below during the long-term period (Photo: I.Štefančík)

THE POSSIBILITY OF BEECH STAND TENDING RATIONALIZATION BASED ON EVALUATION OF LONG-TERM THINNING RESEARCH

Principal investigator: doc. Ing. Igor Štefančík, CSc.
 Applicant organisation: National Forest Centre – Forest Research Institute Zvolen
 Term of solution: July 2012 – December 2015
 Budget from agency: 232 973 EUR
 Project ID: APVV-0262-11

Subject of research

The project evaluates changes resulting from the long-term (45 to 50 years) tending of beech stands in selected areas of the 3rd and 4th altitudinal vegetation zone from the viewpoint of stand structure, as well as quantitative and qualitative production. The results were compared with plots left to self-development. Special attention was paid to trees of selective quality (promising and crop trees), which are an important parameter of qualitative production and/or total stand stability.

Objectives of the project

The objective of the project was to summarize the results of more than 50 years of consecutive measurements related to beech growth and development in stands tended by different methods, which will be the basis for improved methods of their tending in order to reduce costs.

Results

The best results were achieved by the free crown thinning method and the worst by heavy thinning from below, through which the “levelling” of height structure

was found. This fact is considered to be negative in terms of stability. On the contrary, a stand with the appropriate height, diameter and space structure is characterized as suitable. The stands tended by free crown thinning, mostly approximate this. The results of quantitative production did not clearly favour some of the investigated methods. Moreover, some parameters in control plots showed the highest values as a result of the lowest total decrease found in plots with no thinning (planned interventions). The assessment of the “mass quality” in a beech stand showed better results by the application of heavy thinning from below in comparison with the free crown thinning and plots without tending. The cultivation of “selective quality,” which is first-rate in beech stands, showed the best outcomes for individual tending by the free crown thinning of promising and target tree methods.

Benefits for practice

The results will be used in forest practice by means of principles for beech forest management, as well as in forest management planning for “the plan of care of forests”. Additionally, felling or tending and regeneration will also be useful under the “Framework planning” part of the management measures.



01. Plot tended by free crown thinning during the long-term period (Photo: I. Štefančík)



02. Plot left to self-development (Photo: I. Štefančík)



03. High quality beech tree at the age of 100 years on a plot with long-term tending (Photo: I. Štefančík)



Pinzgauer cattle.



Zobor rabbit.

APPLICATION OF BIOTECHNOLOGICAL METHODS FOR CONSERVATION OF ANIMAL GENETIC RESOURCES

Principal investigator: prof. Ing. Peter Chrenek, DrSc.
 Applicant organisation: Research Centre for Animal Production Nitra
 Participating organisation: Faculty of Biotechnology and Food Science, Slovak University of Agriculture in Nitra
 Term of solution: July 2012 – June 2015
 Budget from agency: 249 942 EUR
 Project ID: APVV-0556-11

Subject of research

The necessity and importance of projects dealing with the preservation and use of the gene pools of farm animals are based on the biological, economic, landscaping and cultural needs of each country using the cryopreservation of samples in national gene banks (NGB). To date, the effective biological material cryo-conservation of some farm animal species is not fully under control. This can result in the reduced survival or quality of the frozen/thawed farm animal spermatozoa and embryos.

Objective of the project

The objective of the project was to optimise some cryopreservation methods of sperms, embryos and stem cells for routine use, primarily for endangered farm animal breeds.

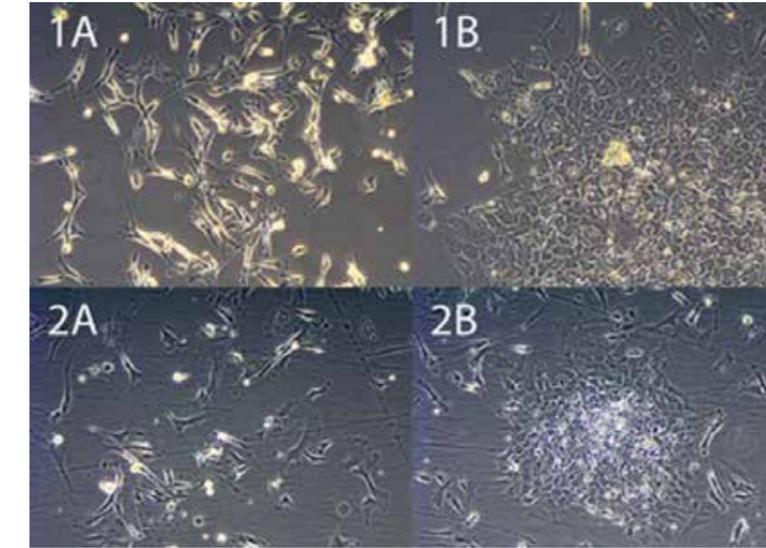
Results

This project was conducted in three stages. Stage 1: Throughout the project period, regular consultations with farmers were arranged in order to monitor the population of the breeds and to update the EFABIS database. Stage 2: The genetic markers determining the

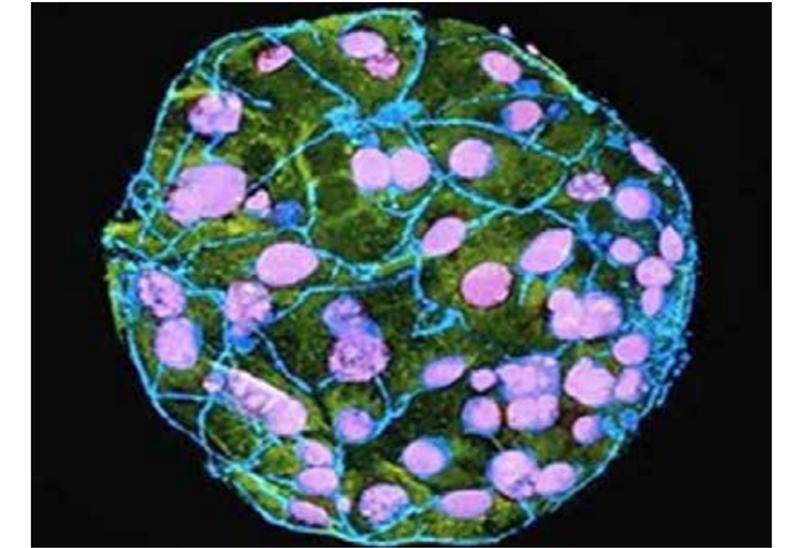
origin of sheep and rabbits in Slovakia were optimized and validated using molecular genetic analyses. Stage 3: The optimized conditions for the cryopreservation of rabbit sperm, embryos and stem cells enabled the creation of the first gene bank of animal genetic resources in Slovakia. The achievement of the relevant results was confirmed by numerous publications in foreign journals. An international conference focused on animal genetic resources was organized during the course of the project. Furthermore, this project enabled the cryopreservation of biological material from most breeds reared in Slovakia, thus fulfilling the real conditions of the contract signed between SR and FAO in 1994 related to genetic resources.

Benefits for practice

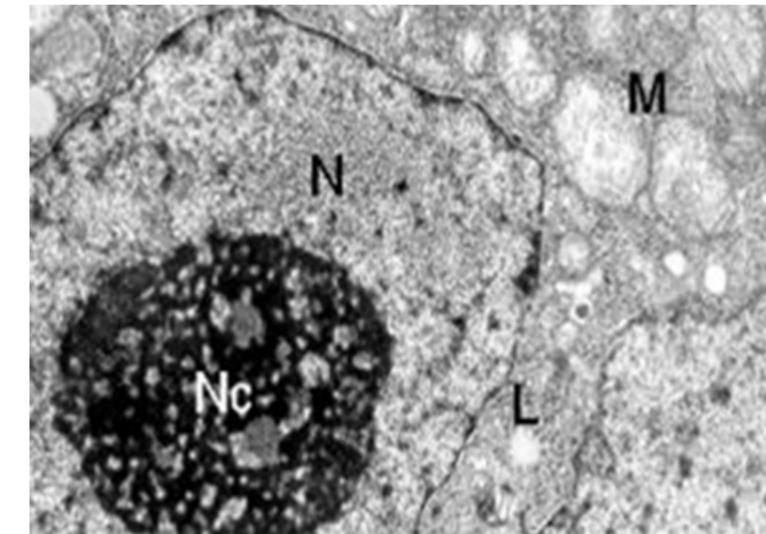
The results are applied to the newly built gene bank of animal genetic resources in the VÚŽV NPPC Nitra where cryopreserved embryos, sperm and stem cells of Slovak several breeds (Pinzgauer cattle, original Wallachian sheep, Nitra rabbits and Zoborský rabbits) are stored. These samples will be available to breeders and farmers for the purposes insemination or embryo transfer.



Rabbit stem cells isolated from amniotic fluid.



Rabbit embryo analysis of quality by confocal microscopy.



Rabbit embryo analysis of quality by electron microscopy.



Gene bank of animal genetic resources in NAFC RIAP Nitra.



M.Sc. L. Juhásová, Ph.D. student of the Comenius University in Bratislava and D.V.M. Barčák, Ph.D. student of the University of Veterinary Medicine and Pharmacy in Košice participating in the project.

SPECIES BOUNDARY DELIMITATION IN FISH PARASITES: MORPHOLOGY VERSUS GENES AND CHROMOSOMES

Principal investigator: RNDr. Vladimíra Hanzelová, DrSc.
 Applicant organisation: Institute of Parasitology, Slovak Academy of Sciences, Košice
 Term of solution: July 2012 – December 2015
 Budget from agency: 222 476 EUR
 Project ID: APVV-0653-11

Subject of research

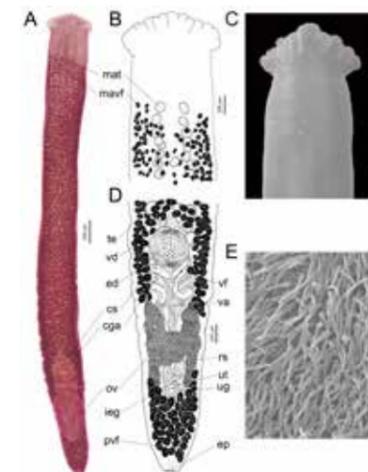
Species delimitation and correct species identification are essential objectives of taxonomy and a key pre-requisite for any further biological study. A failure in this task could lead to contradictory systematic conclusions or questionable biodiversity information. These questions are important for neglected animal groups, including multicellular parasitic organisms. Most represent serious parasitic disease agents of humans, animals and plants.

Objectives of the project

The project strove to address the important question of identifying species boundaries. To achieve this objective, the optimal synergy of morphological, molecular and genetic approaches, including the development of microsatellite markers, was applied. On this basis and using appropriate parasitic models, the proper set of traits was defined for unequivocal species identification. The research also involved generic revisions within the model group of parasites and original descriptions of new tapeworm species.

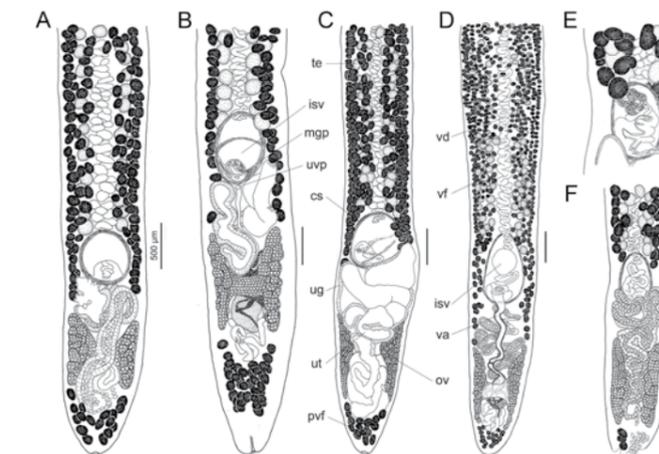
Results

The problem of species demarcation remains a crucial taxonomic task, particularly in evolutionary basal parasitic organisms, to which tapeworms of the order Caryophyllidea parasitizing freshwater fish belong; and as our biological models, they met the demands for addressing the issue of the project. Taking into account the high degree of morphological variability of these tapeworms, the application of specific nuclear and mitochondrial genes led to the discovery of four new tapeworm species - *Khawia abbotinae* n. sp., *Paracaryophyllaeus vladkae* n. sp., *Promonobothrium currani* n. sp. and *P. papiliovarium*. Genera *Caryophyllaeus*, *Monobothrium* and *Promonobothrium* were critically revised and several complexes of multiple species and cryptic species were described. Several tapeworm species were characterized by the use of specific cytogenetic and ultrastructural traits. Microsatellites were designed to resolve more complex problems of species delimitation and short repetitive DNA fragments. Their application in population-genetic studies of the tapeworm *Caryophyllaeus laticeps* from Europe enabled the discovery of two geographically isolated genetic lines of the parasite. The other population of *C. laticeps* from the common (*Chondrostoma nasus*) from Austria differed significantly from two former European populations. The high degree of morphological and genetic



Khawia japonensis, an invasive fish tapeworm of Asian origin - a potential health risk for carp breeding - was first recorded in Slovakia.

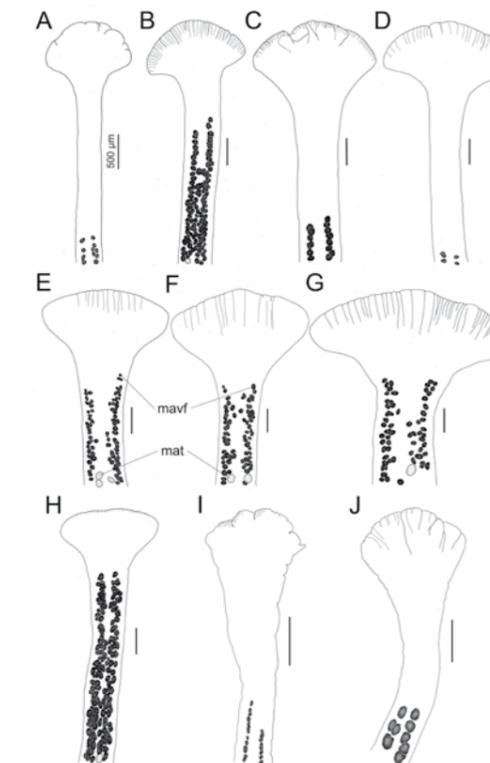
Morphological variability associated with genetic uniformity creates serious difficulties in species identification and represents a serious problem for current taxonomy.



speciation specimens of the Austrian line indicates a subsistence of the new, not yet described tapeworm species. Another benefit of the extensive spatial monitoring of fish parasites performed during this project is the discovery of a new invasive, potentially pathogenic tapeworm in Slovakia (*Khawia japonensis*) and the findings of new transmission routes of two other tapeworms, *Atractolytocestus huronensis* and *Schyzocotyle acheilognathi*, previously introduced to the aquacultures and wild from Asia, to Europe and Africa. Species identification methodologically based on morphology in its traditional meaning is complex in highly polymorphic organisms. The application of advanced molecular techniques in species detection represents a very good alternative, but there are difficulties in the correct gene selection and subjective evaluation of the informativeness of molecular data. This was precisely proven by the results of our project. In hermaphroditic organisms, even this integrative morphological and molecular approach might not be sufficient and clearly interpretable. Results showed that population analyses using microsatellites as genetic markers represent an exacting, but promising trend in addressing species delimitation. The integrated approach that was used in the project is original and unique in parasitological research.

Benefits for practice

The reliable identification of parasitic organisms is an essential prerequisite for the effective control of any parasitic disease. One of the specific results of the project is the improvement of the diagnostics of parasitic diseases, particularly cestodoses found in economically important carp. The discovery of non-native, invasive species of fish parasites recently spreading across Europe is essential for biodiversity conservation and fish farming in Slovakia. We believe that some results and generally drawn conclusions of the project will be relevant not only to agents of parasitic diseases, but for other groups of invertebrate organisms.





Fermentation tank for solid state fermentations.

BIOTECHNOLOGICAL PREPARATION OF NEW TYPES OF FUNCTIONAL CEREALS AND CEREAL PRODUCTS ENRICHED WITH POLYUNSATURATED FATTY ACIDS AND PIGMENTS

Principal investigator: Assoc. Prof. Milan Čertík, PhD.
 Applicant organisation: Faculty of Chemical and Food Technology, Slovak University of Technology in Bratislava
 Participating organisations: National Agricultural and Food Centre, Lužianky - Plant Production Research Centre, Piešťany, Institute of Chemistry, Slovak Academy of Sciences, Bratislava
 Term of solution: July 2012 - December 2015
 Budget from agency: 250 000 EUR
 Project ID: APVV-0662-11



Various types of prefermented bioproducts enriched with polyunsaturated fatty acids and pigments prepared by fungal solid state fermentation and their application for the preparation of bakery and pasta products.

Subject of research

This project involved the biotechnological evaluation of cereal materials and various domestic agricultural waste materials for the preparation of products with targeted nutritional and functional properties.

Objectives of the project

The project focused on three main fields:

- a) the preparation of new types of cereal bio-products enriched with polyunsaturated fatty acids (PUFA) and carotenoid pigments by fermentation;
- b) the functional expression of microbial genes encoding PUFA formation in selected types of cereals; and
- c) the study of the molecular, biochemical and physiological mechanisms of PUFA regulation and pigment biosynthesis in microorganisms.

Results

Fungi from the order *Mucorales* were selected as the producers of polyunsaturated fatty acids (PUFA). Some of these fungi were characterised by the dual production of PUFAs and beta-carotene. A biotechnological

process for the enrichment of cereal materials with PUFA (almost 25 g of gamma-linolenic acid or arachidonic acid 31.5 g per 1 kg of bioproduct) and carotenoid pigments (260 mg of β -carotene per 1 kg of bioproduct) was developed and a pilot plant was tested by using the physiological optimization of fermentation conditions, and by increasing the nutrient availability in cereals by semi-solid fermentations of filamentous fungi. "Scale-up" studies (transfer of experimental results from laboratory to pilot plant volumes) were carried out in co-operation with King Mongkut's University of Technology Thonburi in Bangkok, Thailand for several years. These studies showed that critical factors in the fermentation process include engineering and physiological parameters such as reaction heat removal during fermentation, the maintenance of the optimum moisture content, pH, oxygen levels, substrate gradient and the organoleptic properties of fermented material. In conclusion, the project also led to a number of applications of fermented cereal bioproducts containing PUFAs and pigments. Bioproducts containing gamma-linolenic acid were tested for their effects on rumen fermentation of ruminants, as dietary supplements in

the growth of poultry, as well as for the preparation of bakery products. These studies suggest that fermented cereal products may find their application as a supplementary diet in food and livestock production and veterinary practice. Since these newly prepared functional cereal bioproducts containing PUFAs are subject to oxidation degradation changes during storage or further processing technology, a method for testing the thermooxidation stability of fermented cereal materials by differential scanning calorimetry has been developed. Experiments indicate not only a very slight decrease in the stability of bioproducts during the drying process of these products, but also show their thermooxidation stability during subsequent storage.

Fungi from the order *Mucorales* were selected as suitable donors of genes encoding the fatty acid desaturases involved in the biosynthesis of individual PUFAs. After the preparation of sufficient quantities of plant explants for transformation as the most suitable genotypes, hexaploid varieties of barley and wheat were selected. The presence of a fungal gene encoding a delta 6-desaturase with an optimized genetic code for cereals was confirmed in all monitored generations (T0 - T2) of cereals at the genomic, metabolomic and transcription levels in mature seeds.

Benefits for practice

This project uniquely links microbial biotechnology and agricultural biotechnology for the preparation of new types of cereal bioproducts with targeted nutritional and functional properties and high added value. Transgenic cereals (barley, wheat) containing gamma-linolenic acid and stearidonic acid were prepared for the first time in the world by the transformation and functional expression of fungal genes encoding the fatty acid desaturases. The results of this project have been published and presented in 16 CC / WOS articles (including 15 foreign articles), 4 scientific peer-reviewed articles (3 of them foreign), 26 foreign conference papers (including 11 invited lectures), 25 conference papers in the Slovak Republic, a foreign scientific book publication and 27 SCI citations. Two prototypes of transgenic plants were prepared. Several PhD, master and bachelor students were involved in the project, which increased their practical skills and valuable experimental experience. Thus, research results have been applied to the educational process.



Transgene cereals containing polyunsaturated fatty acids prepared by the functional expression of fungal fatty acid desaturase genes (collaboration with Plant Production Research Centre in Piešťany).



Various types of prefermented bioproducts enriched with polyunsaturated fatty acids and pigments prepared by fungal solid state fermentation and their application for the preparation of bakery and pasta products.





Innovative, extruded products, based on non-traditionally coloured wheat genotypes from the category of functional food.

BIOLOGICAL ACTIVE AND VALUABLE COMPONENTS OF CEREALS, PSEUDOCEREALS AND FORAGES FOR FUNCTIONAL FOODS PRODUCTION

Principal investigator: Ing. Tibor Maliar, PhD.
 Applicant organisation: University of Ss. Cyril and Methodius in Trnava
 Participating organisation: National Agricultural and Food Centre
 Research Institute of Plant Production in Piešťany
 Term of solution: July 2012 – December 2014
 Budget from agency: 228 368 EUR
 Project ID: APVV-0758-11

Subject of research

This project involved the broad screening, selection and possible application of valuable biological activity of extracts, prepared from cereals, pseudocereals and forages for functional foods.

Objectives

- the development and modernization of methods for the determination of biologically active compounds and their *in vitro* biological activity, the particular determination of antioxidant activity, the inhibition activity of selected enzymes, and antimicrobial activity,
- the broad screening of cereals, pseudocereals and forages possessing these compounds, and the chemometric processing of experimental data,
- the identification of biologically active compounds by LC techniques in potential donors within the group of typical and “coloured” plant genotypes,
- the proposed composition of functional foods and drinks, based on subjected extracts.

Results

A set of innovative methods based on key, bioactive substances as well as *in vitro* biological activities utilizing the microplate technique, in particular, composite parameters, activity parameters - antioxidant, enzyme

inhibition, antibacterial and antifungal activities was implemented. All of the collections of agrarian crops were created based on the decision of the relevant crop curators, following such actual purpose within the breeding programs with the relevant argumentation of the genotype selection based upon specific crop phenotype and genetic characterization. Collections of extract samples of both native grain and young plant matters were examined for the following crops: wheat, barley, and oats (n=100), as well as a collection of forage crops (n=266) according to the mentioned parameters. Supporting analytical studies aimed at determining polyphenolic acids, flavonoids and avenanthramides in extract samples were conducted. Questions were answered regarding the stability of the mentioned properties, in particular whether they were of a constitutive or induced nature, and the probability of finding the specific genotype of a chosen activity level through the analysis of frequency histograms established by the Gauss function. Further, a pre-test was conducted related to the simulated digestion of the collection of colour wheat genotypes (n= 100) mainly by the determination of total polyphenol content and antioxidant activity after digestion in acidic and subsequent basic pH treatment. The following functional food products were selected for the preparation: KARKULKA coloured wheat for the branch of extruded products, DUNAJEC oats for innovative drinks based

The presentation of various grain genotypes (Triticum sp.), subjected to extract sample preparation, *in vitro* biological evaluation and application to the form of innovative food products, entire spikelet /A/ grain detail /B/.



on malt and brewing processes and finally FATRAN barley and JANA C1 buckwheat for drinks based on “green barley” products. A broad team of investigators from both institutions was engaged in the project which resulted in 4 manuscripts in CC journals and 20 contributions to other scientific journals and conferences on the international level, 2 results for practice, educational courses, 12 final theses for students and 2 PhD dissertations. It also resulted in a partnership with commercial subjects and the submission of 3 related projects.

Benefits for practice

- benefits for breeding engineers who can choose from specific genotypes from numerous collections of wheat, barley, oat, buckwheat and forage genotypes based on a wide palate of established descriptors of biologically valuable substances and *in vitro* biological activity for subsequent breeding programmes;
- benefits for farmers, primarily for agrarian production, and the basic aspects and direction for special plant production with higher added value,
- benefits for nutrition supplements producers and functional food producers, the selection of genotypes with high biologically valuable substances and *in vitro* biological activity.



▼
SOCIAL
SCIENCES





Presentation of research findings at international conferences.

SOCIAL DETERMINANTS OF HEALTH IN SCHOOL-AGED CHILDREN

Principal investigator: prof. Mgr. Andrea Madarasová Gecková, PhD.
 Applicant organisation: Department of Health Psychology, Faculty of Medicine, Pavol Jozef Šafárik University in Košice
 Participating organisations: University of Groningen, UMCG, The Netherlands
 University Palackého in Olomouc, Czech Republic
 Term of solution: July 2012 – December 2015
 Budget from agency: 247 245.98 EUR
 Project ID: APVV-0032-11

Subject of research

The subject of the research was to analyse the socio-psychological determinants of health and health-related behaviour of adolescents.

Aims of the project

The project was intended to update and validate data on health and health-related behaviour of Slovak adolescents, to monitor trends in the prevalence of selected health, social and behavioural indicators of healthy development as well as the factors which may affect them.

Results

The obtained data were used to examine the socio-demographic and intrapersonal characteristics within their social context (family environment, school environment, peer group) and their contribution to the successful management of developmental changes during the transition from childhood to adolescence, and to assess the health and behavioural indicators of a successful transition. Special attention was paid to the associations of nutritional behaviour (e.g., the consumption of sugary drinks and energy drinks, dieting) with sedentary and violent behaviour, but also to the role of parental rules; to the potential benefit of participation in organized leisure-time activities; intrapersonal but also environmental factors associated with physical activity; the role of parental monitoring in

the education of adolescents; the association of preferences of selected youth subcultures with the risky behaviour of adolescents, as well as the impact of socio-demographic factors and extreme socio-economic deprivation on the health and health-related behaviour of adolescents. The impact of the economic crisis on the health of adolescents, as well as association of the school environment with the active lifestyle of school-children was investigated through the use of multi-level analysis methods. Contributions to research methodology, where several research protocols, questionnaires and measurement tools were verified in terms of the preparation of psychometric properties, were also important.

Benefits for practice

The project updated and validated data on the health and social determinants of adolescents and promoted a better understanding of socio-demographic, intrapersonal factors of the health and health-related behaviour of adolescents in their social context. The project results were used in the preparation of more than 40 scientific papers for SSCI journals (44 already published), active participation in 37 international and national conferences and 5 scientific monographs or scientific publications. 29 educational activities were prepared for professional audiences. The acquired knowledge was used for teaching undergraduate students in general medicine and public health but also in the conduct of theses (5 defended and 3 ongoing).

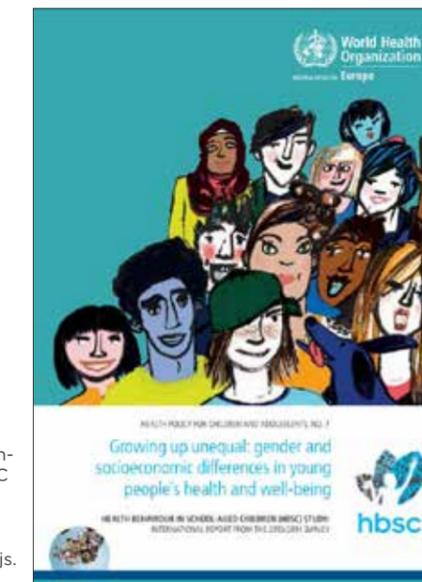
Meeting of stakeholders and the media on the occasion of the publishing of the International and national report on health and the health-related behaviour of 11, 13 and 15 year old students within the social context. Results of the study entitled Health Behaviour of School-age Children 2013/2014. Bratislava, June 2015



Doctoral students in the field of public health, kinanthropology and health sciences were also involved (7 defended and 5 ongoing dissertation projects) in the project. The findings were disseminated to the general public through 3 press releases, 3 press conferences, 2 infographics, 1 video spot, a website, and dozens of posts and responses in television, radio, internet and the print media. The project results were used in 16 activities designated for stakeholders (workshops, seminars, invited presentations, the development of strategic documents). A database of nationally representative data about school-age children was created and included in the international database comparing school-age children from more than 45 countries. An international and national report on the health and health-related behaviour of school-age children was prepared and disseminated. This gave rise to more than 20 projects, 3 of which were supported within an international competition and 3 within Slovakia. Part of the project was devoted to the development of various measures and the verification of their psychometric attributes (e.g., Family affluence scale, Health literacy questionnaire, Questionnaire of organized leisure-time activities, Questionnaire of motives for physical activity, Questionnaire of physical activity and sedentary behaviour of school-aged children, Spirituality scale, Questionnaire of risky behaviour) as well as the development of a protocol for a national HBSC study including questionnaires. The acquired knowledge has the potential to fill gaps in knowledge, indicate the direction and dynamics of current social changes, and on this basis provide a wider theoretical and methodological reflection on the research of the social determinants of health among schoolchildren.



International and national report on health and the health-related behaviour of 11, 13 and 15 year old students within the social context. Results of the study entitled Health Behaviour of School-age Children 2013/2014.



Meeting of the international HBSC team in Košice, 25-27 October 2012.
<http://www.lf.upjs.sk/hbsckosice/>





Project activities included the purchase, Slovak translation and validation of tools for the objective and standardized diagnosis of autism. Subsequently, the staff was trained in these new diagnostic techniques

SOCIAL, EMOTIONAL AND COGNITIVE MIRROR IMAGE OF AUTISM FROM INTERDISCIPLINARY PERSPECTIVE

Principal investigators: MUDr. Katarína Babinská, PhD., MSc.
(RNDr. Silvia Lakatošová, PhD. until 8/2013)

Applicant organisation: Comenius University, Faculty of Medicine in Bratislava

Participating organisations: Trnava University in Trnava, Faculty of Philosophy and Arts
Comenius University, Jessenius Faculty of Medicine in Martin

Term of solution: July 2012 – December 2015

Budget from agency: 188 789 EUR

Project ID: APVV 0254-11

Subject of research

The project focused on the topic of autism. Autism is a neurodevelopmental disorder characterized by social interaction and communication impairments and restrictive and stereotyped behaviour and interests. Autism represents a serious health problem due to its serious symptoms, numerous comorbidities and increasing prevalence. Its etiology and pathomechanisms are only poorly explained, and no biomarker of autism has been identified. Diagnosis is based on a comprehensive examination of the behavioural patterns of the child.

Objectives of the project

a/ to create a standardized set of psycho-diagnostic tests for autism spectrum disorders in Slovakia;
b/ to investigate the associations between sex hormone and oxytocine levels with individual categories within diagnostic scales of autism, systemizing and cognitive abilities, IQ level, as well as to assess the psychopathology of family relations;
c/ to examine selected biomarkers in children with autism and analyse their associations with psychological and behavioural variables with the aim to find biological correlates of behavioural traits.

Results

To the best of our knowledge, this is the first study that showed an association between the autistic traits of parents and the oxytocine levels of their children with autism. This indicates that abnormalities associated with oxytocine may be the link that connects the autistic traits of the parents and the severity of autism in their children. We have shown a positive correlation between oxytocine levels and maladaptive behaviour in children with autism. Our results show an association between testosterone levels and aggressive behaviour in autism, as well as an association between androgene receptor sensitivity and hyperactivity, which indicates that psychiatric comorbidities in autism may be associated with increased androgen activity. The high prevalence of gastrointestinal comorbidities that was found and their correlation with aggressive behaviour and elevated levels of inflammatory markers in plasma supports the hypothesis about the role of inflammation in the pathomechanisms of autism. A positive effect of a 4-month probiotic supplementation on the concentration of inflammatory marker TNF-alpha in the faeces of children with autism was found. The objective diagnostic tools for autism spectrum disorders and their validation for the Slovak population



The project and its results were an inspiration for the publishing of the book *We have a child with autism - a compass for the parents*, which was a joint effort involving many of the research team members.

were translated into Slovak, which is considered one of the most significant results. Our data show that the comprehensive diagnostic process and the determination of autism severity require standard and objective diagnostic methods. We found that IQ values and age must be taken into consideration in scoring in specific diagnostic tools.

Benefits for practice

Project activities included the purchase, Slovak translation and validation of diagnostic tools ADOS-2, ADIR, CARS a GADS. These tests represent the gold standard method in autism diagnosis abroad. However, they had never been used in Slovakia. We also succeeded in introducing these methods in several diagnostic clinics and establishing the Academic Research Centre for Autism (ARCA) at the Comenius University Faculty of Medicine. The centre will integrate research activities aimed at autism spectrum disorders in Slovakia into a network of collaborating institutions that will introduce evidence-based diagnostic and therapeutic methods and coordinate interaction with patients, their families and the relevant institutions. As the only educational basis for the ADOS-2 diagnostic tool, ARCA directly introduces the results of the project into practice. Due

to the high prevalence of digestive and nutritional problems that has been found in autism, a web page was created for providing advice regarding nutritional issues. Based on the results, we can presume that the treatment of digestive problems can help to suppress challenging behaviour and other behavioural problems associated with autism. The results of the project have been disseminated among paediatricians, neurologists, psychologists, speech therapists, teachers and special education teachers in order to raise the rather low level of knowledge about autism; this may help in the earlier detection of the disorder, more efficient early intervention and a better perspective for individuals with autism and their families. The project and its results were the inspiration for the publishing of the book *We have a child with autism - a compass for parents*. Many of the research team members co-authored the book.

OPTIMIZATION OF THE PROCESSES OF DEVELOPMENT AND EVALUATION OF DIGITAL EDUCATIONAL PROGRAMMES AND ELECTRONIC LEARNING TOOLS.

Principal investigator:
Applicant organisation:
Term of solution:
Budget from agency:
Project ID:

RNDr. Štefan Karolčík, PhD.
Comenius University in Bratislava, Faculty of Natural Sciences
July 2012 – December 2015
166 696 EUR
APVV-0266-11

Subject of research

The ambition of the investigators in the research project entitled *Optimization of the Processes of the Development and Evaluation of Educational Programmes and Electronic Learning Tools* was to develop a theoretical-methodological platform for an evaluation system to enable the objective assessment of the quality of software products and various kinds of learning tools based on precisely defined and constantly updated scientific criteria, in an electronic form exclusively in relation to the educational requirements and needs.

Aim of the project

To develop an objective evaluation system of educational software, educational environments and electronic learning tools by means of scientifically defined and parameterized evaluation criteria. To draft, describe and test the methods and procedures which will ensure a high level of objectivity and validity of the chosen evaluation criteria and the precision of the results. To develop procedures for the certification of educational programmes and electronic learning tools.

Objectives of the project

- Draft methodology of evaluation of pedagogical-psychological and didactic aspects of software applications.
- Comprehensively assess the quality of selected educational software and existing electronic learning tools designed for natural sciences.
- Draft a model of a suitable educational software environment with multimedia interactive and comprehensive content.
- Draft an accreditation procedure for the issuance of certificates on software product testing, including the test results.
- Inform both experts and the general public on the activities and results of the project solution; publish information on the evaluated software products and a database

of interesting educational programmes and interactive educational environments on a web site.

Results

- Development of a theoretical model of a suitable educational software environment with multimedia, interactive and comprehensive content.
- Development of an accreditation procedure for the issuance of certificates on software product testing, including the test results.
- Comprehensive psychological-didactic and pedagogical analysis of selected educational technology and electronic learning tools.
- Promotion of research activities and evaluation outcomes with respect to the relevant software products. Intensification of the general awareness of pedagogues in terms of the selection of technological solutions which are suitable in terms of processing and content, and constructive for educational purposes.
- Proposal for the creation of a specialised institute – a research & development centre for the creation and evaluation of educational programs and electronic teaching materials – that reviews commercial digital products and educational environments.

Benefits for practice

During the course of the project (07/2012 - 12/2015) the investigators:
Conducted research (the Delphi method) aimed at gathering the views of specialists concerning the third circle of issues related to the most important expected features of software applications and electronic materials specifically designed and developed for the needs of education and learning support.
Conducted research on a representative sample of teachers – graduates of training sessions organized within the national project *Modernization of the Educational Process in Primary and Secondary Schools*. This numerically large

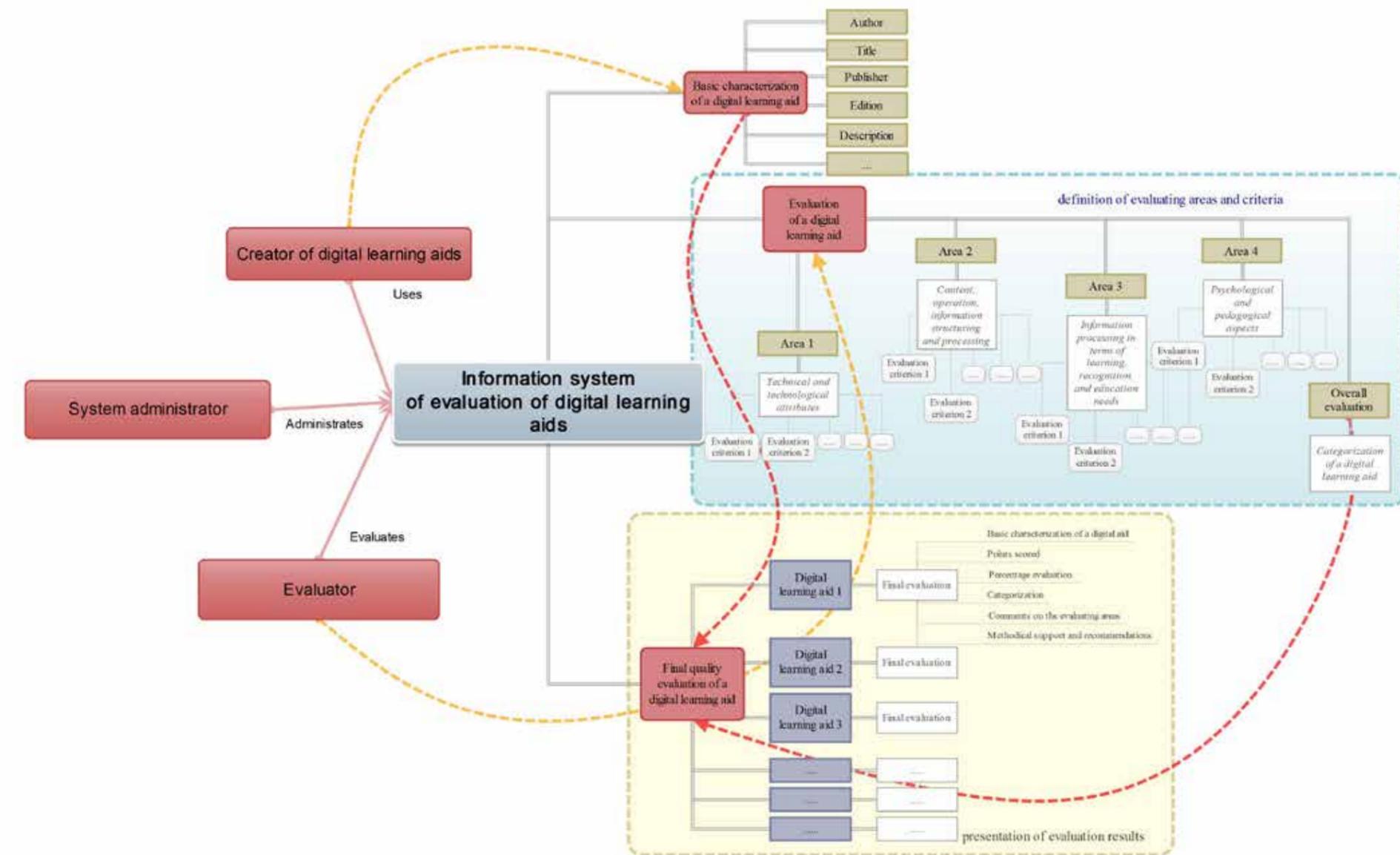
research activity (1842 respondents) involved gathering teachers' opinions and attitudes on the importance of the professional evaluation of the quality of educational software, the desired features of software solutions, the optimal form of publishing assessment results, as well as the most widely used sources of information on existing and available educational software products.

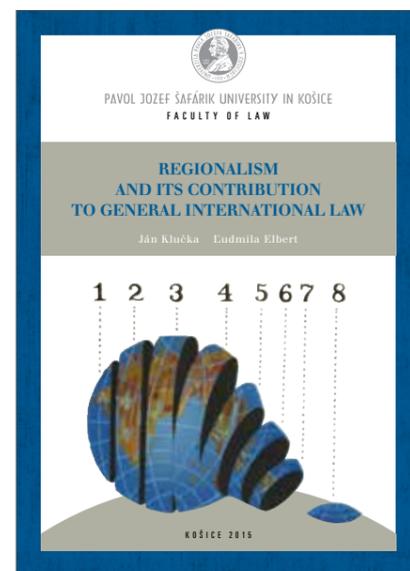
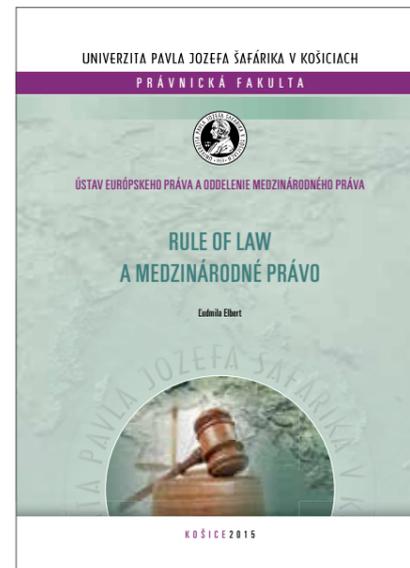
Created the *Comprehensive Evaluation of Electronic Learning Tools and Educational Software – CEELTES*. This evaluation tool is designed for the comprehensive assessment of the quality of digital teaching aids. It has undergone international and domestic review and was subject to an approval procedure by the National Institute for Education. It was also discussed by the relevant sections of the Ministry of Education, Science, Research and Sport of the Slovak Republic and shall become part of the evaluation of digital teaching aids used in schools. Developed *comprehensive evaluation models* of the available and most commonly used digital teaching aids in schools.

Developed a draft organizational structure concerning staffing and technical equipment as well as the specialisation of individual departments of the *Educational Technology R&D Centre*.
Develop a draft *Model of the appropriate, educationally oriented software environment* with digital educational content.

Developed a draft *accreditation procedure for the issuance of certified documents on the evaluation of a digital teaching aid*. The procedure provides for the amendment of Directive No. 10/2011, which regulates the procedure of the Ministry of Education, Science, Research and Sport of the Slovak Republic and directly managed organizations in the selection and approval of textbooks.

Developed a *database of qualified experts who are able to objectively assess the quality of educational technology*, taking into account the learning needs in individual subjects.





REGIONALISM AND ITS CONTRIBUTION TO UNIVERSAL PUBLIC INTERNATIONAL LAW

Principal investigator: prof. JUDr. Ján Klučka, CSc.
 Applicant organisation: Pavol Jozef Šafárik University in Košice (Faculty of Law, Institute of European Law and department of International Law)
 Term of solution: July 2012 – December 2015
 Budget from agency: 174 619 EUR
 Project ID: APVV-0823-11

Subject of research

The team of researchers focused on the influence of regionalism on contemporary general international law. They analysed institutional regionalism, and within this context the role of the regional organisations were evaluated in the system of contemporary international law, their mutual interactions, cooperation and interaction with an international organization of a universal nature – The United Nations (UN). Treaty regionalism and the phenomena of interregionalism, the history of regionalism, its present position and perspectives of regional systems of international law in respect of its fragmentation and the processes of the institutionalization of regional arrangements, regionalism in the fields of human rights, the rule of law, international trade and the enforcement of international peace and security were also examined.

Aims of the project

The aims of the project were to identify the similarities and differences between specific regional systems, to examine the rules of the integration process that are valid for international organizations in general and to identify the circumstances that have an influence on the achievement of the desired level of regional integration in the regions of the world by employing the means of legal science. Another goal of the research was to identify and analyse the horizontal and vertical relations between regional systems of international law and between the individual regional systems and systems of general international law directed from the regional level to the level of general international law and *vice versa*. This

issue was analysed from the normative perspective and from the perspective of the practice of subjects of international law. The interaction between regional and universal organs and organisations was also examined.

Results

The research of regionalism and its influence on general international law clarified the relationship of regional and general international law and their mutual interaction, especially the influence of regionalism on universal international law. During their examination of regionalism in general, the researchers succeeded in identifying several institutions that are developing within the regional framework predominantly under the influence of globalisation. They also explored the substantial influence of regionalism in various fields of international law.

A comparison of old and new regionalism, treaty and institutional regionalism was also carried out. Interregionalism and the relations existing within its framework were examined with a special emphasis on international regional organisations and their operation, as well as the relationship between the legal rules of a regional nature with the legal rules of general international law.

Research showed that specifically international organisations are crucial for creating and influencing international regional law. This is seen in the relationship between human rights and the rule of law; they overlap within regional international law because the development of human rights protection was the basis for the development and strengthening of the concept of the rule of law. Specifically, the regional integration system

Guarantors of the quality of student symposia was panel presided by the responsible researcher prof. JUDr. Ján Klučka, CSc.)

Within the student symposia, various topics were analysed, where the influence of the regionalism had been identified such as the protection of cultural heritage or international airspace and space law.

of the European Union is based on the rule of law in which the protection of fundamental rights is the key pillar. The crucial role of regionalism was also explored in the field of the enforcement of international peace and security, especially when the operation of the UN is influenced or even hampered by the inability of its key organs such as the Security Council to act. While in many instances cooperation between regional organs and the UN works well, examples were presented in which the inability of the UN Security Council became a reason for the initiative of the regional organs. In this area, the cooperation of the UN and regional arrangements had been identified where the UN provides the legitimacy (political as well as legal) for actions of regional arrangements that are more agile and operative in responding to issues at the regional level. This shows that there is a will to find such solutions.

Benefits for practice

The knowledge acquired during research clarified new terms that are developing in the newest system of international law. Such terms include interregionalism, treaty regionalism, regional rule of law, etc. The knowledge acquired through this research can be applied to the resolution of issues related to the relationship of regional and universal bodies in international law, human rights, international trade as well as the safeguarding and enforcement of international peace and security. The results of this research are of high value not only in the fields of international law and European Union law but also in the fields of the theory of law, constitutional law as well as trade law.



The resources of the project were used for the educational events such as the organisation of the student symposia. The picture presents the participants of the Student symposium of international law in 2015.



Workshop participants (including prof. David Zilberman, University of California, Berkeley, USA - first left; prof. Alan Matthews, Trinity College Dublin, Ireland - fifth left; prof. Joachim von Braun, Director of ZEF-Center, University of Bonn, Germany - third right).

GLOBAL COMMODITY PRICES, PRICE TRANSMISSION, AND FOOD SECURITY

Principal investigator: prof. Ing. Ján Pokrivčák, PhD., M.S.
 Applicant organisation: Slovak University of Agriculture in Nitra - Faculty of Economics and Management - Department of Economic Policy
 Participating organisation: National Agricultural and Food Centre - Research Institute of Agricultural and Food Economics, Bratislava
 Term of solution: July 2012 - December 2015
 Budget from agency: 179 776 EUR
 Project ID: APVV-0894-11

Subject of research

Within this project we have created comprehensive international databases on monthly producer and consumer prices, which were together with household budget surveys used in our empirical analyses. The databases covered Slovakia, Romania, Kosovo but also Tajikistan or Uzbekistan. Using quadratic almost ideal demand system methodology we have estimated demand elasticities for key food groups and compared elasticities over different years and countries.

Aims of the project

From our analysis it follows that food security situation in Slovakia has been improving since Slovakia's accession into the EU. However, there is still huge heterogeneity between segments of population. Government policies stimulating income growth are preferred to policies affecting prices to improve food security of vulnerable groups (rural households, ethnic minorities,...) in Slovakia. The project has also empirically estimated how economic, social, demographic, and cultural factors affect

the quality of food diets. Furthermore, we have studied the rising trend of food consumption away from home and estimated the determinants behind its growth. Advanced time series econometrics techniques were used to compute price transmission elasticities from world to domestic prices and from producer to consumer prices. The effects of market structure, policies, and exogenous shocks on price transmission was evaluated.

Our results were published in Energy Policy, Post-Communist Economies, Applied Economics, Economic Journal, etc. We presented results at international conferences: Congress of the European Agricultural Economists in Ljubljana, International Congress of Agricultural Economists in Milano, Conferences in Alghero, Ancona, Wageningen, Rome etc.

Benefits for practice

The results of the project were incorporated in new courses at the Faculty of Economics and Management of SUA in Nitra: Agricultural Policy, Behavioural Economics and Agricultural Economics.



Workshop participants (standing, project coordinator, prof. Jan Pokrivcak, Faculty of Economics and Management, SUA in Nitra).



Presentation by prof. Johan F. M. Swinnen, Director of LICOS Center for Institutions and Economic Performance at the University of Leuven, Belgium.

▼
HUMANITIES





D. Kováč and P. Šoltés proofreading the text for the book Slovak society in the "long" 19th century.

SLOVAKIA IN THE 19TH CENTURY

Principal investigator: PhDr. Dušan Kováč, DrSc.
 Applicant organisation: Institute of History, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 208 385 EUR
 Project ID: APVV-0119-11



The project leader Dušan Kováč with Eva Kowalská and Peter Šoltés, the editors of the first volume of publication Slovakia in 19th century.

Subject of research

The subject of the project was Slovak history in the "long 19th century". The 19th century had been the best searched period by Slovak historiography in the past because it was the period of modern Slovak nation building. However, new theoretical approaches in world historiography, ethnology and in political science have brought a new stimulus to the research of the 19th century. New views on nationalism and the ethnogenesis of modern nations and on the period of modernization have inspired Slovak historiography to look for new documents and re-evaluate previous research in the sense of the new theoretical approaches.

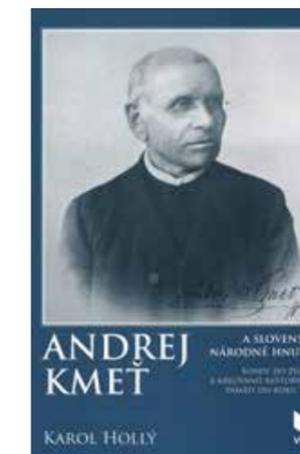
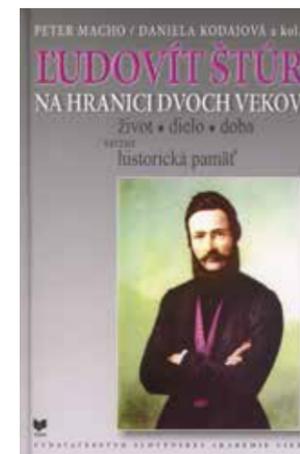
Objectives of the project

The goals of the project were to carry out basic and thoroughgoing research and to process the results in particular case studies, monographs and ultimately, three scientific syntheses; in other words, to expand and complete the knowledge of Slovak history of the "long" 19th century (1780-1900). This should create space to write manuscripts of three qualitatively new scientific syntheses summarizing the years from 1780 to 1867. Another goal was to publish scientific papers

and monographs about the period from 1867 to the end of the 19th century. In addition to the publication of these scientific outcomes, the research group intended to organize professional conferences and workshops and present their results at academic conferences organized by other institutions, especially at the 22nd World congress of historical sciences in Jinan (China) in 2015.

Results

After more than twenty years (the last historical synthesis of Slovak history was published in 1992), the comprehensive historical work, *Slovensko v 19. storočí* [Slovakia in the 19th century] brings a new in-depth view of the history of Slovakia in the 19th century. Three volumes, which will be published by VEDA, together with four volumes of *Slovensko v 20. storočí* [Slovakia in the 20th century], will present a new interpretation of the history of Slovakia in the modern period. Above all, research associated with the project brought new findings in areas which have only been partially explored. For example, this publication examines social history, which is understood as the history of an entire society, an individual within it and his everyday life,



including family life and available social and medical care. In addition to examining village life, the publication thoroughly examines the urban environment. Moreover, the research of economic history, which examines the economic processes in Slovakia in the European and Central European context, brings innovation. This work also brought new perspectives on projects with traditional topics: politics and culture. In the area of politics, the emphasis is on the relationship between Slovak political programs and the international context. In terms of politics and culture, research advanced from examining political and cultural elites to the perception of political programs and culture by common people in Slovakia. This project brought a new and deeper understanding of the society in Slovakia in the 19th century, which was its main aim. The project's findings are available in three volumes (which are prepared for publication), as well as numerous publications (15 monographs, 52 studies and articles). The research team was especially productive in popularizing the findings of their research.

The most important publications include:
 KOVÁČ, Dušan – KOWALSKÁ, Eva – ŠOLTÉS, Peter a kol. Spoločnosť na Slovensku v dlhom 19. storočí. [Society in Slovakia in the 19th Century]. Bratislava 2015.
 HOLEC, Roman. Štát s dvoma tvármi. (K hospodárskemu vývoju monarchie, Uhorska a Slovenska 1848-1867.) [The State with Two Faces. (The economic development of the monarchy, Hungary and Slovakia 1848-1867.)] Bratislava 2014.
 KOVÁČ, Dušan a kol. Sondy do slovenských dejín v dlhom 19. storočí. [Survey of Slovak History in the Long 19th Century.] Bratislava 2013.
 Pramene k dejinám Slovenska a Slovákov XI. a [Sources of History of Slovakia and Slovaks XI. a]. (ed. Dušan Kováč). Slováci po rakúsko-uhorskom vyrovnaní. [Slovaks after the Austro-Hungarian Compromise.] Bratislava 2012.
 MACHO, Peter – KODAJOVÁ, Daniela a kol. Ludovít Štúr na hranici dvoch vekov. [Ludovít Štúr on the Border of Two Ages.] Bratislava 2015.



International Conference „Patočka and History of Philosophy“ - July 2015.



An Interview of R. Stojka with Ivan Chvatík on the Occasion of the 25th Anniversary of Jan Patočka's Archive which was published in the journal „Philosophy“.

PATOČKA'S ASUBJECTIVE PHENOMENOLOGY AND HISTORY OF PHILOSOPHY

Principal investigator: Mgr. Róbert Stojka, PhD.
 Applicant organisation: Faculty of Arts, Pavol Jozef Šafárik University in Košice
 Term of solution: July 2012 – December 2015
 Budget from agency: 205 068 EUR
 Project ID: APVV-0480-11

Subject of research

The philosophical heritage and the personality of Jan Patočka, the most important Czech (Czechoslovak) philosopher of the last century in the context of the history of Greek philosophy, modern philosophy and the philosophy of the 20th century.

Objectives of the project

To explore the philosophical work of Jan Patočka in relation to the most significant figures of the history of philosophy and to present research on the major outputs of the project (3 collective monographs, an international scientific conference) and secondary outputs (2 separate monographs, 2 textbooks, establishing a library and organising an exhibition).

Results

Preparation and publication of the major outputs of the project - collective monographs:

Patočka and Greek Philosophy (Košice: UPJŠ 2013, 379 p.)
 Patočka and Modern Philosophy (Košice: UPJŠ 2014, 540 p.)
 Patočka and Philosophy of 20th Century (Košice: UPJŠ 2015, 696 p.)

Patočka and Modern Philosophy received the Literary Fund's prize for scientific and technical literature in 2014 in the category of social sciences.
 Patočka and Philosophy of 20th century received the Literary Fund's prize for scientific and technical literature in 2015 in the category of social sciences.
 The Institute of Philosophy in Prague, Czech Republic hosted a public presentation of all three major monographs as well as the proceedings from the international conference Patočka and the History of Philosophy. Establishing and expanding a specialised library called Patočkiana (01/13 – 12/15).
 Preparation and realisation of the international conference Patočka a dejiny filozofie (7/15).

Preparation and publication of the following individual monographs:
 Proceedings from the international conference – Stojka, R. – Škára, M. (eds.): Patočka and the History of Philosophy (Košice: UPJŠ 2015, s. 228 p.).
 Stojka, R.: Patočka's Philosophy of History (Košice: UPJŠ 2015, 272 p.).
 Preparation and publication of two textbooks:
 Zouhar, J. – Stojka, R.: „Kapitoly z dějin české filozofie 20. století“ (Košice: UPJŠ 2015, 209 s.).
 Jusko, Š.: „Mýtus v Patočkově filozofii“ (Košice: UPJŠ, 148 s.).



Receive the award (Literary fund) in 2014 – Professor Leško.

Publication of studies, reviews and interviews in peer-reviewed journal Filozofia - a special edition dedicated to the philosophy of Jan Patočka (5 – 6/15):
 Blecha, I.: Patočka's Care of the Soul: From Socrates through Plato to Aristotle
 Leško, V.: Patočka, Heidegger and the Question of Being
 Chvatík, I.: Approaching Patočka's Politics of a Spiritual Person
 Jusko, Š.: Patočka: Patočka: Time, Myth, and Critical Philosophy of History (essay)
 Stojka, R.: Democracy is No Bed of Roses. An Interview with Ivan Chvatík on the Occasion of the 25th Anniversary of Jan Patočka's Archive

Preparation and realisation of the exhibition Život a dielo J. Patočku (11/15 – Košice, 04/16 – Prešov).

In addition to the members of the Department of Philosophy and the History of Philosophy of the Faculty of Arts of Pavol Jozef Šafárik University in Košice, the following foreign and domestic experts in the history of philosophy were involved in the project: Dr. h. c. Ing. Ivan Chvatík (Institute of Philosophy of the Czech Republic – the founder of Jana Patočka's Archive in Prague), Prof. PhDr. Milan Sobotka, Dr.h.c., CSc. (Faculty of Arts of Charles University in Prague), prof. PhDr. Jan Zouhar, CSc. (Masaryk University in Brno), PhDr. Věra Schifferová, CSc. (Institute of Philosophy of the



Opening ceremony of „Life and work of Jan Patočka“ exhibition – Košice, November 2015.



Institute of Philosophy in Prague, Czech Republic held on its premises a public presentation of all three major monographs published under the project - „Patočka and Greek Philosophy“, „Patočka and Modern Philosophy“ and „Patočka and Philosophy of 20th century“, as well as the collections from the international conference „Patočka and History of Philosophy“. The picture shows Dr. Schifferová speech.

Czech Republic), Mgr. Jan Frei, PhD. (Institute of Philosophy of the Czech Republic, Prague), Prof. Dr. hab. Czesław Głombik (University of Silesia in Katowice), Dr. Dariusz Bęben (University of Silesia in Katowice), Dr. Helga Blaschek-Hahn (Charles University in Prague), Dr. Ludger Hagedorn (Institut für die Wissenschaften vom Menschen, Vienna), Mgr. Jozef Sivák, CSc. (Institute of Philosophy of the Slovak Academy of Sciences) and Doc. Erika Lalíková, PhD. (Faculty of Arts of Comenius University in Bratislava).

Benefits for practice

The project comprises the first historical-philosophical analysis, synthesis, deepening and expanding of the conventional understanding of Patočka's theoretical-philosophical legacy in the context of the most important philosophical concepts of the history of philosophy. Until now, no project had devoted any theoretical interest in Patočka's legacy in our domestic or even foreign conditions. Given that Patočka is becoming a more respected philosophical figure especially in foreign philosophical circles, this effort proved to be fully justified. Specific outputs (monographs, anthologies, textbooks and studies) will surely become a subject of interest to all university workplaces with a philosophical orientation. Last but not least, the project brings Patočka's personality to wider public awareness

STATE BORDERS AND IDENTITIES IN MODERN SLOVAK HISTORY IN CENTRAL EUROPEAN CONTEXT

Principal investigator: PhDr. Slavomír Michálek, DrSc.
 Applicant organisation: Institute of History, Slovak Academy of Sciences
 Term of solution: July 2012 – December 2015
 Budget from agency: 231 304.70 EUR
 Project ID: APVV-0628-11

Subject of Research

Within the framework of integration and disintegration processes, the investigation of the phenomenon of borders is again on the rise. State borders and their historical, economic, cultural, ethnic contexts are regularly discussed in EU and non-EU European states. In this case, the most violent changes in the last 100 years took place in Central and South-eastern Europe. This project represents the first attempt to sum up published results regarding Slovakia, and lays the groundwork for the future comprehensive elaboration of this matter in comparative research. It is an attempt at a new conceptualization of the border phenomenon from the point of view of social and cultural history, and represents one of the newest trends in current international historiography.

The project deals with economic history and the history of diplomacy and politics in Slovakia and the Central European region in the 19th and 20th centuries.

Objectives of the project

The aims of the project were to conduct a complex analysis of the state borders phenomenon – from the political, diplomatic, social, and micro-historical points of view. In such a conception borders do not constitute only a geopolitical problem, but also social, cultural and

economic phenomena and influence the public sphere. Another aim is to examine the impact of the creation and changes of state borders on the identities and identifications of the population.

Results

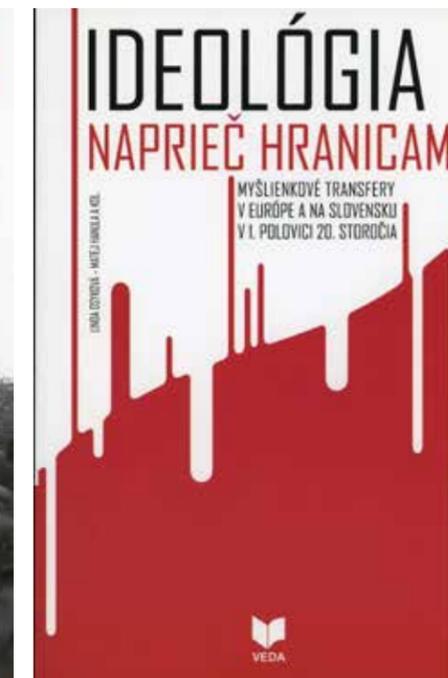
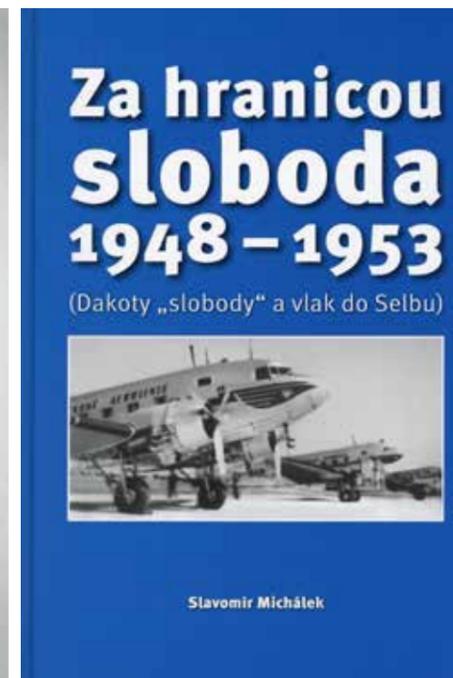
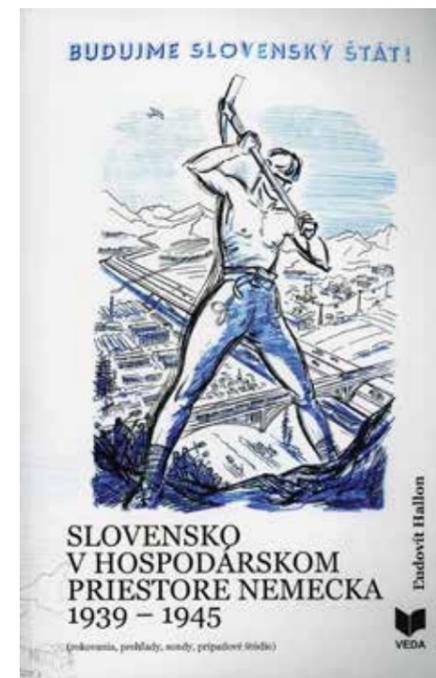
During the three-year project period, 19 scientific (and 2 specialized) monographs, as well as many scientific papers home and abroad – including 11 in CC journals were published. The knowledge acquired through the project has been used in the educational process (lectures and seminars on the 1st and 2nd levels of university education and doctoral studies). The project participants have popularized this theme in electronic and print media and their public lectures have drawn numerous visitors.

The published books included:
 OSYKOVÁ, Linda – HANULA, Matej. *Ideológia naprieč hranicami : myšlienkové transfery v Európe a na Slovensku v 1. polovici 20. storočia*. [Ideology across Borders: transfers of ideas in Europe and Slovakia in the 1st half of the 20th century.] Bratislava 2015.
 HUDEK, Adam – VÖRÖS, Ladislav a kol.: *Overcoming the Old Borders: beyond the paradigm of Slovak nation-*

al history. Bratislava 2013.
 MICHÁLEK, Slavomír. *Za hranicou sloboda 1948-1953* [Freedom beyond the Borders 1948-1953.] Bratislava 2013.
 MICHELA Miroslav – VÖRÖS László: *Rozpad Uhorska a Trianonská mierová zmluva: K politikám pamäti na Slovensku a v Maďarsku*. [The Disintegration of Hungary and the Peace Treaty of Trianon: on the Policies of Memory in Slovakia and Hungary.] Bratislava 2012.
 HALLON, Ľudovít. *Slovensko v hospodárskom priestore Nemecka 1939-1945*. [Slovakia in the Economic Space of Germany 1939-1945.] Bratislava 2015.

Benefits for practice

The project results are intended for the academic community, including other disciplines of social sciences and humanities, for students and teachers in the educational process, for the decision-making sphere, for journalists and publicists and the general public. In 2017, the book *Hranice a identity v moderných slovenských dejinách* (Borders and Identities in Modern Slovak History) will be published. The text will also include photographs, original documents and a list of publications.



CONTRIBUTION OF SLOVAKIA FOR ECONOMIC AND SOCIAL DEVELOPMENT OF EUROPEAN METAL AGE

Principal investigator: Dr.h.c. prof. PhDr. Václav Furmánek, DrSc.
 Applicant organisation: Institute of Archaeology, Slovak Academy of Sciences
 Term of solution: July 2012 – June 2015
 Budget from agency: 235 039 EUR
 Project ID: APVV-0736-11

Subject of research

The subject of the project was the historical development of Slovak and European Metalicium (from the end of the 3rd millennium BC to the beginning of the 1st millennium BC). This involved the elaboration of the absolute and relative chronology of each culture in the Bronze Age and the specification of the inter-ethnic relations of the civilizations in material and spiritual culture and the incorporation of late prehistoric society into the cultural-historical development of Middle Europe.

Aim of the project

The goal of the project was to evaluate the situation of the findings and the inventory from archaeological excavations in all their complexity (pottery, bone and horn finds, metal finds, osteological and botanical finds) from the following settlements (Partizánske, Radzovce, Rybník, Santovka, Včelince, Vráble); hillforts (Ilija-Sitno, Cinobaňa-Strieborná); hoards of bronze finds (Ilija-Sitno, Nitrianska Blatnica, Žilina-Považský Chlmec, Radzovce); cult places (Topoľčany-Továrniky, Slovak Karst caves); and cemeteries (Cinobaňa, Ilava, Kyjatice, Mikušovce, Radzovce, Silica, Tornaľa, Trenčín, Varín, Žitavany-Kňazice). Modern analytical methods of natural sciences (anthropology, archaeozoology, archaeobotanics, palynology, petrography, etc.) and mathematic-statistical methods were used. The analysis provides a solid basis for detailed studies and an understanding of the economic and social level of contemporary society, settlement urbanism, hillforts and its fortifications, as well as demonstrations of the

social structure of Late Prehistory, demographic and socio-economic development and its demonstrations in religion. Another goal was to elaborate the chronology and synchronization of each archaeological culture of the Late Bronze Age, as well as to specify the inter-ethnic relations of the civilizations in material and spirit culture and to incorporate the late prehistoric society into cultural-historical development of contemporary Europe.

Results

The project achieved several significant results. We continued in the systematic archaeological field research of the Southeastern Urnfields cemetery in Cinobaňa. In 2012 and 2014 we excavated other urn graves to bring the total to 314 graves. We worked on the grave catalogue in Radzovce, which was prepared for print in 2016. We finished field survey analyses, archaeological finds analyses and ecofacts analyses from the settlements in Radzovce and Tornaľa, while implementing the same approach that was used in working out the settlement in Partizánske and the Ilija-Sitno hillfort. Project researchers dealt with a huge funeral findings inventory. We finished the analysis of the Lusatian Culture urnfield cemeteries in Ilava and Žitavany-Kňazice and the Southeastern Urnfield Culture cemetery in Radzovce (a total of 1725 graves), while material from the urnfield cemeteries in Cinobaňa, Mikušovce, Trenčín, Varín (together 3000 graves) is in the process of being analysed.

Bronze industry was worked out within the framework of studied settlement agglomerations, urnfield cem-

eteries as well as bronze artefacts hoards: Ilija-Sitno, Nitrianska Blatnica, Žilina-Považský Chlmec. The above-mentioned science disciplines assisted in achieving a better understanding of urnfield civilization. Burnt human bones from cemeteries in Cinobaňa, Kyjatice, Mikušovce and Silica (together 750 samples) were analysed. A relevant demographic model of the urnfield civilization in Slovakia was created from these analyses. The model was used to establish the age and gender of more than 2700 individuals. The first steps in clarifying the production technology of the bronze finds were achieved in cooperation with Slovak metallographs. Project members participated in international conferences (Hriňová-Polana, Košice, Levice, Nitra) and foreign conferences (Opava, Plzeň, Sedlec-Prčice, Wrocław). They prepared archaeological exhibitions in Hodejov, Filakovo, Rimavská Sobota and Rožňava, where the young metalicium presentation was dominant. The project was also promoted in popular-scientific lectures, articles, and radio and tv presentations.

Benefits for practice

The results will be useful for history lectures in elementary and secondary schools. They will also be used in archaeological departments of universities in Slovakia and abroad. They may also be used to make science more attractive and to improve the national knowledge level in this field. Together they will exemplify the high professional and scientific level of Slovak archaeology in the context of European archaeological research.



Members of XXIIIth International colloquium „Old Bronze Age in Bohemia, Moravia and Slovakia“ in year 2013. Photo Archives of Museum in Levice.



Cinobaňa. Excavation of burial ground from Late Bronze Age in year 2012. Photo V. Mitáš.

Cinobaňa. Popularization and presentation of archaeological excavation in Cinobaňa for teachers and pupils of elementary school. Photo V. Mitáš.

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