CEITEC | Central European Institute of Technology
BRNO | CZECH REPUBLIC

NEWSLETTER

Dear CEITEC Friends,

CEITEC continues to make significant progress during this initial phase of establishing our institute. As a symbol of this, the opening of the first buildings at the Masaryk University Bohunice Campus will take place in September. This will bring many of our research groups plus the excellent instrumentation in the life sciences area into the same location.

CEITEC has been very active in organising international scientific events. The recent 3rd Congress on Epilepsy, Brain & Mind, as well as the INBIOR Conference: Integrated Approaches to Structural Biology, hosted several dynamic speakers, and were very well attended. We are also proud to have had The EMBO Young Scientists Forum organised by CEITEC Group Leaders. Looking into the future, we would like to extend an invitation to participate in the CEITEC Annual Conference - Frontiers in Life and Materials Sciences which will take place in Brno on 21-24 October. The many scientific events that CEITEC is involved in are an important mechanism to exchange the latest research and technology concepts and to bring the international scientific community together with CEITEC.

In September we will have a very important evaluation of our scientific activities which will be conducted by an international team of experts along with our International Scientific Advisory Board members. These evaluations are an important step to ensure that the quality of science within CEITEC is mandated and encouraged to grow.

We thank all of you, both within and outside of our organisation, who have helped CEITEC realize its goals of becoming an Institute for high-quality research.

Best,

Markus Dettenhofer

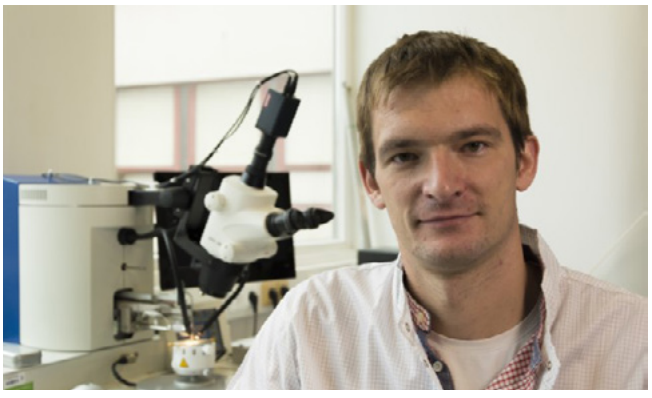
CONTENT

CEITEC is a Prime Example of the Synergy of Regional and EU Research Policies

A microscope that is unique even by world standards. This is one of the outcomes of scientific research at CEITEC BUT, which also serves as an example of how to access European funds. Thanks to well-chosen instruments and technology acquired through the targeted support of the European Regional Development Fund for large-scale infrastructure and approved by the Czech government, they have been able to obtain and implement research projects awarded directly by the European Commission.

The result of the synergy of national and European grant policy is exemplified by the participation of CEITEC scientists in the UnivSEM scientific research project. The project was successful at the European competition, among almost 30 applications, and obtained financing for the project to develop a new type of electron microscope with a wide spectrum of applications. The main actor in this project is the Czech company Tescan, a.s., which produces electron microscopes – CEITEC is one of the co-partners along with 6 other major companies and academic institution from Germany and Switzerland. The common goal is to develop a unique electron microscope capable of a number of structural, atomic and molecular analyses concurrently. UnivSEM is now halfway through the project and CEITEC can already celebrate publication in the prestigious journal *Nano Letters*.

More information can be found HERE



Michal Urbánek, UnivSEM project investigator

Three New SoMoPro Fellowships Have Started at CEITEC

The South Moravian Programme for Distinguished Researchers (SoMoPro) has allowed three more researchers who succeeded in its fourth call to integrate into the research teams at CEITEC. The SoMoPro programme combines funding from the South Moravian Region and the European Commission (via the Marie Curie COFUND Action) with the aim of creating appropriate conditions for returning or incoming scientists. Let us briefly introduce the new SoMoPro fellows and their research projects:

Dr. Jozef Hritz joined the research group of Biomolecular NMR Spectroscopy at the Structural Biology research programme under the supervision of Prof. Vladimír Sklenář in 2012 as a Marie-Curie IOF (International Outgoing Fellowship) fellow in the last, reintegration year of his project. He spent the two preceding years in the laboratory of Prof. Angela Gronenborn at the University of Pittsburgh School of Medicine, US. The topic of his SoMoPro project is the structural determination of the human 14-3-3ζ in a complex with a double phosphorylated human tyrosine hydroxylase 1.

Dr. Silvie Trantírková is a postdoctoral fellow in the research group of Biomolecular NMR Spectroscopy at the Structural Biology research programme, under the supervision of Dr. Lukáš Trantírek since he joined CEITEC in 2012 (see interview). Her previous career was oriented toward medical oncology in the laboratory of Dr. Susanne M.A. Lens at the UMC Utrecht, in the Netherlands. The topic of her current work and SoMoPro project is focused on selective targeting of DNA G-quadruplexes by small molecule ligands within the human genome.

Dr. Phil Jackson has recently joined the research group Functional Genomics and Proteomics of Plants under the leadership of Assoc. Prof. Jan Hejátko. He will work on his successful project *"S/T kinases implicated in the cytokinin signalling pathway and cytokinin control of root growth"* which has been granted by SoMoPro II. Dr Jackson has come to CEITEC from ITQB in Oerias, Portugal, where he led the Plant Cell Wall research group. With his expertise in plant cell wall development and almost 30 years of scientific experience in the USA and Portugal he will significantly enhance the host research group for the next three years.

Karel Říha Fully Takes up the Post of Group Leader at CEITEC

On July 1, 2014, the new research group for the research programme Genomics and Proteomics of Plant Systems with title Plant Molecular Biology under the leadership of Dr. Karel Říha, will begin work in earnest. Dr. Říha is joining CEITEC after 12 years spent at two prestigious foreign institutions - Texas A&M University, College Station, USA and the Gregor Mendel Institute of Molecular Plant Biology, Vienna, Austria. At CEITEC Dr. Říha will concern himself with research in the field of telomeres and genome stability, the regulation of meiosis and the role of RNA decomposition in genome regulation.

EU-LIFE Community Meeting

The second EU-LIFE Community Meeting was held from May 14 to 15, 2014, at the CRG in Barcelona. During the meeting, 85 EU-LIFE members presented the main results of the seven Working groups EU-LIFE has established, focusing on Grants, Science Communication, Translational Research, Technology Transfer, Training, IT and Indicators of Excellence. In addition to sharing best practice and benefiting from each other's expertise and experience in all these domains, several joint actions were initiated and presented during the meeting.

The EU-LIFE alliance was honoured by the presence of two distinguished guests:

- **Alessandra Luchetti**, European Commission, Head of Unit, Marie Skłodowska-Curie actions, who presented her vision of how an alliance such as EU-LIFE could be an interesting partner for the European Commission.
- **Iain Mattaj**, Director General of EMBL, who as the scientific advisor gave thorough feedback on the organisation and achievements of the alliance.

AWARDS

The Best Poster Award Given to Lenka Zajíčková from CEITEC MU

Lenka Zajíčková from CEITEC MU won the 2014 Best Poster Award for her presentation, „Bioactive Amine-Containing Thin Films Prepared by Plasma Polymerization" at the 2014 Society of Vacuum Coaters Technical Conference (SVC TechCon), which was held on May 3-5, 2014, in Chicago, USA. The SVC TechCon explores the latest advances in vacuum coating and surface engineering technologies, including process and materials development, engineering solutions and industrial applications.

Prof. Radek Marek Receives the Petr Sedmera Prize for the Best Publication in the Category of NMR

The Jan Marek Marci Spectroscopy Association each year awards a prize for the best specialist work in the field of the molecular structure of substances, as studied with the aid of mass spectrometry or NMR. In the NMR spectroscopy category this year the Petr Sedmera Prize was won by Prof. Radek Marek from the Biomolecular NMR Spectroscopy research group for work entitled *Intermolecular Interactions in Crystalline Theobromine as Reflected in Electron Deformation Density and ^{13}C NMR Chemical Shift Tensors* (authors Kateřina Bouzková, Martin Babinský, Lucie Novosadová and Radek Marek) published in the *Journal of Chemical Theory and Computation*. In this contribution a theoretical approach to the interpretation of the influence of intermolecular interactions on NMR chemical shift tensors and their correlation with experimental NMR data was proposed.

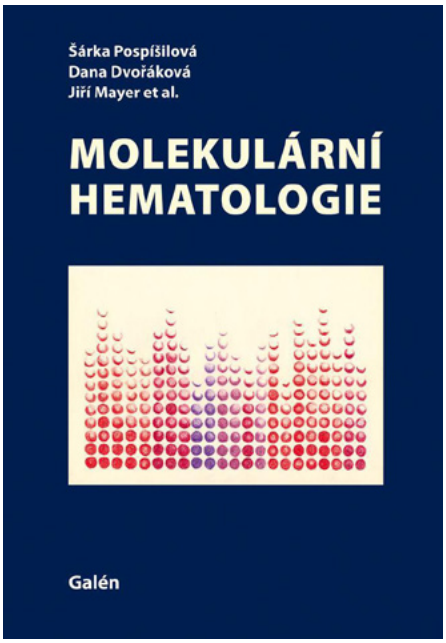
The results of the competition were announced at the 29th Central European NMR Meeting in Valtice, where one of the authors of the winning work, Dr. Martin Babinský, gave a lecture on this topic.

On the left Prof. Viktor Kanický, chairman of the Jan Marek Marci Spectroscopy Association, on the right the award recipient Prof. Radek Marek

Monograph *Molecular Hematology* Awarded the Hlávka Prize

The Foundation of Czech Literature Fund together with the Hlávka Foundation decided to award the team of scientists led by Prof. Šárka Pospíšilová, Ing. Dana Dvořáková and Prof. Jiří Mayer for their monograph *Molecular Hematology*, published in 2013.

The Hlávka Prize promotes excellent scientific literature from various disciplines published in the Czech Republic. The awards ceremony traditionally takes place in the Castle of Lužany, near Pilsen, and this year was held on June 16.



Despite the fact that the field of haematology was established decades ago, the importance of molecular aspects of haematological diseases has recently grown rapidly. In haematology in particular we can observe a close connection between laboratory research and clinical application. The authors of the book are reacting to the current situation and offer a consistent and thorough overview of the molecular mechanisms of haematological pathogenesis. The content of the monograph is divided into four parts: a general introduction to cell biology, molecular-biological methods used for investigation in haematology, molecular pathogenesis of the most frequent haematological malignities and molecular pathogenesis of severe haematological non-malignant pathogenesis. The book helps deepen our understanding of a topic that is nowadays an essential prerequisite not only for the clinical haematologist but for any molecular biologist.

Dr. Roman Řemínek Wins the Sanofi Prize for Pharmacy

Roman Řemínek, PhD, a researcher from the CEITEC Metabolomics research group received on June 19 at the French Embassy in Prague an award for his research in the pharmaceutical sciences. He reached the final from the nationwide competition, where the quality of his work was judged by an expert commission made up of French and Czech scientists. The prize was presented to him by the holder of the 1987 Nobel prize for chemistry, Jean-Marie Lehn, in the presence of His Excellency Jean-Pierre Asvazadourian, France's ambassador in the Czech Republic.

Dr. Řemínek looked at the metabolic processing of drugs using capillary electrophoresis. As winner he gets both financial support and a chance to travel on a one-month placement with the French research laboratory of his choice.

On the left the award recipient Dr. Roman Řemínek, on the right Prof. Zdeněk Glatz, Metabolomics research group leader

EVENTS

The EMBO Young Scientists Forum

The EMBO Young Scientists Forum organized by CEITEC research group leaders Dr. Štěpánka Vaňáčová (RNA Quality Control research group) and Dr. Richard Štefl (Structural Biology of Gene Regulation research group) was held at the University Campus Bohunice on May 29-30, 2014. The meeting provided an opportunity to our PhD students and postdocs to interact with Europe's most promising young scientists, members of the EMBO Young Investigator Programme, and motivate them to pursue a career and education in the life sciences. PhD students had a chance to present their work through poster sessions and discuss some of the policies and practices for undertaking world-class science. The best posters were awarded EMBO certificates for attendance at international meetings and conferences. We would like to thank to all the students and speakers who actively participated at EYSF!

A photo gallery can be found HERE.

INBIOR Conference: Integrated Approaches to Structural Biology

On May 15, the conference on Integrated Approaches to Structural Biology organized by research programme coordinator, Prof. Vladimír Sklenář, was held in the Augustinian Abbey in Brno. Eight prominent European scientists including Anne Imberty (CERMAV, CNRS, Grenoble), Dmitri Svergun (EMBL, Hamburg) and Simon Bullock (MRC, Cambridge) presented their recent achievements and state-of-the-art results in the field. The meeting was attended by almost 100 participants.

A photo gallery is available HERE.

esf european social fund in the czech republic
EUROPEAN UNION
MINISTRY OF EDUCATION, YOUTH AND SPORTS
OP Education for Competitivness
INVESTMENTS IN EDUCATION DEVELOPMENT

The conference was funded from the project INBIOR (CZ.1.07/2.3.00/20.0042) co-financed by the European Social Fund and the state budget of the Czech Republic.

3rd Congress on Epilepsy, Brain & Mind

In the period April 3–5, 2014 the third annual international congress Epilepsy, Brain & Mind was held. For the first time the congress was held in Brno, at the International Hotel.

The congress took place under the patronage of the president of the Czech Republic, the governor of the South Moravian region, the rector of Masaryk University and the mayor of Brno. The main organiser was the Brain and Mind Research programme of CEITEC.

The congress also took place under the patronage of the Commission on European Affairs of the International League Against Epilepsy (ILAE), The Czech League Against Epilepsy and ILAE branches from other European countries. The congress dealt with aspects of epilepsy outside the framework normally discussed and covered themes on the borders of epilepsy and philosophy, religion, art, history and other areas. The main subject of the congress was issues of psychological disorders, depression, cognitive disorders, psychosocial situation and behavioural problems in people with epilepsy (LSE). Participants focussed on the possibilities of treatment of these disorders and the influence of antidepressant, antipsychotic and cognitive medication,

as well as the influence of antiepileptics on attention, cognition, mood and behaviour. A total of 302 delegates from 28 countries took part, and they not only participated in the professional side but also enjoyed the evening social activities. The congress was chaired by Prof. Ivan Rektor from Brno and Prof. Amos Korczyn from Tel Aviv.

Both professionally and socially the congress was a great success.

A photo gallery can be found HERE.

Invitation: CEITEC Annual Conference - Frontiers in Material and Life Sciences

This will be our first annual conference bringing together international scientific speakers in the fields of the life sciences and materials sciences with speakers from within CEITEC to explore the interface of these two disciplines. The programme is designed to maximise the time for scientists from multiple disciplines to discuss common ideas in solving some of the most important scientific questions of today. The programme includes keynote lectures, plenary sessions, topic specific workshops, poster session with PhD students competition, educational session and more.

WHEN: October 21-24, 2014

WHERE: Best Western International Hotel, Brno, Czech Republic

Frontiers in Material and Life Sciences

KEYNOTE SPEAKERS:
- **Jack Johnson**, The Scripps Research Institute, USA
- **Jochen Feldmann**, Ludwig-Maximilians-Universtität München, Germany

More information can be found HERE.

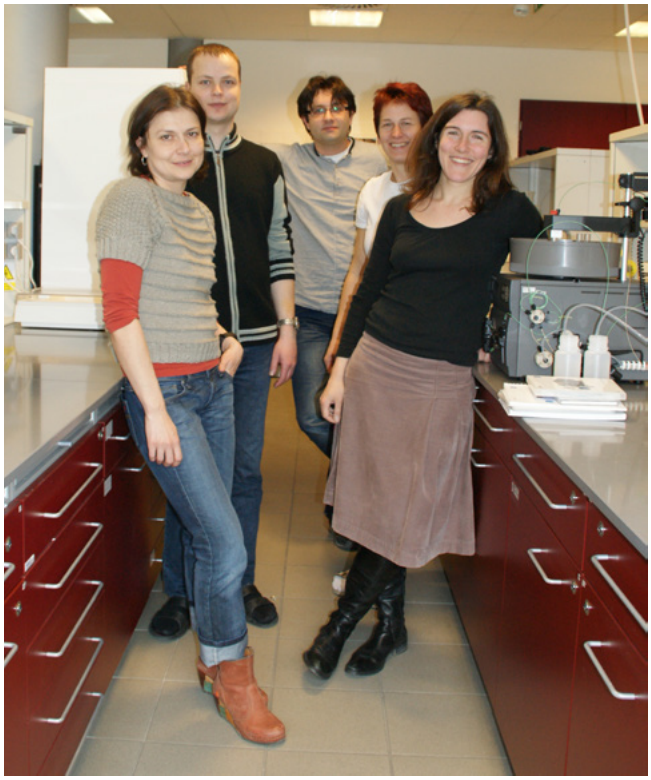
INTERVIEW WITH CEITEC SCIENTIST

Lukáš Trantírek , PhD

Research Group **Biomolecular NMR Spectroscopy**
Research Programme **Structural Biology**

To start with could you outline the main focus and aims of your research, and explain why you chose to work at CEITEC on your return to the Czech Republic two years ago?

Our laboratory focusses on the identification of regulating elements and mechanisms in the non-coding part of the genome, in which we assume there is potential for its use as a therapeutic target in a wide range of pathological states from cancer to various developmental diseases. In simpler terms: we are studying certain areas of genomic DNA, which control something in the cell. We will then try to find out how we might through the DNA influence that control.



Beginning at CEITEC - the composition of the group in 2012 (from the left: Silvie Trantírková, Jan Ryneš, Lukáš Trantírek, Barbora El-Ghanammová, Lola Bajard)

There were basically three reasons for choosing CEITEC. In the first place was the factor of a strong scientific community, and an inspiring environment linked to it. Primarily I work in the field of DNA research and Brno is a kind of 'Mecca' in this area and not only within the Czech Republic. In Brno, and in CEITEC, there is a whole range of internationally renowned scientists in this field such as for example Prof. Vladimír Sklenář (NMR spectroscopy of nucleic acids), Prof. Jiří Šponer (computational chemistry of nucleic acids), Prof. Michaela Vorlíčková (CD spectroscopy of nucleic acids), or Prof. Jiří Fajkus and Dr. Karel Říha working with the non-coding parts of the genome responsible for its integrity. From the younger generation a range of talented scientists are working in CEITEC such as Ass. Prof. Richard Štefl, Dr. Peter Lukavsky and Ass. Prof. Štěpánka Vaňáčová, who are looking into closely connected problems involving RNA. A second factor in the choice was the equipment of the newly -established Josef Dadok National NMR Centre, which can stand comparison with the world's best and makes possible the most demanding NMR measurements (the NMR spectrometer is a basic instrument for our research). A third, and for me very important, factor was the attractive start-up package allowing me to establish an independent research group.

You spent four years at Utrecht University in the Netherlands and so are well placed to compare the situation there and in the Czech Republic. How would you rate conditions for scientists, support at the national level, competition for grants, etc.?

I will reply in a roundabout way because a fair comparison of research in the Czech Republic and the Netherlands would take up many pages. It certainly isn't the case that research financing in the Netherlands was much better than in the Czech Republic. Dutch universities have suffered a kind of minor crisis in the last five years, caused by an unfortunate change in the rules for

their financing, and that of research overall. Specifically this involved the transfer of what was previously institutional financial means to the grant agency. The original intent of the Dutch government was to strengthen excellence in research with the assumption that excellent universities would gain money while the less good would either improve or disappear. The new system certainly made possible an increase in funds for excellent scientists and research groups, but without any visible correlation with a growth in research quality. Excellent groups simply continued to be excellent. It is important to be aware that the money does not flow into the institutions as such, but to a small group of their employees. As a result this shift from institutional money to grant money had a very negative impact on the delivery of education and the running of the whole institution. All of a sudden there wasn't money to pay lecturers and not even for administrative assistants. At the University of Utrecht, which has been repeatedly assessed as the best in the Netherlands, this led to the closing of whole areas and departments, and thanks to redundancies even to a transfer of teaching and admin to the scientists that were successful in gaining grants. And since I was a first-hand witness to this, I am now disconcerted to hear in the Czech Republic plans for the strengthening of excellence that sound dangerously similar to the Dutch model I have described.

Lukáš Trantírek was born in Moravská Třebová, in the Czech Republic, in 1975. He obtained his MSc in organic chemistry from Masaryk University in Brno in 1998. In 2001, he obtained his Ph.D. from Masaryk University under the direction of Prof. Vladimír Sklenář. He was an EMBO postdoctoral fellow in the group of Juli Feigon at the University of California in Los Angeles from 2002 to 2003. In 2012, following his independent career at the University of Utrecht, The Netherlands, he joined CEITEC as a junior group leader in the research group of Biomolecular NMR Spectroscopy. His research is focused on the structural biology of nucleic acids and NMR spectroscopy.

What on the other hand should be an inspiration for the Czech Republic is their strategy for the education of students at university, especially at postgraduate level. In the Netherlands there is a great deal of competition for places on courses at all levels in comparison with here. Therefore the demands on students during their studies are, and can be, significantly higher. The consequence is that the quality and capacities of the average Utrecht University graduate are substantially better than those of the average graduate from any Czech university. Much of the responsibility for this state of affairs lies at the door of our accreditation commission.

To return to the question – I see the conditions for scientific workers in the Czech Republic as being good. Or I should say that they are no better or worse than anywhere else in the world.

You yourself have been very successful in gaining scientific grants and your wife was successful in the latest call for SoMoPro. Could you let us know what lies behind these excellent results?

Luck, tens of hours spent preparing grant applications and, we kind of kid ourselves, also the original approaches we propose for the resolution of scientific problems. Among other factors undoubtedly belongs what the scientific community refers to as "track record", including experience from top foreign laboratories and good publication output.

For a time you were involved in the running of the Faculty of Science of the University of South Bohemia. What did you gain from this experience and how did it influence your view of the bureaucracy which is often connected with Czech science?

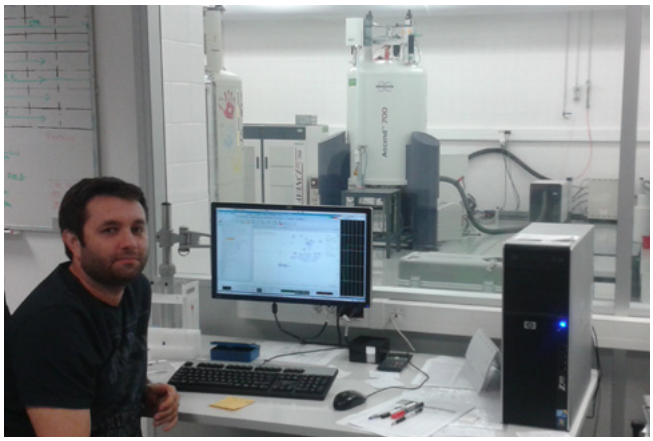
From today's perspective I see taking up the function of vice-dean for the operation of the faculty as important experience. I accepted the post from pure naivety and at a time when I was still starting up my laboratory. The multitude of duties and administration connected to the role kept me busy 8-10 hours a day. And alongside that teaching as well. Both the laboratory and my family suffered. Nonetheless every cloud has a silver lining: Firstly I learned how important it is when running things to be able to delegate (provided there is someone to delegate to), consistency and predictability in decision-making (something I use both when testing students as well as in running the laboratory), and communication with others. Since that time I have had a deep respect for those doing good work in academic roles – it is a service to the community and not all by any means show gratitude.

My perspective on bureaucracy was changed by taking on the role of vice dean in that I have learned to distinguish between essential and non-essential administration. At present, admin takes up 60-70% of my time. I think I can say that about 50% of this admin can be put in the unnecessary group, the group that really should not exist. Reducing this excess admin, in my opinion would be one of the first steps toward the more efficient functioning of Czech universities.

Returning several years back, what was the main impulse behind your scientific career? Did you enjoy chemistry already at primary/secondary school?

Did I enjoy chemistry? Certainly not at primary school. At secondary school yes. After girls and outdoor sports it was my favourite area of interest. :-)

My scientific career, even if I do not like the term, began I guess in the first year postgraduate studies. Under Prof. Vladimír Sklenář I had the chance to work on the characterisation of a new type of DNA helix, which was one of those projects that even after successful resolution generated a whole range of further problems, questions and projects. I guess that then I felt, 'my god I have to see it through to completion'. And I'm still trying to complete it even now. :-)



By what criteria did you choose a location for your post-doctoral placement?

I chose my post-doctoral placement on a combination of two factors: a) topic – I wanted to continue with the NMR spectroscopy of nucleic acids, and b) location. California was simply more attractive for me than for example Sweden or the Netherlands, where I also had offers. If you ask whether the prestige of the laboratory was an important factor in my choice, then I have to say it wasn't. Nonetheless if I were a student today looking for a foreign placement, I would also take this factor into consideration. Fortunately for me the laboratory of Prof. Juli Feigon at the University of California Los Angeles was at the top of the field.

What do you see as the most important aspect of a well-functioning scientific team?

This is not a simple question. The most important aspects of a well-functioning group are its productivity and recognition in the international scientific community. These two factors imply that such a group works on important problems or, thanks to their originality, come out with a completely new discovery. In the ideal case a combination of the two. From a different perspective – the most important aspects for a well-functioning scientific group are stable financing for a period of more than three years, a minimum of administration and access to students with a good grasp of the fundamentals. In each of these areas we have a certain amount of ground to make up in the Czech Republic.

And finally an obligatory question – what do you see as the greatest success of your career? And what are your ambitions and further scientific plans within CEITEC?

Concerning the first question. Personally I would see it as the development of two approaches which made possible the structural characterisation of nucleic acids, and that at the level of resolving individual atoms, in the complex environment of the living cell. Since the structure of DNA reacts very sensitively to a range of physico-chemical factors in its surroundings, these approaches have turned out to be fundamental in identifying the bioactive conformation of DNA, which is an essential precondition for their rational therapeutic targeting.

As to the second question: Our research is fundamental in nature. Nonetheless I would be happy if we managed to find applications for at least some of our discoveries. That however is very much for the long term. In terms of fundamental research my ambition remains to find the principle allowing for the rational development of medicines having specificity for a particular position on the genome. Currently all known medicines are non-specific, which means that they have a whole range of undesirable side effects for potential patients.

Thank you for the interview!

SELECTED RECENT PUBLICATIONS

ADVANCED NANOTECHNOLOGIES AND MICROTECHNOLOGIES

Optics Express

Coherence-controlled holographic microscopy in diffuse media

Lošťák M., **Chmelík R.**, **Slabá M.**, Slabý T.

Research Group: Experimental Biophotonics

Summary: Low-coherence interferometric microscopy (LCIM) enables to image through scattering media by filtration of ballistic light from diffuse light. The filtration mechanism is called coherence gating. We show that coherence-controlled holographic microscope (CCHM), which belongs to LCIM, enables to image through scattering media not only with ballistic light but also with diffuse light. The theoretical model was created which derives the point spread function of CCHM for imaging through diffuse media both with ballistic and diffuse light. The results of the theoretical model were compared to the experimental results. In the experiment the resolution chart covered by a ground glass was imaged. The experimental results are in the good agreement with the theoretical results. It was shown both by experiments and the theoretical model, that with ballistic and diffuse light we can obtain images with diffraction limited resolution.

NANO LETTERS

Real-Time Observation of Collector Droplet Oscillations during Growth of Straight Nanowires.

Kolíbal M., Vystavěl T., **Varga P.**, **Šikola T.**

Research Group: Fabrication and Characterisation of Nanostructures

Summary: A liquid droplet sitting on top of a pillar is crucially important for semiconductor nanowire growth via a vapor–liquid–solid (VLS) mechanism. For the growth of long and straight nanowires, it has been assumed so far that the droplet is pinned to the nanowire top and any instability in the droplet position leads to nanowire kinking. Here, using real-time in situ scanning electron microscopy during germanium nanowire growth, we show that the increase or decrease in the droplet wetting angle and subsequent droplet unpinning from the growth interface may also result in the growth of straight nanowires. Because our argumentation is based on terms and parameters common for VLS-grown nanowires, such as the geometry of the droplet and the growth interface, these conclusions are likely to be relevant to other nanowire systems.

ADVANCED MATERIALS

Catalysis Today

Preparation and characterization of doped titanium dioxide printed layers

Králová M., **Dzik P.**, **Veselý M.**, **Cihlář J.**

Research Group: Advanced Polymers and Composites

Summary: Thin layers of doped titanium dioxide on Pyrex glass were prepared by the material printing technique. Titanium dioxide was synthesized by the sol–gel method employing titanium(IV)isopropoxide as the precursor. A dedicated experimental inkjet printer Fujifilm Dimatix 2831 was used for the coating process. The influence of various solvents onto sol jettability was investigated. The mixture of absolute ethanol and 2-butanol was finally adopted because of its optimum viscosity and rate of evaporation. A series of experiments with different printing conditions was carried out, the optimum printing settings were determined. Consequently, iron and silver dopants were incorporated into the sol. The influence of doping on the photocatalytic activity of TiO_2 as well as the shift of absorption edge towards high wavelengths was investigated. The quality of all layers was studied by optical microscopy. The surface topology was evaluated by atomic force microscopy. The study of surface structure was performed using scanning electron microscopy. Crystallite phases of prepared TiO_2 were investigated by X-ray diffraction analysis. Band gap energy was determined by UV–vis reflection spectroscopy. The photocatalytic activity of printed thin films was examined as a degradation rate of stearic acid and 2,6-dichloroindophenol under UV radiation.

STRUCTURAL BIOLOGY

Nucleic Acids Research

MotiveValidator: interactive web-based validation of ligand and residue structure in biomolecular complexes

Vařeková Svobodová R., **Jaiswal D.**, **Sehnal D.**, **Ionescu C.**, **Geidl S.**, **Pravda L.**, Horský V., **Wimmerová M.**, **Koča J.**

Research Group: Computational Chemistry & Glycobiochemistry

Summary: Structure validation has become a major issue in the structural biology community, and an essential step is checking the ligand structure. This paper introduces MotiveValidator, a web-based application for the validation of ligands and residues in PDB or PDBx/mmCIF format files provided by the user. Specifically, MotiveValidator is able to evaluate in a straightforward manner whether the ligand or residue being studied has a correct annotation (3-letter code), i.e. if it has the same topology and stereochemistry as the model ligand or residue with this annotation. If not, MotiveValidator explicitly describes the differences. MotiveValidator offers a user-friendly, interactive and platform-independent environment for validating structures obtained by any type of experiment. The results of the validation are presented in both tabular and graphical form, facilitating their interpretation. MotiveValidator can process thousands of ligands or residues in a single validation run that takes no more than a few minutes. MotiveValidator can be used for testing single structures, or the analysis of large sets of ligands or fragments prepared for binding site analysis, docking or virtual screening. MotiveValidator is freely available via the Internet at http://ncbr.muni.cz/MotiveValidator.

Nucleic Acids Research

Structure and semi-sequence-specific RNA binding of Nrd1

Bačíková V., **Pasulka J.**, **Kubíček K.**, **Štefl R.**

Research Group: Structural Biology of Gene Regulation

Summary: In *Saccharomyces cerevisiae*, the Nrd1-dependent termination and processing pathways play an important role in surveillance and processing of noncoding ribonucleic acids (RNAs). The termination and subsequent processing is dependent on the Nrd1 complex consisting of two RNA-binding proteins Nrd1 and Nab3 and Sen1 helicase. It is established that Nrd1 and Nab3 cooperatively recognize specific termination elements within nascent RNA, GUA[A/G] and UCUU[G], respectively. Interestingly, some transcripts do not require GUA[A/G] motif for transcription termination *in vivo* and binding *in vitro*, suggesting the existence of alternative Nrd1-binding motifs. Here we studied the structure and RNA-binding properties of Nrd1 using nuclear magnetic resonance (NMR), fluorescence anisotropy and phenotypic analyses *in vivo*. We determined the solution structure of a two-domain RNA-binding fragment of Nrd1, formed by an RNA-recognition motif and helix–loop bundle. NMR and fluorescence data show that not only GUA[A/G] but also several other G-rich and AU-rich motifs are able to bind Nrd1 with affinity in a low micromolar range. The broad substrate specificity is achieved by adaptable interaction surfaces of the RNA-recognition motif and helix–loop bundle domains that sandwich the RNA substrates. Our findings have implication for the role of Nrd1 in termination and processing of many non-coding RNAs arising from bidirectional pervasive transcription.

GENOMICS AND PROTEOMICS OF PLANT SYSTEMS

Mass Spectrometry Reviews

Numerical modeling of capillary electrophoresis - electrospray mass spectrometry interface design.

Jarvas G., Guttman A., **Foret F.**

Research Group: Bioanalytical Instrumentation

Summary: Capillary electrophoresis hyphenated with electrospray mass spectrometry (CE-ESI-MS) has emerged in the past decade as one of the most powerful bioanalytical techniques. As the sensitivity and efficiency of new CE-ESI-MS interface designs are continuously improving, numerical modeling can play important role during their development. In this review, different aspects of computer modeling and simulation of CE-ESI-MS interfaces are comprehensively discussed. Relevant essentials of hydrodynamics as well as state-of-the-art modeling techniques are critically evaluated. Sheath liquid-, sheathless-, and liquid-junction interfaces are reviewed from the viewpoint of multidisciplinary numerical modeling along with details of single and multiphase models together with electric field mediated flows, electrohydrodynamics, and free fluid-surface methods. Practical examples are given to help non-specialists to understand the basic principles and applications. Finally, alternative approaches like air amplifiers are also included.

Science Signaling

Huwe1-mediated ubiquitylation of Dishevelled defines a negative feedback loop in the Wnt signaling pathway

De Groot R. E. A., Ganji R. S., Bernatik O., Lloyd-Lewis B., Seipel K., **Šedová K.**, **Zdráhal Z.**, Dhople V. M., Dale T. C., Korswagen H. C., Bryja V.

Research Group: Proteomics

Summary: Wnt signaling plays a central role in development, adult tissue homeostasis, and cancer. Several steps in the canonical Wnt/β-catenin signaling cascade are regulated by ubiquitylation, a protein modification that influences the stability, subcellular localization, or interactions of target proteins. To identify regulators of the Wnt/β-catenin pathway, we performed an RNA interference screen in *Caenorhabditis elegans* and identified the HECT domain-containing ubiquitin ligase EEL-1 as an inhibitor of Wnt signaling. In human embryonic kidney 293T cells, knockdown of the EEL-1 homolog Huwe1 enhanced the activity of a Wnt reporter in cells stimulated with Wnt3a or in cells that overexpressed casein kinase 1 (CK1) or a constitutively active mutant of the Wnt co-receptor low-density lipoprotein receptor-related protein 6 (LRP6). However, knockdown of Huwe1 had no effect on reporter gene expression in cells expressing constitutively active β-catenin, suggesting that Huwe1 inhibited Wnt signaling upstream of β-catenin and downstream of CK1 and LRP6. Huwe1 bound to and ubiquitylated the cytoplasmic Wnt pathway component Dishevelled (Dvl) in a Wnt3a- and CK1ε-dependent manner. Mass spectrometric analysis showed that Huwe1 promoted K63-linked, but not K48-linked, polyubiquitination of Dvl. Instead of targeting Dvl for degradation, ubiquitylation of the DIX domain of Dvl by Huwe1 inhibited Dvl multimerization, which is necessary for its function. Our findings indicate that Huwe1 is part of an evolutionarily conserved negative feedback loop in the Wnt/β-catenin pathway.

MOLECULAR MEDICINE

Nature Methods

Towards error-free profiling of immune repertoires

Shugay M., Britanova O. V., Merzlyak E. M., Turchaninova M. A., **Mamedov I. Z.**, Tuganbaev T. R., Bolotin D. A., Staroverov D. B., Putintseva E. V., **Plevova K.**, Linnemann C., Shagin D., **Pospisilova S.**, Lukyanov S., Schumacher T. N., **Chudakov D. M.**

Research Group: Adaptive Immunity Group & Medical Genomics

Summary: Deep profiling of antibody and T cell–receptor repertoires by means of high-throughput sequencing has become an attractive approach for adaptive immunity studies, but its power is substantially compromised by the accumulation of PCR and sequencing errors. Here we report MIGEC (molecular identifier groups–based error correction), a strategy for high-throughput sequencing data analysis. MIGEC allows for nearly absolute error correction while fully preserving the natural diversity of complex immune repertoires.

Nature Communications

The structure and substrate specificity of human Cdk12/Cyclin K.

Bösken C. A., Farnung L., Hintermair C., Merzel Schachter M., Vogel-Bachmayr K., **Blazek D.**, Anand K., Fisher R. P., Eick D., Geyer M.

Research Group: Inherited Diseases II - Transcriptional Regulation

Summary: Phosphorylation of the RNA polymerase II C-terminal domain (CTD) by cyclin-dependent kinases is important for productive transcription. Here we determine the crystal structure of Cdk12/CycK and analyse its requirements for substrate recognition. Active Cdk12/CycK is arranged in an open conformation similar to that of Cdk9/CycT but different from those of cell cycle kinases. Cdk12 contains a C-terminal extension that folds onto the N- and C-terminal lobes thereby contacting the ATP ribose. The interaction is mediated by an HE motif followed by a polybasic cluster that is conserved in transcriptional CDKs. Cdk12/CycK showed the highest activity on a CTD substrate prephosphorylated at position Ser7, whereas the common Lys7 substitution was not recognized. Flavopiridol is most potent towards Cdk12 but was still 10-fold more potent towards Cdk9. T-loop phosphorylation of Cdk12 required coexpression with a Cdk-activating kinase. These results suggest the regulation of Pol II elongation by a relay of transcriptionally active CTD kinases.

BRAIN AND MIND RESEARCH

Journal of Alzheimer's disease

Disturbed Default Mode Network Connectivity Patterns in Alzheimer's Disease Associated with Visual Processing

Krajcovicova L., **Mikl M.**, **Marecek R.**, **Rektorova I.**

Research Groups: Applied Neuroscience (main author) & Multi-modal and Functional Neuroimaging

Summary: Changes in connectivity of the posterior node of the default mode network (DMN) were studied when switching from baseline to a cognitive task using functional magnetic resonance imaging. In all, 15 patients with mild to moderate Alzheimer's disease (AD) and 18 age-, gender-, and education-matched healthy controls (HC) participated in the study. Psychophysiological interactions analysis was used to assess the specific alterations in the DMN connectivity (deactivation-based) due to psychological effects from the complex visual scene encoding task. In HC, we observed task-induced connectivity decreases between the posterior cingulate and middle temporal and occipital visual cortices. These findings imply successful involvement of the ventral visual pathway during the visual processing in our HC cohort. In AD, involvement of the areas engaged in the ventral visual pathway was observed only in a small volume of the right middle temporal gyrus. Additional connectivity changes (decreases) in AD were present between the posterior cingulate and superior temporal gyrus when switching from baseline to task condition. These changes are probably related to both disturbed visual processing and the DMN connectivity in AD and reflect deficits and compensatory mechanisms within the large scale brain networks in this patient population. Studying the DMN connectivity using psychophysiological interactions analysis may provide a sensitive tool for exploring early changes in AD and their dynamics during the disease progression.

Frontiers in Behavioral Neuroscience

Pregnanolone glutamate, a novel use-dependent NMDA receptor inhibitor, exerts antidepressant-like properties in animal models

Holubova K., Nekovarova T., Pistovcakova J., **Sulcova A.**, Stuchlík A., Vales K.

Research Groups: Experimental and Applied Neuropsychopharmacology

Summary: Results of the study showed that pregnanolone glutamate (PG) did not induce hyperlocomotion, whereas both dizocilpine and ketamine significantly increased spontaneous locomotor activity in the open field. In the elevated plus maze, PG displayed anxiolytic-like properties. In forced swimming, PG prolonged time to the first floating. Acute treatment of PG disinhibited suppressed locomotor activity in the repeatedly defeated group-housed mice. Aggressive behavior of isolated mice was reduced after the chronic 30-day administration of PG. PG showed antidepressant-like and anxiolyticlike properties in the used tests, with minimal side-effects. Since PG combines GABAA receptor potentiation and use-dependent NMDAR inhibition, synthetic derivatives of neuroactive steroids present a promising strategy for the treatment of mood disorders.

MOLECULAR VETERINARY MEDICINE

Parasites & Vectors

Hidden threat of tortoise ticks: high prevalence of Crimean-Congo haemorrhagic fever virus in ticks Hyalomma aegyptium in the Middle East.

Siroky P., Belohlavek T., Papousek I., Jandzik D., Mikulicek P., Kubelova M., Zdrazilova-Dubska L.

Research Group: Molecular Bacteriology

Summary: It is the first time that Crimean-Congo haemorrhagic fever virus (CCHFV), causing potentially lethal disease of humans, has been reported from the Middle East region and from the tortoise tick *Hyalomma aegyptium* from a tortoise host, whose epidemiological significance may have remained almost completely overlooked so far. We used RT-PCR to screen for 245 ticks collected from 38 *Testudo graeca* tortoise individuals. Results of our genetic screening provide unambiguous evidence of occurrence of CCHFV in this region and host, suggesting a potentially important role of *H. aegyptium* in CCHF epidemiology.

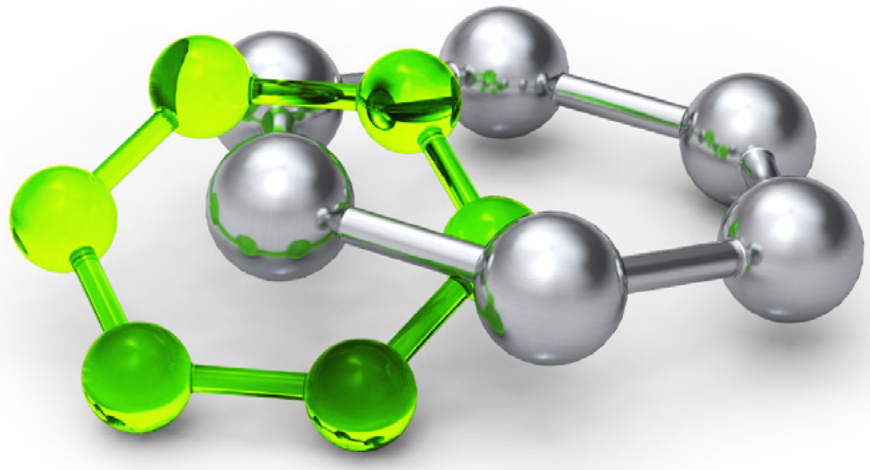
Environmental Microbiology

American crows as carriers of vancomycin-resistant enterococci with vanA gene

Oravcova, V., Zurek, L., Townsend, A., Clark, A.B., Ellis, J.C., **Cizek, A.**, **Literak, I.**

Research Group: Molecular Bacteriology

Summary: We studied the *vanA*-carrying vancomycin-resistant enterococci (VRE) isolated from American crows in the United States during the winter 2011/2012. Faecal samples from crows were cultured selectively for VRE and characterized. Pulsed-field gel electrophoresis (PFGE) and multilocus sequence typing (MLST) were used to examine epidemiological relationships of *vanA*-containing VRE. Isolates were tested *in vitro* for their ability to horizontally transfer the vancomycin resistance trait. VRE with the *vanA* gene were found in 15 (2.5%) of 590 crows samples, from which we obtained 22 different isolates. Enterococcal species were *Enterococcus faecium* (14) and *E. faecalis* (8). One, two and 19 isolates originated from Kansas, New York State and Massachusetts, respectively. Based on MLST analysis, *E. faecium* isolates were grouped as ST18 (6 isolates), ST555 (2), and novel types ST749 (1), ST750 (3), ST751 (1), ST752 (1). *Enterococcus faecalis* isolates belonged to ST6 (1), ST16 (3) and ST179 (4). All isolates were able to transfer the vancomycin resistance trait via filter mating with very high transfer range. Clinically important enterococci with the *vanA* gene occur in faeces of wild American crows throughout the United States. These migrating birds may contribute to the dissemination of VRE in environment over large distances.



Please send us your comments and ideas to **pavla.vyhnankova@ceitec.cz**