CEITEC news

NEWSLETTER No. 3/2013

Electronic Newsletter, October 2013

Dear CEITEC friends,

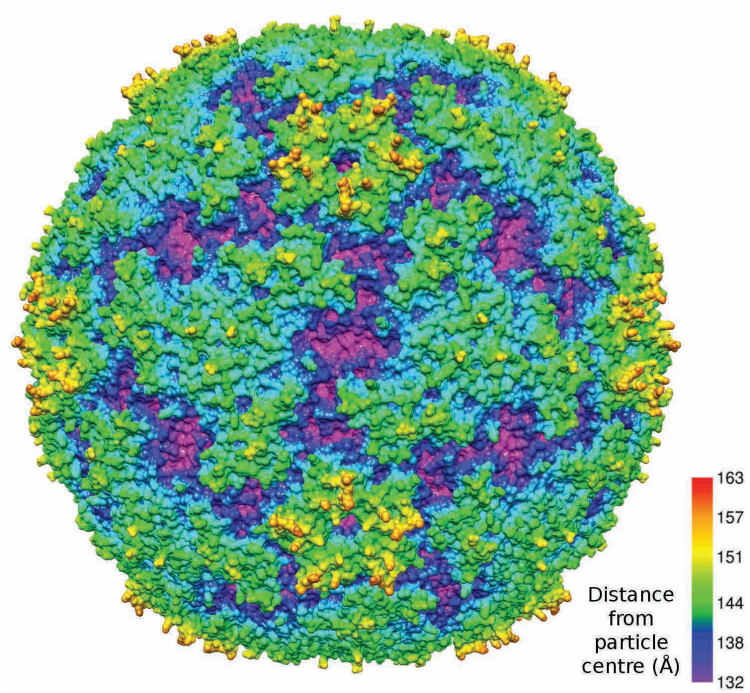
In the last quarter we have accomplished much, however there are still many challenges ahead. In our first CEITEC Retreat in Chateau Valtice, our Group Leaders had the opportunity to hear Gregory Weiss from UC Irvine and Pascal Ruffieux from EMPA Zurich give inspiring research seminars. Additionally our colleagues from both EMBL and VIB joined us to discuss how their highly successful organizations are run. This occasion allowed us to acknowledge our progress thus far, but also to reflect on the road ahead for CEITEC as our organization matures. Our successes have been many, capping it off with the awarding of our first ERC grant, which is judged by an international review panel solely based on excellence in science. As our investment in equipment continues and our organization gains momentum, we have launched the opening of another core facility - Single-crystal X-ray Diffraction. Also, this quarter we hosted several international events which are detailed in this newsletter. Thanks go to all of our supporters for making CEITEC a choice institute for basic and applied research.

Best wishes,
Markus Dettenhofer

Content

Most prestigious European research grant goes to CEITEC

Young scientist, Pavel Plevka of CEITEC MU, has received the most prestigious European scientific grant awarded by the European Research Council (ERC). This makes him the only scientist working in the Czech Republic who has received financial support from the ERC in the category of "Starting Grants" this year. ERC awards "Starting Grants" to the most talented European researchers based on the scientific excellence of their innovative research proposal. Pavel Plevka has succeeded with his project entitled "Structural Study of Human Picornaviruses" and he is only the sixth ERC "Starting Grants" recipient in the Czech Republic since 2007 and the very first in Brno.



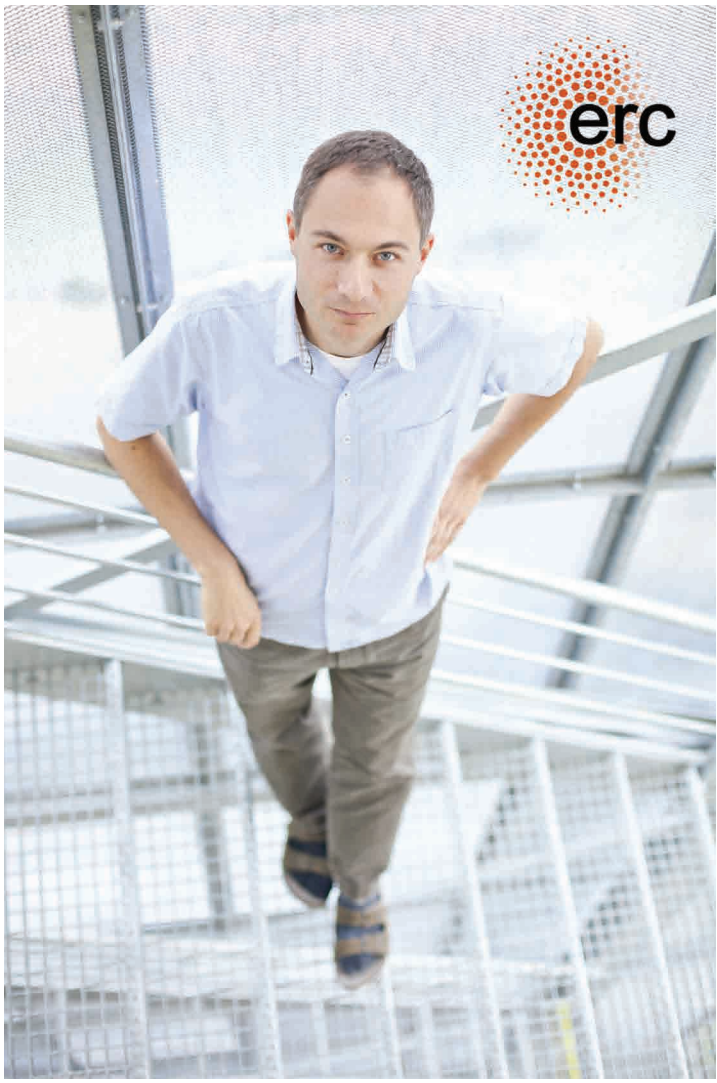
Molecular surface rendering of EV71 (human enterovirus 71) virus. The picture is based on atomistic model of the EV71 capsid. The surface is coloured according to the distance from the virus centre (valleys are purple mountains are red).

> *ERC grants represent an important indicator of the quality of research institutions, as well as the quality of research in various countries. Obtaining this grant represents confirmation for CEITEC that we are on the right track and that we are competitive with all other scientific institutions."*
>
> *Markus Dettenhofer*
> *CEITEC Executive Director*

The ERC "Starting Grants" are awarded each year to support researchers who intend to establish their own research teams and commence their own independent research in Europe. Obtaining an ERC grant is very difficult because the usual success rate is 10% for applicants from all over the world and only 3% for applicants from the Czech Republic. The important thing is to prepare a research project that has the potential to shift the frontiers of human knowledge in one of the key research areas.

More information about Pavel Plevka and his research can be found in the interview on page 8 of this Newsletter.

The press release can be found **HERE**.



Pavel Plevka
© foto: Tomáš Škoda, Hospodářské noviny

CEITEC acquires unique device to researching complex biological processes

The Single-crystal X-ray Diffraction core facility has been ceremonially inaugurated on September 12, 2013 at the Masaryk University Campus Bohunice. The laboratory has been newly equipped with small angle X-ray scattering (SAXS) camera BioSAXS-1000, from Rigaku and two diffractometers Rigaku HighFlux HomeLab™, the first robotized (sample changer ACTOR) and optimized for work at biomolecular Cu-K_α wavelength, the second with a dual wavelength (Mo-K_α and Cu-K_α) X-ray source. The ceremonial opening consisted of several contributions of CEITEC management and scientific lectures on how the modern methods of structural biology; high-field NMR spectroscopy, X-ray diffraction, Bio-SAXS, and cryo-EM; are employed in CEITEC research. The inauguration was followed by the scientific symposium aiming at the new trends and advancement in X-ray diffraction and biological SAXS which was held on September 13, at the same place.

The Singe-crystal X-ray Diffraction Laboratory is one of the core facilities of the Structural Biology research programme focused on key technology using X-ray for the study of molecular structures in crystals. The new biological SAXS camera will allow us to understand the interconnection of structural data and, consequently, it will provide vital information about the quaternary structure of molecular complexes not only in the crystal, but also in solution.

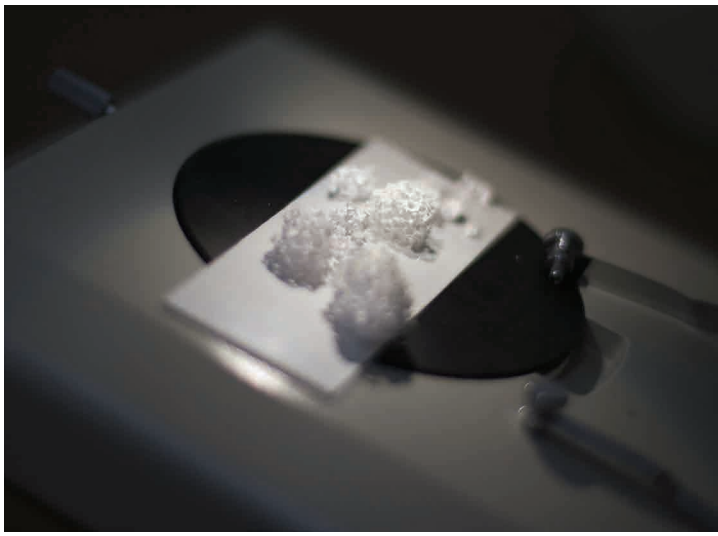
More information and photos can be found **HERE**.

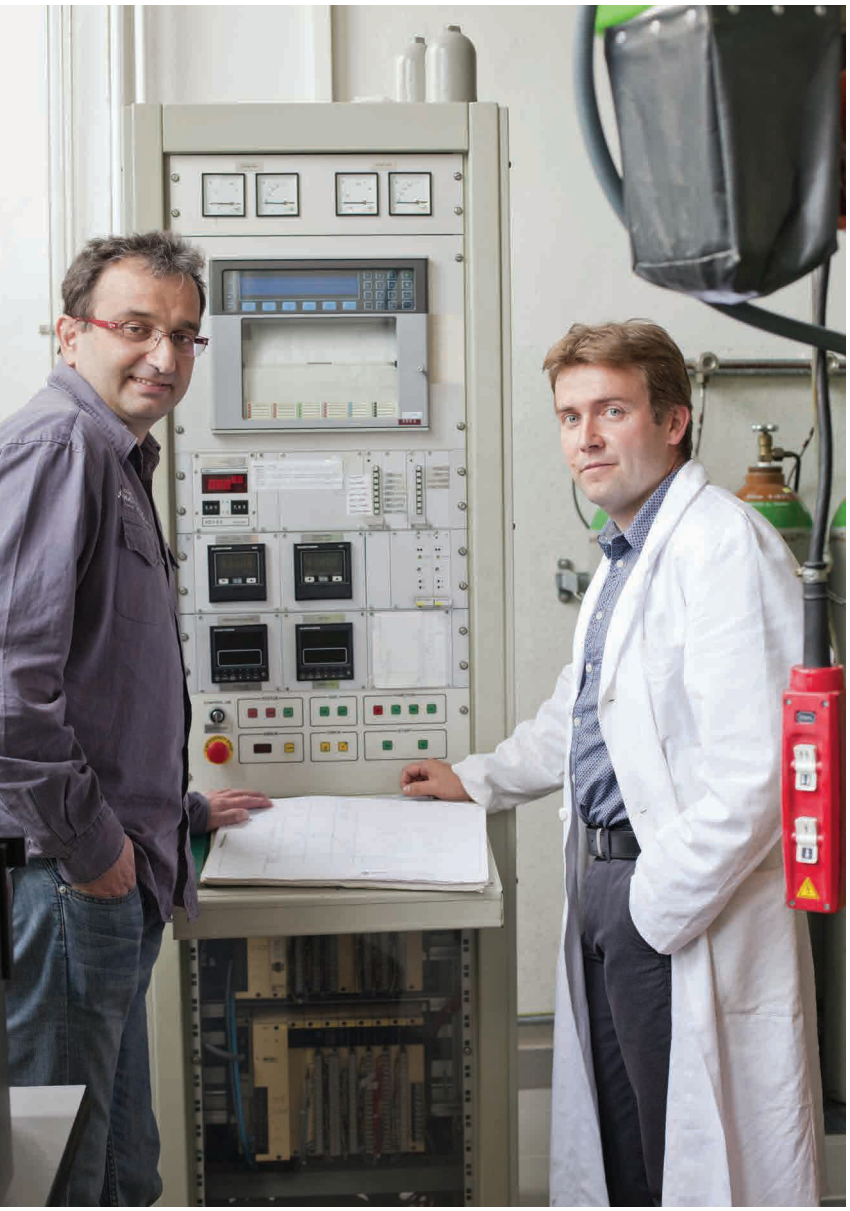
Ceremonial inauguration, toast

BioSAXS-1000

CEITEC develops special bioactive replacement for the jaw bone

Scientists Karel Maca and David Salamon from the Advanced Ceramic Materials research group at CEITEC BUT are developing special ceramic materials to replace jaw bone. They are manufacturing ceramic granules which can be filled with a unique biopolymer and in the form of a solution use them as "ink" in 3D printers. Scientists from Moravia's metropolis won FP7 grant in cooperation with German, Swedish, Spanish and Chinese experts. The research combines several technologies that are already in use and utilises them in medicine in line with current trends towards reducing treatment costs.





The aim is to replace damaged jaw with ceramics in order to meet the precise needs of the patient. Thus the researchers have to make an exact copy which they then fill with a substance that supports healing. Thanks to this approach, a specific patient receives a tailor-made replacement jaw bone created from a scan. Thanks to the bioactive polymer in the ceramic granules, the body is able to accept the implanted jaw bone without suffering unwelcomed side-effects - moreover, the healing process can begin quickly .

More information can be found **HERE**.

Researchers Karel Maca and David Salamon
© foto: Tomáš Škoda, Hospodářské noviny

CEITEC Scientific Retreat

On 3rd and 4th October, the first CEITEC Scientific Retreat took place, designed for all CEITEC research group leaders. The objective of this event was not only to meet each other and to discuss the current issues within this broad plenum, but also to inform the research group leaders how other research centres and core facilities function and to let them know about the news in the Horizon 2020 grant programme.

One of our esteemed guests was the Director of Core Facilities and Services of EMBL, Christian Boulin, who introduced the structure and operations at the core facilities at one of the most reputable institutions within Europe and abroad. Prof. Gregory Weiss, from University of California, Irvine, with his presentation entitled "Single Molecule Enzymology with Nanometer-scale Electronics", and Dr. Pascal Ruffieux, from Empa - a Research Institute of the ETH Domai, with his presentation entitled "Atomically Precise Graphene Nanostructures", introduced scientific topics indicating potential for co-operation between life and material sciences.

Lieve Ongena, Science Policy Manager of VIB, presented the steps that VIB had to take along its path towards becoming a reputable scientific institute, which could serve as inspiration for CEITEC. Eleonora Billi, an attendee of an international PhD program at VIB, spoke about PhD studies at VIB. Another highly beneficial contribution was the introduction of the new grant possibilities within the scope of Horizon 2020 – this was presented by Lotte Jaspers of Yellow Research.

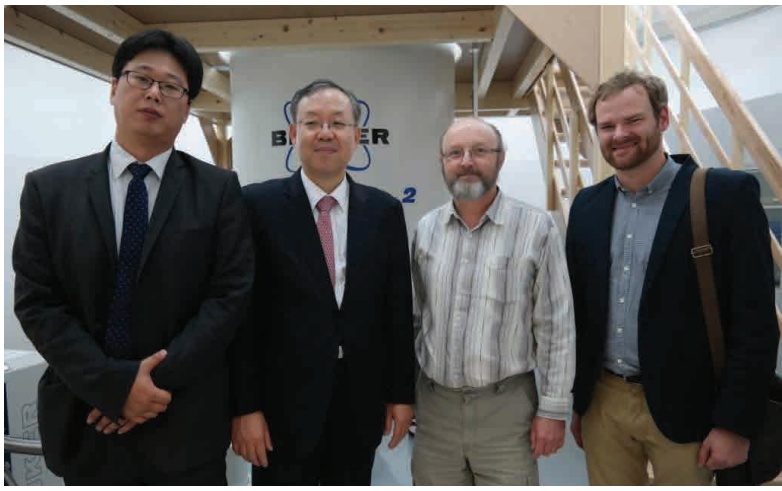
We would like to thank all participants and guests.

Cooperation

CEITEC management welcomes Korean Ambassador, Mun Ha-yong, in Brno

On 25th September, representatives of CEITEC met with the Korean Ambassador, Mun Ha-yong. They showed him around scientific laboratories on the campus of Masaryk University and talked about possibilities of future cooperation.

The aim of the meeting with the Korean Ambassador, which took place with the participation of the CEITEC's Executive Director, Markus Dettenhofer; Marketing and Communication Manager, Jakub Ondroušek; and Head of the Josef Dadok National NMR Centre, Radovan Fiala, was to introduce the CEITEC project, its goals, strategy and research areas. Possibilities for cooperation between Czech and Korean scientists and educational exchanges were also on the agenda.



Park Jong Kil, Mun Ha-yong, Radovan Fiala, Jakub Ondroušek

CEITEC begins further cooperation with international companies

On Monday, 9th September, the X-ray Micro CT and Nano CT research group from CEITEC BUT co-organized an international brokerage event where industrial representatives met with scientists and looked for possibilities for cooperation. Representatives of significant companies involved in the field of modern technology, GE Measurement & Control, Bruker, Carl Zeiss - X-ray Microscopy Group and Rigaku, took part in this event.

It was the Japanese company, Rigaku, the leading producer of scientific analytical devices using X-radiation, which officially introduced its latest product in this event – a computer tomograph with submicron resolution. Over and above its other features, it is the accessible native voxel resolution of less than 0.5 micrometers in the tomography mode that puts it at the top of commercially available devices.

Events

Past events

Core Facility Genomics Workshop: Next-gen Sequencing Technologies and Applications

The CEITEC Genomic Core Facility organized a workshop on 25th September entitled Next-Gen sequencing technologies and applications. Event took place at Hotel International and was thematically focused on theoretical and practical aspects of next generation sequencing. More than 170 Czech and international participants from both, industry and basic research were in attendance for presentations from biotechnology companies developing new tools for NGS. Later, scientists had opportunities to discuss their experiences in these methods in different fields of research and their applications in medical diagnostics. The high number of participants reflects the substantial level of interest in the topic of NGS, which is a key service offered by our Genomics Core Facility.

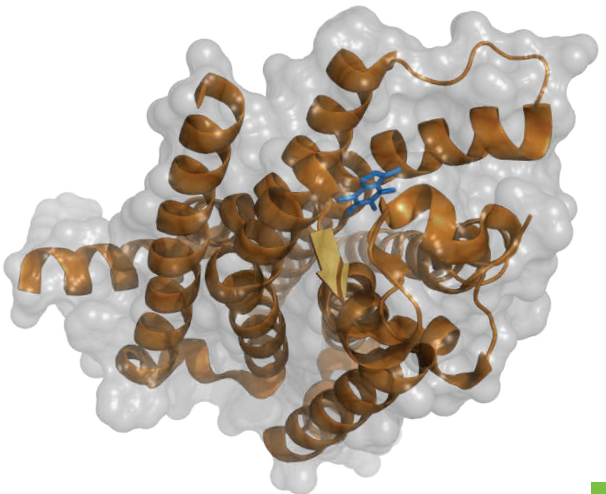
5th IgCLL Educational Workshop on Immunoglobulin Sequence Analysis in Chronic Lymphocytic Leukemia

On 26th and 27th September, Prof. Pospisilova (research programme Molecular Medicine) organized the 5th Workshop Immunoglobulin Sequence Analyses in Chronic Lymphocytic Leukemia under the auspices of European Research Initiative on CLL (ERIC). Speakers from 7 countries discussed analyses of immunoglobulin genes and their applications in the diagnosis and prognosis of chronic lymphocytic leukemia. Attendees learned about the newest bioinformatics tools for sequence analyses of immunoglobulins and discussed interpretations of results while participating in practical exercises. In total, researchers from 12 European countries and the USA participated in the workshop.

Researchers' Night

CEITEC once again participated in the European Researchers' Night, which took place on 27th September. The Computational Chemistry research group of the Structural Biology research programme prepared presentations related to chemo-informatics and bio-informatics. There was a station at the Faculty of Science of MU called "What chemo-informatics specialists look for in coffee and tea". It focused on the history, cultivation and preparation of these two popular beverages and in particular on rich caffeine content of these natural products. The visitors could learn how caffeine works as a stimulant, addictive substance and drug, and how scientists are attempting to use it to improve treatments for Parkinson's disease. The second station of CEITEC MU was situated at the Faculty of Informatics and was called "The bio-chemical puzzle or how to hack a cell". It focused on the use of computers in molecular biological and medical research, that is, how a chemical experiment can be replaced by a calculation or how chemical data can be transfer-red to a computer for further work.

The scientists of CEITEC BUT also participated in the event and presented in the Technical Museum the Foucault pendulum and the Tesla transformer, which made a fluorescent tube light up in the hands of children. Another curiosity was the Stirling motor, where compression when the working gas is at low temperatures and expansion when at the high temperatures results in the transformation of the heat energy into mechanical work. Experiments showed that it also works with the heat of a candle. At MENDELU, CEITEC was represented with a demonstration of a four-wheel Orpheus robot.



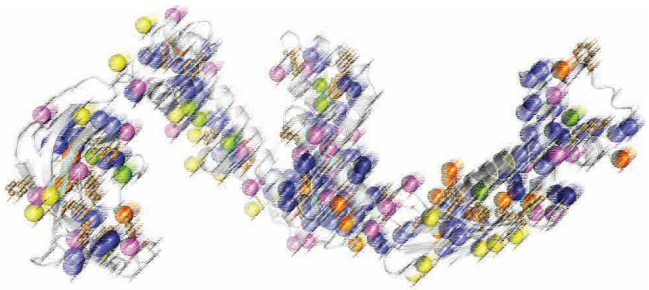
Upcoming events

Structural Biology Seminar Series

You are cordially invited to the CEITEC Structural Biology Seminar Series organized by the Structural Biology research programme coordinator, Prof. Vladimír Sklenář.

WHEN: Thursday, October 17, at 2 p.m.

WHERE: lecture room 132 of pavilion A11, University Campus Bohunice, Brno



The lecture **NMR of Large Proteins: Molecular Chaperones** will be delivered by **Prof. Charalampos G. Kalodimos**, Department of Chemistry & Chemical Biology, Rutgers University, Piscataway, New Jersey, USA.

Molecular chaperones are necessary for maintaining a functional proteome in the cell in that they prevent the aggregation of unfolded proteins and/or assist with their folding. Despite the central importance of binding chaperones to unfolded substrates, the structural basis of their interaction remains to be poorly understood. The scarcity of structural data pertaining to complexes between chaperones and unfolded client proteins is primarily due to technical challenges originating in the dynamic nature of these complexes.

He will discuss how NMR spectroscopy can be used as an extremely powerful tool to determine the structural and dynamic basis for the recognition and interaction of unfolded proteins by molecular chaperones.

More information and the programme for 2013 can be found **HERE**.

Workshop: Cerebellum, Basal, Ganglia and Cortical Connections Unmasked in Health and Disorder

Behavioural and Social Neuroscience research group would like to invite you to the workshop Cerebellum, Basal, Ganglia and Cortical Connections Unmasked in Health and Disorder.

WHEN: Thursday, October 17, 2013, 9:00 - 13:30

WHERE: Lecture Hall, Moravian Gallery Brno, Museum of Apllied Arts, Husova 14, Brno

The programme can be found **HERE**.

Workshop: Advanced Microscopy Systems and Image Analysis

We would like to invite you to several lectures on advanced microscopy systems and image analyses.

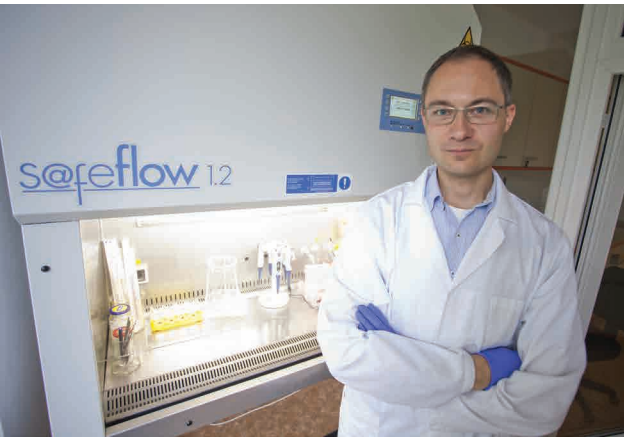
WHEN: Thursday, October 31, 2013

WHERE: Pavilion A3, University Campus Bohunice, Brno

More information and event programme can be found **HERE**.

Interview with CEITEC scientist

Pavel Plevka



CEITEC Masaryk University

Research Group Leader - Structural Virology
Research Programme – Structural Biology

Pavel Plevka graduated from Charles University in Prague where he specialised in molecular biology and virology. In 2009, he earned a PhD from Uppsala University in Sweden. In the period of 2009-2012, he worked as a post-doctoral researcher at Purdue University in the USA. Since July 2013 he has been working as the head of the Structural Virology research group that is a part of the Structural Biology research programme at CEITEC MU. Pavel Plevka focuses on the study of molecular structures of human picornaviruses, viruses contributing to the exacerbation of Leishmaniasis disease symptoms, and viruses contributing to the collapse of honeybee colonies. He is the author of a number of scientific papers in journals such as Science, PNAS, EMBO Reports, or the Journal of Virology.

Congratulations on gaining the most prestigious European scientific grant ERC, which you will use to study picornaviruses. Can you tell us how difficult it was to get an ERC grant?

Thank you. On average only three per cent of Czech scientists that apply for it are successful. I did prepare carefully, taking two months to write the application. Many colleagues helped me to write it. Particularly I'd like to mention Veronika Papoušková, Roman Badík, Peter Šebo, Jana Roithová and Markus Dettenhofer. Then I had to defend the project in Brussels. My presentation was made up of 12 slides and each of them took me on average one day to prepare.

What do you see as most interesting about your project?

I think my project involves an interesting combination of structural biological methods which we use to study the life cycle of picornaviruses. It is also important that we will be studying viruses that cause diseases in people, meaning that our results might contribute to an increase in the quality of human life.

Can you describe exactly what you are going to study with your ERC Starting Grant?

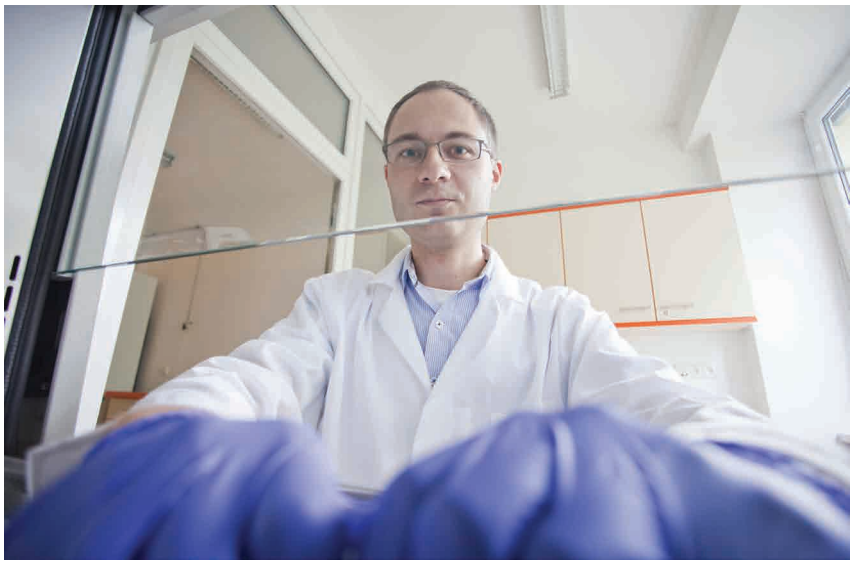
We will study viruses from the picornavirus group, which are responsible for a range of human diseases from the common cold to life-threatening encephalitis. More specifically we will look into how the virus enters cells, what happens in the cell in the course of infection, how the virus replicates, etc. The analysis will be so detailed that we will be able to describe these processes on the level of individual molecules and atoms. Understanding the mechanism allowing virus replication will help us to identify targets for antiviral inhibitors. It will then be possible to prepare substances preventing entry of viruses to cell or virus replication. The techniques that we will use – x-ray crystallography, electron microscopy and computer image analysis - will allow us to study viruses with a resolution approaching the size of individual atoms (1/10 000 000 000 metre).

Why exactly did you decide to study picornaviruses?

Picornaviruses cause a whole range of illnesses, from the common cold, often mistaken for influenza, up to more serious conditions such as hand, foot and mouth disease which can be accompanied by fever or encephalitis. Since on average each of us gets three or four colds a year, we encounter picornaviruses quite often. In addition these viruses are relatively easy to investigate, being simple, and a great deal of work has already been done on them, giving us an advanced point of departure.

Your research interests are much broader. What else are you working on?

Another area of research for us is to look at the problem of honeybees dying out. Colony numbers in Europe and America are falling. In 1950 there were some 5.5 million domesticated colonies, while at present there are only 2.1 million. Furthermore, in the same period, the area of land used for growing crops needing pollination has grown. One of the causes of the dying out of bees is viral infection. It is interesting to note that most bee viruses are distant relatives of human picornaviruses. Determining their structure will help us to modify the active ingredients in substances that are effective against human picornaviruses so that they will work against bee viruses.



What brought you to the study of structural virology? What had the greatest influence on your choice of scientific specialisation?

I first became interested in viruses at secondary school. I liked how simple they are, meaning that we can understand them on a molecular level. At the Faculty of Natural Sciences at Charles University there was a very good virology group lead by Professor Jitka Forstová, where I worked on my thesis. I went to Sweden for the chance to learn x-ray crystallography. The most exciting part of my scientific career so far was my post-doctoral work at Purdue University in Michael Rossmann's laboratory. It was very motivating to work with someone as enthusiastic about research as Michael.

You have spent much time abroad, particularly in Sweden and the USA. What has brought you back to the Czech Republic?

The decisive factor for me was the equipment for structural biology that CEITEC is purchasing. The costs are in the range of hundreds of millions of Czech crowns and it will be the equal of the world's top laboratories. In fact it will be better equipment than what we had in American laboratories. Although obviously the equipment is only as good as the people working on it, so it will be a great challenge for us. When we left for the States, I promised my wife that it would not be forever. Winning a place at CEITEC made it possible for me to keep my word.

Could you compare the scientific environment here with that for example in the USA?

I see the main differences in work ethic. In top research groups in the US it is standard to work ten or twelve hours a day, frequently even over the weekend. It's also normal for scientists to get home, have their supper, and then study articles in scientific journals. They get to work in the morning in right frame of mind – with what they plan to do already thought through. Czech science could also do with being more open. Research teams in the US and in Sweden are much more multinational. It is good if in the course of his or her career, a scientist works in a variety of institutions, since it gives a chance to gain many scientific contacts as well as an opportunity to learn new methods.

Thanks to the ERC grant you can set up your own research team. How many people will be in your group? How difficult is it to find suitable candidates?

Nine scientists will work in the group – four post-docs, three PhD students and a technician. Aside from these I want to involve several master's students. So far I have taken on a lab assistant and two post-docs, one from France and the other from India. I placed an advert in an international exchange for scientific jobs. Almost thirty people went for each position. Some five applicants had good CVs and references. I followed up by calling them and discussing how I see the work and how my laboratory will operate.

In CEITEC you work as head of the Structural Virology research group – who are you going to be cooperating with inside CEITEC? Who are you planning to work with outside CEITEC?

Within CEITEC I am collaborating with Robert Vácha, a computational biologist interested in simulations of whole virus particles. I am also going to work with the electron microscopists Daniel Němeček and Tanvir Shaikh. We will study the Leishmania RNA virus 1 and the dynamics of genome release from picornavirus particles. I will collaborate with Štěpánka Vaňáčová on studies of the role of small non-coding RNA molecules in viral infections. Outside CEITEC I will work with Daniel Růžek from the Veterinary Research Institute, who is studying alphaviruses and flaviviruses such as tick borne encephalitis.

Thank you for the interview. •●

© foto: Tomáš Škoda, Hospodářské noviny

Funding opportunities

National	Deadline
CEITEC - Open Access	29th Nov 2013
Ministry of Education, Youth and Sports - GESHER / MOST	6th Dec 2013
Ministry of Education, Youth and Sports - Strengthening the research capacity of R&D centres	January 2014 (TBC)
Technology Agency of the Czech Republic - ALFA	January 2014 (TBC)
Czech-Norway Research Fund	January 2014 (TBC)

International	
Sciex-NMSch fellowships	1st Nov 2013
Human Brain Project Competitive Calls Programme	6th Nov 2013
Graphene Flagship Open Call	3rd Feb 2014
ERC Starting Grants	25th Mar 2014 (TBC)

First calls under HORIZON 2020 will be published on 11th December 2013.
For more information, please contact your **grant office staff**.

Grants-related events taking place in Brno

11th Nov	Joint Research Centre (JRC) Information Day
27th Nov	European Research Council (ERC) Information Day
November (TBC)	Future and Emerging Technologies (FET) Information Day
December (TBC)	Nanosciences, Nanotechnologies, Materials and New Production Technologies (NMP) Information Day

Selected CEITEC Publications

Current Drug Metabolism

Nanocarriers for anticancer drugs - New trends in nanomedicine

Drbohlavova J., Chomoucka J., Adam V., Ryvolova M., Eckschlager T., Hubalek J., Kizek R.

Research Group: Smart Nanodevices
Research Programme: Advanced Nanotechnologies and Microtechnologies

Abstract

This review provides a brief overview of the variety of carriers employed for targeted drug delivery used in cancer therapy and summarizes advantages and disadvantages of each approach. Particularly, the attention was paid to polymeric nanocarriers, liposomes, micelles, polyethylene glycol, poly(lactic-co-glycolic acid), dendrimers, gold and magnetic nanoparticles, quantum dots, silica nanoparticles, and carbon nanotubes. Further, this paper briefly focuses on several anticancer agents (paclitaxel, docetaxel, camptothecin, doxorubicin, daunorubicin, cisplatin, curcumin, and geldanamycin) and on the influence of their combination with nanoparticulate transporters to their properties such as cytotoxicity, short life time and/or solubility.

The Journal of Neuroscience

In vivo Stimulus-Induced Vasodilation Occurs without IP3 Receptor Activation and May Precede Astrocytic Calcium Increase

Nizar K., Uhlirova H., Tian P., Saisan P., Cheng Q., Reznichenko L., Weldy K., Steed T., Sridhar V., MacDonald C., Cui J., Gratiy S., Sakadzic S., Boas D., Beka T., Einevoll G., Chen J., Masliah E., Dale A., Silva G., Devor A.

Research Group: Experimental Biophotonics
Research Programme: Advanced Nanotechnologies and Microtechnologies

Abstract

Calcium-dependent release of vasoactive gliotransmitters is widely assumed to trigger vasodilation associated with rapid increases in neuronal activity. Inconsistent with this hypothesis, intact stimulus-induced vasodilation was observed in inositol 1,4,5-triphosphate (IP3) type-2 receptor (R2) knock-out (KO) mice, in which the primary mechanism of astrocytic calcium increase—the release of calcium from intracellular stores following activation of an IP3-dependent pathway—is lacking. Further, our results in wild-type (WT) mice indicate that *in vivo* onset of astrocytic calcium increase in response to sensory stimulus could be considerably delayed relative to the simultaneously measured onset of arteriolar dilation. Delayed calcium increases in WT mice were observed in both astrocytic cell bodies and perivascular endfeet. Thus, astrocytes may not play a role in the initiation of blood flow response, at least not via calcium-dependent mechanisms. Moreover, an increase in astrocytic intracellular calcium was not required for normal vasodilation in the IP3R2-KO animals.

NANO LETTERS

Control and Near-Field Detection of Surface Plasmon Interference Patterns

Dvorak P., Neuman T., Brinek L., Samoril T., Kalousek R., Dub P., Varga P., Sikola T.
Research Group: Fabrication and Characterisation of Nanostructures
Research Programme: Advanced Nanotechnologies and Microtechnologies

Abstract

The tailoring of electromagnetic near-field properties is the central task in the field of nanophotonics. In addition to 2D optics for optical nanocircuits, confined and enhanced electric fields are utilized in detection and sensing, photovoltaics, spatially localized spectroscopy (nanoimaging), as well as in nanolithography and nanomanipulation. For practical purposes, it is necessary to develop easy-to-use methods for controlling the electromagnetic near-field distribution. By imaging optical near-fields using a scanning near-field optical microscope, we demonstrate that surface plasmon polaritons propagating from slits along the metal– dielectric interface form tunable interference patterns. We present a simple way how to control the resulting interference patterns both by variation of the angle between two slits and, for a fixed slit geometry, by a proper combination of laser beam polarization and inhomogeneous far-field illumination of the structure. Thus the modulation period of interference patterns has become adjustable and new variable patterns consisting of stripelike and dotlike motifs have been achieved, respectively.

Journal of the European Ceramic Society

Two-stage master sintering curve applied to two-step sintering of oxide ceramics

Pouchly V., Maca K., Shen Z.

Research Group: Advanced Ceramic Materials
Research Programme: Advanced Materials

Abstract

Tetragonal (3 mol% Y_2O_3) and two cubic zirconia (8 mol% Y_2O_3) as well as alumina green bodies were used for the construction of the Master Sintering Curve (MSC) created from sets of constant-rate-of-heating (CRH) sintering experiments. The activation energies calculated according to the MSC theory were 770 kJ/mol for Al_2O_3, 1270 kJ/mol for t-ZrO_2, 620 kJ/mol and 750 kJ/mol for c-ZrO_2. These values were verified by an alternative approach based on an analysis of the densification rate in the intermediate sintering stage. The MSCs established from the Two-Step Sintering (TSS) experiments showed at high densities a significant deflection from those constructed from the CRH experiments. This deflection was explained by lower sintering activation energy in the closed porosity stage. A new two-stage MSC model was developed to reflect the change in sintering activation energy and to describe TSS. The efficiency of TSS of four materials under investigation was correlated with their activation energies during the final sintering stage.

IEEE Transactions on Industrial Electronics

AC Drive Observability Analysis

Vaclavek P., Blaha P., Herman I.

Research Group: Cybernetics in Material Science
Research Programme: Advanced Materials

Abstract

AC induction motors and permanent magnet synchronous drives became very popular for motion control applications due to their simple and reliable construction. Sensorless drive control is required in many applications to reduce drive production costs. While many approaches to magnetic flux, rotor speed, or other quantities needed to control electrical machine were proposed, conditions under which these quantities can be estimated are not often sufficiently investigated. In this paper; induction machine and permanent-magnet-synchronous-machine drive state observability analysis is presented, together with conditions allowing reliable rotor speed and position estimation. A method based on the nonlinear dynamical system state observability theory is proposed, resulting in a unified approach to the ac drive observability analysis.

Journal of Alloys and Compounds

Beneficial effect of carbon on hydrogen desorption kinetics from Mg–Ni–In alloy

Cermak J., **Kral L.**

Research Group: **Advanced Materials**
Research Programme: **Advanced Metallic Materials and Metal Based Composites**

Abstract

In the present paper, hydrogen desorption kinetics from hydrided Mg–Ni–In–C alloys was investigated. A chemical composition that substantially accelerates hydrogen desorption was found. It was observed that carbon improves the hydrogen desorption kinetics significantly. Its beneficial effect was found to be optimum close to the carbon concentration of about $c_C \approx 5$ wt.%. With this composition, stored hydrogen can be desorbed readily at temperatures down to about 485 K, immediately after hydrogen charging. This can substantially shorten the hydrogen charging/discharging cycle of storage tanks using Mg–Ni-based alloys as hydrogen storage medium. For higher carbon concentrations, unwanted phases precipitated, likely resulting in deceleration of hydrogen desorption and lower hydrogen storage capacity.

Structure

Subunit Folds and Maturation Pathway of a dsRNA Virus Capsid

Nemecek D., **Boura E.**, **Wu W.**, **Cheng N.**, **Plevka P.**, **Qiao J.**, **Mindich L.**, **Heymann J.B.**, **Hurley J.H.**, **Steven A.C.**

Research Group: **CryoEM & Structural Virology**
Research Programme: **Structural Biology**

Abstract

The cystovirus φ6 shares several distinct features with other double-stranded RNA (dsRNA) viruses, including the human pathogen, rotavirus: segmented genomes, nonequivalent packing of 120 subunits in its icosahedral capsid, and capsids as compartments for transcription and replication. φ6 assembles as a dodecahedral procapsid that undergoes major conformational changes as it matures into the spherical capsid. We determined the crystal structure of the capsid protein, P1, revealing a flattened trapezoid subunit with an α-helical fold. We also solved the procapsid with cryo-electron microscopy to comparable resolution. Fitting the crystal structure into the procapsid disclosed substantial conformational differences between the two P1 conformers. Maturation via two intermediate states involves remodeling on a similar scale, besides huge rigid-body rotations. The capsid structure and its stepwise maturation that is coupled to sequential packaging of three RNA segments sets the cystoviruses apart from other dsRNA viruses as a dynamic molecular machine.

ChemBioChem

Structural Study of the Partially Disordered Full-Length δ Subunit of RNA Polymerase from *Bacillus subtilis*

Papouskova V., Kaderavek P., Otrusinova O., Rabatinova A., Sanderova H., Novacek J., Krasny L., Sklenar V., Zidek, L.

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

Abstract

The partially disordered δ subunit of RNA polymerase was studied by various NMR techniques. The structure of the well-folded N-terminal domain was determined based on inter-proton distances in NOESY spectra. The obtained structural model was compared to the previously determined structure of a truncated construct (lacking the C-terminal domain). Only marginal differences were identified, thus indicating that the first structural model was not significantly compromised by the absence of the C-terminal domain. Various 15N relaxation experiments were employed to describe the flexibility of both domains. The relaxation data revealed that the C-terminal domain is more flexible, but its flexibility is not uniform. By using paramagnetic labels, transient contacts of the C-terminal tail with the N-terminal domain and with itself were identified. A propensity of the C-terminal domain to form β-type structures was obtained by chemical shift analysis. Comparison with the paramagnetic relaxation enhancement indicated a well-balanced interplay of repulsive and attractive electrostatic interactions governing the conformational behavior of the C-terminal domain. The results showed that the δ subunit consists of a well-ordered N-terminal domain and a flexible C-terminal domain that exhibits a complex hierarchy of partial ordering.

Journal of the American Chemical Society

Relative Stability of Different DNA Guanine Quadruplex Stem Topologies Derived Using Large-Scale Quantum-Chemical Computations

Sponer J., Mladek A., Spackova N., Cang X., Cheatham T.E., Grimme S.
Research Group: **Structure and Dynamics of Nucleic Acids**
Research Programme: **Structural Biology**

Abstract

We provide theoretical predictions of the intrinsic stability of different arrangements of guanine quadruplex (G-DNA) stems. Most computational studies of nucleic acids have applied Molecular Mechanics (MM) approaches using simple pairwise-additive force fields. The principle limitation of such calculations is the highly approximate nature of the force fields. In this study, we for the first time apply accurate QM computations (DFT-D3 with large atomic orbital basis sets) to essentially complete DNA building blocks, seven different folds of the cation-stabilized twoquartet G-DNA stem, each having more than 250 atoms. The solvent effects are approximated by COSMO continuum solvent. We reveal sizable differences between MM and QM descriptions of relative energies of different G-DNA stems, which apparently reflect approximations of the DNA force field. Using the QM energy data, we propose correction to earlier free energy estimates of relative stabilities of different parallel, hybrid, and antiparallel G-stem folds based on classical simulations. The new energy ranking visibly improves the agreement between theory and experiment. We predict the 5´-*anti-anti*-3´ GpG dinucleotide step to be the most stable one, closely followed by the 5´-*syn-anti*-3´ step. The results are in good agreement with known experimental structures of 2-, 3-, and 4-quartet G-DNA stems. Besides providing specific results for G-DNA, our study highlights basic limitations of force field modeling of nucleic acids. Although QM computations have their own limitations, mainly the lack of conformational sampling and the approximate description of the solvent, they can substantially improve the quality of calculations currently relying exclusively on force fields.

Plant Physiology

Proteome analysis in Arabidopsis reveals shoot- and root-specific targets of cytokinin action and differential regulation of hormonal homeostasis

Zdarska M., Zatloukalova P., Benitez M., Sedo O., Potesil D., Novak O., Svacinova J., Pesek B., Malbeck J., Vasickova J., Zdrahal Z., Hejatko J.

Research Group: **Functional Genomics and Proteomics of Plants & Core Facility – Genomics**

Research Programme: **Genomics and Proteomics of Plant Systems**

Abstract

The plant hormones cytokinins (CKs) regulate multiple developmental and physiological processes in Arabidopsis (*Arabidopsis thaliana*). Responses to CKs vary in different organs and tissues (e.g. the response to CKs has been shown to be opposite in shoot and root samples). However, the tissue-specific targets of CKs and the mechanisms underlying such specificity remain largely unclear. Here, we show that the Arabidopsis proteome responds with strong tissue and time specificity to the aromatic CK 6-benzylaminopurine (BAP) and that fast posttranscriptional and/or posttranslational regulation of protein abundance is involved in the contrasting shoot and root proteome responses to BAP. We demonstrate that BAP predominantly regulates proteins involved in carbohydrate and energy metabolism in the shoot as well as protein synthesis and destination in the root. Furthermore, we found that BAP treatment affects endogenous hormonal homeostasis, again with strong tissue specificity. In the shoot, BAP up-regulates the abundance of proteins involved in abscisic acid (ABA) biosynthesis and the ABA response, whereas in the root, BAP rapidly and strongly up-regulates the majority of proteins in the ethylene biosynthetic pathway. This was further corroborated by direct measurements of hormone metabolites, showing that BAP increases ABA levels in the shoot and 1-aminocyclopropane-1-carboxylic acid, the rate-limiting precursor of ethylene biosynthesis, in the root. In support of the physiological importance of these findings, we identified the role of proteins mediating BAP-induced ethylene production, METHIONINE SYNTHASE1 and ACC OXIDASE2, in the early root growth response to BAP.

Lab on a Chip

Detection of electrochemiluminescence from floating metal platelets in suspension

Juskova P., Neuzil P., Manz A., Foret F.

Research Groups: **Smart Nanodevices & Bioanalytical Instrumentation**

Research Programmes: **Advanced Nanotechnologies and Microtechnologies & Genomics and Proteomics of Plant Systems**

Abstract

We present a generation of electrochemiluminescence (ECL) signal, based on square shaped gold electrodes with a size of 50 µm positioned inside a fused silica capillary. The ECL was generated using electric pulses with duration in the range from 100 ms to 5 s and an electrical field strength from 300 V cm^{-1} to 500 V cm^{-1}. We have demonstrated that the electrochemical reaction with detectable optical output can be produced using freely moving and thus disposable electrodes.

Journal of Experimental Botany

Proteome and metabolome profiling of cytokinin action in *Arabidopsis* identifying both distinct and similar responses to cytokinin down- and up-regulation

Černý M., Kuklová A., Hoehenwarter W., Fragner L., Novák O., Rotková G., Jedelský P.L., Žáková K., Šmehilová M., Strnad M., Weckwerth W., Brzobohatý B.

Research Group: **Developmental and Production Biology – Omics Approaches**

Research Programme: **Genomics and Proteomics of Plant Systems**

Abstract

In plants, numerous developmental processes are controlled by cytokinin (CK) levels and their ratios to levels of other hormones. While molecular mechanisms underlying the regulatory roles of CKs have been intensely researched, proteomic and metabolomic responses to CK deficiency are unknown. Transgenic *Arabidopsis* seedlings carrying inducible barley cytokinin oxidase/dehydrogenase (*CaMV35S*>GR>*HvCKX2*) and agrobacterial isopentenyl transferase (*CaMV35S*>GR>*ipt*) constructs were profiled to elucidate proteome- and metabolome-wide responses to down- and up-regulation of CK levels, respectively. Proteome profiling identified >1100 proteins, 155 of which responded to *HvCKX2* and/or ipt activation, mostly involved in growth, development, and/or hormone and light signalling. The metabolome profiling covered 79 metabolites, 33 of which responded to *HvCKX2* and/or ipt activation, mostly amino acids, carbohydrates, and organic acids. Comparison of the data sets obtained from activated *CaMV35S*>GR>*HvCKX2* and *CaMV35S*>GR>*ipt* plants revealed unexpectedly extensive overlaps. Integration of the proteomic and metabolomics data sets revealed: (i) novel components of molecular circuits involved in CK action (e.g. ribosomal proteins); (ii) previously unrecognized links to redox regulation and stress hormone signalling networks; and (iii) CK content markers. The striking overlaps in profiles observed in CK-deficient and CK-overproducing seedlings might explain surprising previously reported similarities between plants with down- and up-regulated CK levels.

Nature Methods

MiTCR: software for T-cell receptor sequencing data analysis

Bolotin D.A., Shugay M., Mamedov I.Z., Putintseva E.V., Turchaninova M.A., Zvyagin I.V., Britanova O.V., Chudakov D.M.
Research Group: **Adaptive Immunity Group**
Research Programme: **Molecular Medicine**

Abstract

Matrix metalloproteinases (MMPs) are involved in many physiological and pathological processes. Numerous MMPs assays were developed for both clinical and research purposes, but far more attention was turned to understanding their biological functions. In this review, enzymatic, immunochemical and fluorimetric methods as well as in vivo imaging methods are discussed. Moreover, we aimed our attention on additional methods that are now subject to investigation, such as phage display, Multiple-Enzyme/Multiple-Reagent Assay System (MEMRAS) and activity based profiling.

Haematologica

Multiple productive immunoglobulin heavy chain gene rearrangements in chronic lymphocytic leukemia are mostly derived from independent clones

Plevova K., Skuhrova Francova H., Burckova K., Brychtova Y., Doubek M., Pavlova S., Malcikova J., Mayer J., Tichy B., Pospisilova S.
Research Group: **Medical Genomics**
Research Programme: **Molecular Medicine**

Abstract

In chronic lymphocytic leukemia, usually a monoclonal disease, multiple productive immunoglobulin heavy chain gene rearrangements are identified sporadically. Prognostication of such cases based on immunoglobulin heavy variable gene mutational status can be problematic, especially if the different rearrangements have discordant mutational status. To gain insight into the possible biological mechanisms underlying origin of the multiple rearrangements, we performed a comprehensive immunogenetic and immunophenotypic characterization of 31 cases with the multiple rearrangements identified in a cohort of 1147 chronic lymphocytic leukemia patients. For the majority of cases (25/31), we provide evidence for the co-existence of at least two B lymphocyte clones with chronic lymphocytic leukemia phenotype. We also identified clonal drifts in serial samples, likely driven by selection forces. More specifically, higher immunoglobulin variable gene identity to germline and longer complementarity determining region 3 were preferred in persistent or newly appearing clones, a phenomenon more pronounced in patients with stereotyped B cell receptors. Finally, we report that other factors, such as TP53 gene defects and therapy administration, influence clonal selection. Our findings are relevant to clonal evolution in the context of antigen stimulation and transition of monoclonal B-cell lymphocytosis to chronic lymphocytic leukemia.

Leukemia

Distinct patterns of novel gene mutations in poor-prognostic stereotyped subsets of chronic lymphocytic leukemia: the case of SF3B1 and subset #2

Strefford J.C., Sutton L.-A., Baliakas P., Agathangelidis A., Malcikova J., Plevova K., Scarfo L., Davis Z., Stalika E., Cortese D., Cahill N., Pedersen L.B., di Celle P.F., Tzenou T., Geisler C., Panagiotidis P., Langerak A.W., Chiorazzi N., Pospisilova S., Oscier D., Davi F., Belessi C., Mansouri L., Ghia P., Stamatopoulos K., Rosenquist R.

Research Group: Medical Genomics

Research Programme: Molecular Medicine

Abstract

Recent studies have revealed recurrent mutations of the *NOTCH1*, *SF3B1* and *BIRC3* genes in chronic lymphocytic leukemia (CLL), especially among aggressive, chemorefractory cases. Nevertheless, it is currently unknown whether their presence may differ in subsets of patients carrying stereotyped B-cell receptors and also exhibiting distinct prognoses. Here, we analysed the mutation status of *NOTCH1*, *SF3B1* and *BIRC3* in three subsets with particularly poor prognosis, that is, subset #1, #2 and #8, aiming to explore links between genetic aberrations and immune signalling. A remarkably higher frequency of SF3B1 mutations was revealed in subset #2 (44%) versus subset #1 and #8 (4.6% and 0%, respectively; $P<0.001$). In contrast, the frequency of *NOTCH1* mutations in subset #2 was only 8%, lower than the frequency observed in either subset #1 or #8 (19% and 14%, respectively; $P=0.04$ for subset #1 versus #2). No associations were found for *BIRC3* mutations that overall were rare. The apparent non-random association of certain mutations with stereotyped CLL subsets alludes to subset-biased acquisition of genomic aberrations, perhaps consistent with particular antigen/antibody interactions. These novel findings assist in unravelling specific mechanisms underlying clinical aggressiveness in poor-prognostic stereotyped subsets, with far-reaching implications for understanding their clonal evolution and implementing biologically oriented therapy.

Schizophrenia Research

A detailed analysis of the effect of repetitive transcranial magnetic stimulation on negative symptoms of schizophrenia: A double-blind trial

Prikryl R., Ustohal L., Prikrylova Kucerova H., Kasparek T., Venclikova S., Vrzalova M., Ceskova E.

Research Group: Applied Neuroscience

Research Programme: Brain and Mind Research

Abstract

Objective: The aim of the study was to assess the effect of rTMS not only on the general severity of negative schizophrenia symptoms, but also particularly on their individual domains, such as affective flattening or blunting, alogia, avolition or apathy, anhedonia, and impaired attention.
Methods: Forty schizophrenic male patients on stable antipsychotic medication with prominent negative symptoms were included in the study. They were divided into two groups: 23 were treated with active and 17 with placebo rTMS. Both treatments were similar, but placebo rTMS was administered using a purposebuilt sham coil. Stimulation was applied to the left dorsolateral prefrontal cortex (DLPFC). The stimulation frequency was 10 Hz; stimulation intensity was 110% of the individual motor threshold intensity. Each patient received 15 rTMS sessions on 15 consecutive working days (five working days "on" and two weekend days "off" design). Each daily session consisted of 20 applications of 10-second duration with 30-second intervals between sequences. The patients and raters were blind to condition of stimulation treatment.
Results: The active rTMS led to a statistically significantly higher reduction of the Scale for the Assessment of Negative Symptoms (SANS) total score and of all domains of negative symptoms of schizophrenia. After Bonferroni adjustments for multiple testing, the statistical significance disappeared in alogia only.
Conclusion: High-frequency rTMS stimulation over the left DLPFC at a high stimulation intensity with a sufficient number of applied stimulating pulses may represent an efficient augmentation of antipsychotics in alleviating the negative symptoms of schizophrenia.

NeuroImage

Superior temporal sulcus and social cognition in dangerous drivers

Zelinkova J., Shaw D.J., Marecek R., Mikl M., Urbanek T., Peterkova L., Zamecnik P., Brazdil M.
Research Group: Behavioural and Social Neuroscience
Research Programme: Brain and Mind Research

Abstract

Understanding the neural systems underpinning social cognition is a primary focus of contemporary social neuroscience. Using functional magnetic resonance imaging (fMRI), the present study asked if brain activity reflecting socio-cognitive processes differs between individuals according to their social behavior; namely, between a group of drivers with frequent traffic offenses and a group with none. Socio-cognitive processing was elicited by employing videos from a traffic awareness campaign, consisting of reckless and anti-social driving behavior ending in tragic consequences, and control videos with analogous driving themes but without such catastrophic endings. We investigated whether relative increases in brain function during the observation of these campaign stimuli compared with control videos differed between these two groups. To develop the results of our previous study we focused our analyses on superior temporal sulcus/gyrus (STS/STG). This revealed a bigger increase in brain activity within this region during the campaign stimuli in safe compared with dangerous drivers. Furthermore, by thematically coding drivers' verbal descriptions of the stimuli, we also demonstrate differences in STS reactivity according to drivers' scores on two indices of socio-cognitive processing: subjects' perceived consequences of actors' actions, and their affective evaluation of the clips. Our results demonstrate the influence of social behavior and socio-cognitive processing on STS reactivity to social stimuli, developing considerably our understanding of the role of this region in social cognition.

Journal of Neuroinflammation

Bilateral elevation of interleukin-6 protein and mRNA in both lumbar and cervical dorsal root ganglia following unilateral chronic compression injury of the sciatic nerve

Dubovy P., Brazda V., Klusakova I., Hradilova-Svizenska I.
Research Group: Cellular and Molecular Neurobiology
Research Programme: Brain and Mind Research

Abstract

Background: Current research implicates interleukin (IL)-6 as a key component of the nervous-system response to injury with various effects. *Methods*: We used unilateral chronic constriction injury (CCI) of rat sciatic nerve as a model for neuropathic pain. Immunofluorescence, ELISA, western blotting and in situ hybridization were used to investigate bilateral changes in IL-6 protein and mRNA in both lumbar (L4-L5) and cervical (C7-C8) dorsal root ganglia (DRG) following CCI. The operated (CCI) and sham-operated (sham) rats were assessed after 1, 3, 7, and 14 days. Withdrawal thresholds for mechanical hyperalgesia and latencies for thermal hyperalgesia were measured in both ipsilateral and contralateral hind and fore paws. *Results*: The ipsilateral hind paws of all CCI rats displayed a decreased threshold of mechanical hyperalgesia and withdrawal latency of thermal hyperalgesia, while the contralateral hind and fore paws of both sides exhibited no significant changes in mechanical or thermal sensitivity. No significant behavioral changes were found in the hind and fore paws on either side of the sham rats, except for thermal hypersensitivity, which was present bilaterally at 3 days. Unilateral CCI of the sciatic nerve induced a bilateral increase in IL-6 immunostaining in the neuronal bodies and satellite glial cells (SGC) surrounding neurons of both lumbar and cervical DRG, compared with those of naïve control rats. This bilateral increase in IL-6 protein levels was confirmed by ELISA and western blotting. More intense staining for IL-6 mRNA was detected in lumbar and cervical DRG from both sides of rats following CCI. The DRG removed from sham rats displayed a similar pattern of staining for IL-6 protein and mRNA as found in naive DRG, but there was a higher staining intensity in SGC. *Conclusions*: Bilateral elevation of IL-6 protein and mRNA is not limited to DRG homonymous to the injured nerve, but also extended to DRG that are heteronymous to the injured nerve. The results for IL-6 suggest that the neuroinflammatory reaction of DRG to nerve injury is propagated alongside the neuroaxis from the lumbar to the remote cervical segments. This is probably related to conditioning of cervical DRG neurons to injury.

FEMS Microbiology Ecology

Extended spectrum beta-lactamase and fluoroquinolone resistance genes and plasmids among *Escherichia coli* isolates from zoo animals, Czech Republic

Dobiasova, H.; Dolejska, M.; Jamborova, I.; Brhelova, E.; Blazkova, L.; Papousek, I. ; Kozlova, M.; Klimes, J.; Cizek, A. ; Literak, I.

Research Group: **Molecular Bacteriology**

Research Programme: **Molecular Veterinary Medicine**

Abstract

Commensal *Escherichia coli* isolates from healthy zoo animals kept in Ostrava Zoological Garden, Czech Republic, were investigated to evaluate the dissemination of extended-spectrum beta-lactamase (ESBL) and plasmid-mediated quinolone resistance (PMQR) genes. A total of 160 faecal samples of various animal species were inoculated onto MacConkey agar with cefotaxime (2 mg L^{-1}) or ciprofloxacin (0.05 mg L^{-1}) to obtain ESBL- or PMQR-positive *E. coli* isolates. Clonality of *E. coli* isolates was investigated by multilocus sequence typing and pulsed-field gel electrophoresis. Plasmids carrying ESBL or PMQR genes were typed by PCR-based replicon typing, plasmid multilocus sequence typing and restriction fragment length polymorphism. Forty-nine (71%, $n = 69$) cefotaxime-resistant and 15 (16%, $n = 94$) ciprofloxacin-resistant *E. coli* isolates harboured ESBL or PMQR genes. Isolates were assigned to 18 sequence types (ST) and 20 clusters according to their macrorestriction patterns by pulsed-field gel electrophoresis. The genes $bla_{CTX\text{-}M\text{-}1}$ and *qnrS1* were detected on highly related IncI1 plasmids assigned to clonal complex 3 (ST3, ST38) and on non-related IncN plasmids of ST1 and ST3, respectively. The gene *qnrS1* was located on related IncX1 plasmids. Dissemination of antibiotic resistance is associated with spreading of particular *E. coli* clones and plasmids of specific incompatibility groups among various animal species.

Journal of General Virology

Preliminary epitope mapping of Torque teno sus virus 1 and 2 putative capsid protein and serological detection of infection in pigs

Jarosova V., Celer V.

Research Group: **Molecular Virology**

Research Programme: **Molecular Veterinary Medicine**

Abstract

The aim of this work is to identify antigenic regions within the ORF1 protein of *Torque teno sus virus 1* (TTSuV1) and *Torque teno virus sus 2* (TTSuV2) that could be used as antigens to detect virus-specific antibodies following infection in pigs. Protein sequences of TTSuV ORF1 genes were analysed to predict linear antigenic epitopes. Synthesized peptides were analysed for serological reactivity with swine sera. Such an antigenic region was identified at the C terminus of the ORF1 protein of both viruses and showed serological reactivity with 78% (TTSuV1) and 88% (TTSuV2) of swine sera. An ELISA with an immunodominant peptide as antigen was used to examine the sera of piglets, aged 4–20 weeks, and adults. Results indicated that TTSuV1- and TTSuV2-specific antibodies were detectable at 4 weeks. Antibody titres increased from week 10 and peaked at week 20. A relatively high antibody titre persisted to adulthood.

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