CEITEC news

NEWSLETTER No. 2/2013

Electronic Newsletter, June 2013

Dear CEITEC friends,

This last quarter was highlighted by a visit from our International Scientific Advisory Board (ISAB), which included 6 international scientific experts from outside of the Czech Republic. They came for two days to Brno to examine what progress has been made since last year's visit, and provide further useful recommendations to our Research Programme Coordinators. Moreover, the ISAB served as the judging committee to select the three winners out of a field of 20 student finalists for the first CEITEC PhD student competition. Within this newsletter you can learn more about the three finalists' work.

CEITEC has now been included in the EU-LIFE initiative, which is a consortium of 10 recognized European research institutes which strive for the highest-level of scientific performance. CEITEC is thus far the only non-Western European partner, which is a great testament to our growing reputation outside of the Czech Republic.

In the pages of this quarterly update, you will also find some of our recent scientific successes, including publications in top ranking journals within the fields of specialization.

And finally, I would like to announce the launch of our new CEITEC website, www.ceitec.eu (in English), and www.ceitec.cz (in Czech).

Best wishes,
Markus Dettenhofer

Content

International Scientific Advisory Board meeting

The International Scientific Advisory Board (ISAB) is the highest advisory body of CEITEC, which meets twice a year, and at least once physically in Brno. This year the meeting was held on June 10 – 11. The main objective was to provide ISAB members with information about the current state, progress and development of all Research Programmes since the scientific evaluation in 2012. The Research Programme Coordinators focused on their vision, highlights of their top publications, grants and patents and main achievements.

During this two day meeting the Board members refined the rules for the evaluation, which will be held in 2014. This meeting was concluded with a joint meeting with Coordination Board, the highest authority of CEITEC, where ISAB members presented their recommendations.

ISAB and Coordination Board meeting

CEITEC PhD Competition 2013

The first CEITEC PhD Competition was held on Tuesday, 11 June 2013. This competition was attended by 20 young researchers - three PhD students from each of the CEITEC Research Programmes introduced their research topics. CEITEC experts from the International Scientific Advisory Board evaluated presenters according to the importance of their research question, the significance of their findings and their presentation skills. We believe that such competitions provide exposure across scientific disciplines and could trigger exciting collaborations.

Carl Djerassi

The CEITEC PhD Competition was enriched by a lecture delivered by esteemed scientist Carl Djerassi, emeritus professor at Stanford University. Carl Djerassi, born in Vienna and educated in the US, is a writer and professor of chemistry emeritus at Stanford University. Author of over 1200 scientific publications and seven monographs, he is the only American chemist to have been awarded both the National Medal of Science (in 1973, for the first synthesis of a steroid oral contraceptive-"the Pill") and the National Medal of Technology (in 1991, for promoting new approaches to insect control).

Another interesting lecture with the title "To overcome chemorefractoriness in CLL; an inside and outside approach" was delivered by Arnon Kater, Academic Medical Center, Netherlands. This was followed by Paula Stein, University of Pennsylvania, USA, lecturing on: "Possible Adverse Outcomes of Assisted Reproduction", who was a special guest at CEITEC VFU Summer School.

A photogallery can be found **HERE**.

PhD competition criteria

- The importance of the question (why is it worth asking)
- The significance of the findings (examination of the quality of the data)
- Quality of slides and quality of presentation skills (presentation should be clear and compelling)

Prizes:

1st place
International internship in an institution of student's own choice

2nd and 3rd place
International conference of student's own choice

The winners of CEITEC PhD Competition 2013 (from the left):1. Petra Faltejsková, 2. Iva Tomalová, 3. Petr Klenovský

All PhD competitors were great, but there could be just three winners. Petra Faltejsková from the Molecular Medicine Research Programme took first prize, Iva Tomalová and Petr Klenovský, both from the Advanced Nanotechnologies and Microtechnologies Research Programme, placed second and third respectively. How did they like the competition, what is their research about and what are their scientific dreams? For answers to these questions see below.

Interview with PhD Competition winners

Petra Faltejsková, MSc completed her master's degree in Biochemistry at the Faculty of Science at Masaryk University in 2011. She is a post-graduate student of Biochemistry and works at the CEITEC in the Molecular Oncology II – Solid Cancer group under the supervision of Associate Professor Ondrej Slaby, PhD. Her research is focused mainly on the role of non-coding RNAs in colorectal cancer. She is an author of one book and several publications in reputable scientific journals including the Journal of Cellular and Molecular Medicine, the International Journal of Colorectal Disease and the Journal of Translational Medicine.

What are your thoughts on the first CEITEC PhD Competition? What does winning this competition mean to you?

I think this competition is a good opportunity to get acquainted with research projects of one's colleagues who work within CEITEC and at the same time it helps make new contacts and establish forms of cooperation. For me, winning first place is confirmation that area of research our group, Molecular Oncology II – Solid Cancer, is engaged in, managed to gain the interest of experts across various fields and that's why it is important to continue with it.

One of the evaluation criteria was the significance of the research question. Can you explain briefly what you are working on and what could have made the committee interested in your research?

In my PhD studies I am aiming to find out if short non-coding RNAs called microRNAs could serve as new diagnostic, predictive and prognostic biomarkers and also as therapeutic targets with tumour diseases in future. I think this topic is very up-to-date and that's why it could have convinced the committee of experts.

Have you thought of where you might go for an internship after having won?

I haven't thought about the location of the internship yet, but I believe I will find a suitable workplace in the near future which would help move our research even further.

Do you have any dreams related to science which you would like to come true?

I would like our research to find clinical uses in the future so that patients with tumour diseases would have a higher chance of a successful recovery or at least a higher quality of life.

Iva Tomalová studied biochemistry at the Masaryk University in Brno. Since 2010 she has been studying in a doctoral study programme in Analytical Chemistry under the supervission of Assoc. Professor Jan Preisler, PhD. She has had internships in the National Institute for Agricultural Research in Sophia Antipolis (France) and at the National Taiwan University in Taipei (Taiwan). Iva Tomalová deals with the possibilities of using nanomaterials for desorption mass spectrometry for bioanalytical applications. In CEITEC she works in the Advanced Nanotechnologies and Microtechnologies Research Programme.

What are your thoughts on the first CEITEC PhD Competition? What does being the first runner-up mean to you?

The CEITEC PhD Competition was not only a great experience with the presentation of scientific results but it was also inspiring to meet so many interesting people. Even being through to the final in the competition was an unexpected surprise for me. Winning recognition among CEITEC's best PhD students and holding the ISAB members interest is a success I greatly appreciate.

One of the evaluation criteria was the significance of the research question. Can you explain briefly what you are working on and what could have made the committee interested in your research?

We are developing a method for the analysis of metalloproteins. To put it very simply, we apply separations in the form of traction on a suitable carrier and from this separation record we then try to get as much information as possible about present metals and proteins by means of various analytical methods – mainly mass spectrometry. It is interesting to watch how much data we can gain from single separation, at the beginning of which there are several nanolitres of a sample. In addition, methods usually used require a high concentration of expensive instrumentation in one laboratory. Our approach isolates the separation and detection steps from each other in time as well as place, which enables an effective use of instruments.

Have you thought of which conference you would take part in after having won?

The International Mass Spectrometry Conference was first to come to mind. It is to be held in Switzerland in August next year but I am sure there are more possibilities.

Do you have any dreams related to science which you would like to come true?

I have always kept my big wishes and dreams to myself. But I would be glad if we were successful in the development of methods and coming with solutions to help other scientists in their work and not to stop only at being published.

Petr Klenovský has been studying physics with a specialization in solid state physics since 2003 and he received a master's degree in 2008. Since then he has been a PhD student at the Department of Condensed Matter Physics under the supervision of Prof. RNDr. Josef Humlíček, CSc. He has been a researcher at the same institute since 2009 and recently joined the Functional Properties of Nanostructures Research Group in CEITEC's Research Programme Advanced Nanotechnologies and Microtechnologies. During his PhD studies, he spent several months at the Johannes Kepler University in Linz, Austria, as a visiting PhD student in Prof. Thomas Fromherz's group. Petr Klenovský is involved in the research of semiconductor nanostructures, optical spectroscopy and scanning probe microscopy. He is the author of 7 publications in renown physical journals such as the Physical Review B or Applied Physics Letters, to which 37 citations have been given so far (based on Web of Knowledge).

What are your thoughts on the first CEITEC PhD Competition? What does being the second runner-up mean to you?

As a first attempt to compare PhD students from different CEITEC Research Programmes and Groups, the event was quite successful, particularly in presenting the research carried out in different CEITEC groups. However, in order to make this competition even more fair and focused on the scientific research in the future, I would recommend prolonging the time for individual student presentations. Furthermore, it would be nice to compare students studying in like fields of research (e.g. physics, biology, etc.) and those who are in similar years of their PhD studies (e.g. a PhD student in his first year of studies is disadvantaged to one having studied PhD for four or more years). As for myself, the importance of the PhD competition lies in promoting our group and in the development of my presentation skills in English, which for sure will help me when participating in various international research conferences. Particularly because of the latter, the prize for the third place is much appreciated.

One of the evaluation criteria was the significance of the research question. Can you explain briefly what you are working on and what could have made the committee interested in your research?

I am working on theoretical and experimental studies of quantum dots, very small artificial structures in crystal lattices that attract charge carriers (electrons and holes) and thus in turn exhibit properties similar to atoms or molecules. I am particularly interested in type-II dots where the electrons and the holes are spatially separated resulting in intriguing physical properties, some of which have been successfully described by our group. Among those is an occurrence of a natural quantum dot molecule in type-II quantum dots of a particular kind of semiconductor materials (so far we have described it only theoretically) which might be used in the future in the realization of the so-called quantum gate, an essential part of the elusive quantum computer. It was maybe that last proposal that attracted the jury because of the abilities such a machine was proposed to have (calculations of complex structures like pharmaceuticals, DNA, or even a human brain). However, it must be noted that these abilities of such a device have never been confirmed.

Have you thought of which conference you would take part in after having won?

Maybe the International Conference on Quantum Dots 2014, held in Pisa, Italy.

Do you have any dreams related to science which you would like to come true?

An obvious dream would be to develop a working quantum gate for a quantum computer in the way Shockley, Bardeen, and Brattain developed the semiconductor transistor in the 1940s, which is nowadays used in every computer in the world. And then to use such a computer to develop cures for mankind's maladies. However, as nice as this might sound, it is most probably just as impossible. Science is not just about stellar ideas (although some ideas are needed of course), it is usually hard work with only a very few stellar outcomes. •●

CEITEC contributes to development of new type of computer memory. Data saved much faster and without loss.

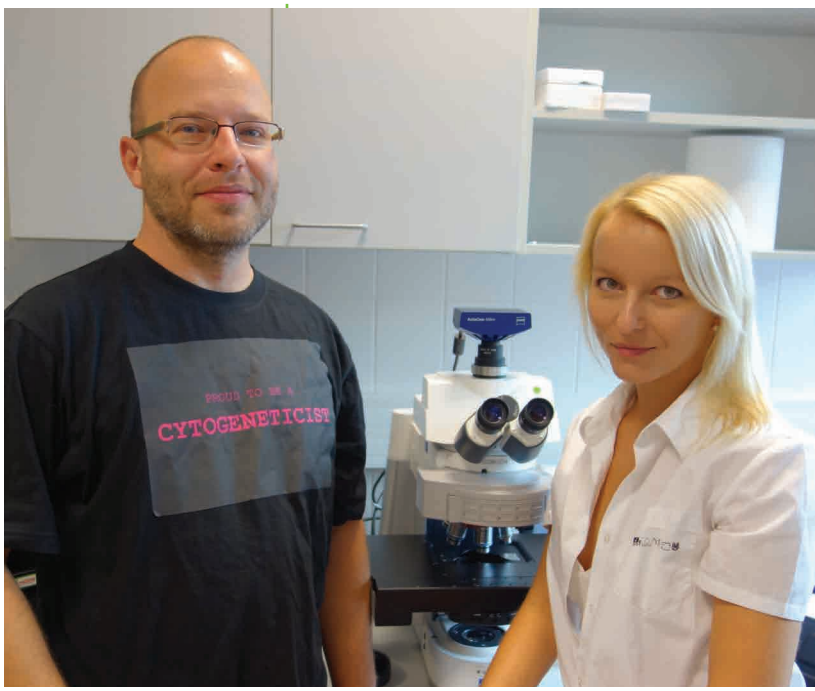
Young scientists from CEITEC BUT and the Institute of Physical Engineering, BUT, Vojtěch Uhlíř and Michal Urbánek, have discovered new ways of controlling magnetic vortices, which can be used, for example, in the fabrication of a new kind of computer memory. The Brno scientists worked on the experimental verification of the corresponding theory with their colleagues from the University of California in San Diego and the synchrotron laboratory in Berkeley. The results of their research were published in the May edition of the prestigious scientific journal, Nature Nanotechnology.

Vortices are physical phenomena found in many forms and scales, from tornadoes or water vortices to vortices at nanometre scale, which can be found in superconducting materials or nanomagnets. The scientists have now managed to rapidly and in a controlled manner switch the spin circulation in magnetic vortices, which opens the door to a multitude of possible applications, especially in the field of IT. Memory cells made from magnetic vortices make it possible to store twice as much information, can work several times faster and, unlike in current memory cells, the information is not lost from the operating memory when disconnected from a power supply. •●

More information can be found **HERE**.

Scientists from CEITEC clarify the ancestral genome structure of the present-day brassicas

Young scientists from CEITEC MU, Terezie Mandáková and Martin A. Lysák, in cooperation with colleagues from the Institute of Vegetables and Flowers in Beijing have reconstructed the ancestral genome structure of the present-day cabbages. The genus *Brassica* comprises several species and varieties of oil-producing plants, forage plants and vegetables, such as oilseed rape, broccoli, cauliflower and cabbage. The study answers the 80-plus-year-old question about a make-up of the ancestral genome of extant brassicas, and will facilitate sequencing and genome analysis of other economically important cruciferous crops. The research was published in the top-ranking journal The Plant Cell in May 2013. •●

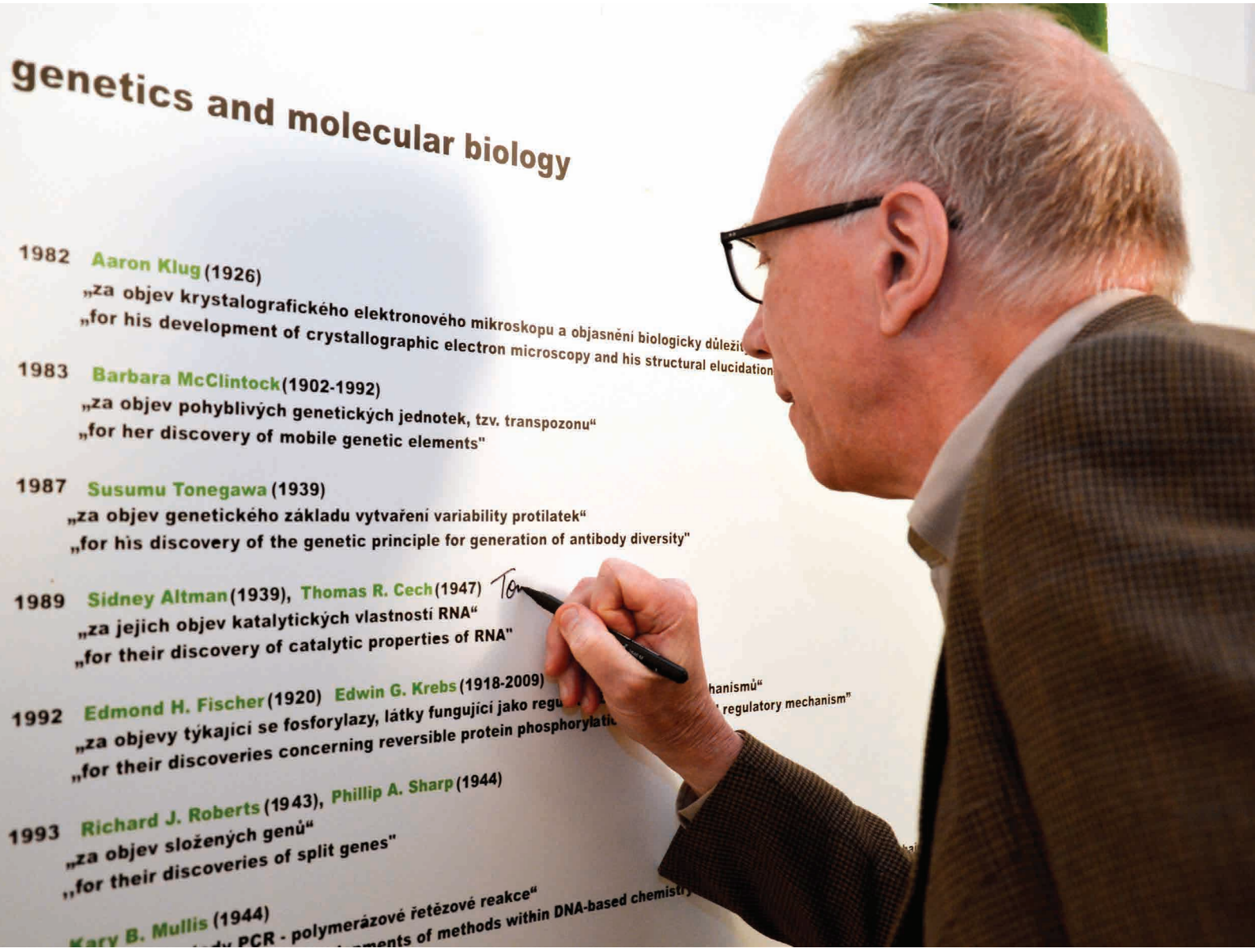


Martin A. Lysák a Terezie Mandáková

Nobel laureate, Thomas R. Cech, in Brno

Another lecture by a Nobel Prize winner took place in Brno under the auspices of CEITEC and Masaryk University. Professor Thomas R. Cech, Howard Hughes Medical Institute and University of Colorado, USA, held a lecture entitled "From the RNA World to the RNP World: Ribozymes, Telomerase and lncRNAs". The lecture was devoted to the functions of Ribonucleic acid (RNA), for the discovery of which Cech was awarded. In 1981-1982 he found out that RNA is not just a passive carrier of genetic information but it can catalyze biochemical reactions like enzymes of protein character. In particular, it was discovered that RNA is able to cut itself without the participation of proteins – a process in which a part of its chain is cut out and remaining parts are reconnected. This discovery was a significant landmark in the study of the origin and development of life.

During his visit, Professor Cech met the Research Programme Coordinator of Genomics and Proteomics of Plant Systems, Jiří Fajkus, whose laboratories cooperate in practice. He also saw the first-class Core Facility at the Josef Dadok National NMR Centre.



Thomas. R. Cech

New Alliance for European Excellence and Competitiveness in Life Sciences

"European research centres in life sciences gather to foster excellence in research, share knowledge, and influence policy."

At the Centre for Genomic Regulation (CRG), in Barcelona, directors and staff from ten top European research institutes, including CEITEC, kicked off a new alliance, called EU-LIFE, that will promote European research. The mission of EU-LIFE is to foster excellence, share knowledge, and influence policies in life sciences. Partners in EU-LIFE are renowned research centres that operate with similar principles of excellence, external reviews, independence, competiveness, and internationality. During difficult economic times and within a highly competitive international research landscape, they believe that they can join forces to better address complex questions, thereby contributing to pushing European science forward.

Current partners of this association are the co-leaders CRG and VIB (Belgium), the Institut Curie (France), the Netherlands Cancer Institute (Netherlands), the Max Delbrück Center for Molecular Medicine; MDC, Berlin-Buch (Germany), Istituto Europeo di Oncologia (Italy), Instituto Gulbenkian de Ciência (Portugal), the CeMM Research Center for Molecular Medicine of the Austrian Academy of Sciences (Austria), CEITEC (Czech Republic), and the Institute for Molecular Medicine Finland (Finland).

FACTS & FIGURES OF THE NETWORK (data at the end of 2012)

- Total number of scientists and support personnel: **7,039**
- Total number of publications: **2,551**
- Total number of running coordinated EU-Projects: **59**
- Total number of running ERC Grants: **75**

More information can be found **HERE**.

Week of Innovatiove Regions Europe

CEITEC was represented at the European Conference Week of Innovative Regions Europe IV (WIRE IV) organised in Cork, Ireland, during Ireland's Presidency of the European Union in 2013. The WIRE IV focused on regional aspects relevant to the final stages of the Horizon 2020 design and legislative process and was positioned primarily as an implementation focused activity in the context of the Cohesion Policy 2014-2020 and Europe 2020. CEITEC presented itself at this high-level forum during Session 2 linking in to Research and Innovation Capacities and Infrastructures. This event was held based on the invitation from the European Commission within the SYLICA project.

Six SoMoPro awards for CEITEC

Six researchers from abroad were recently supported in their integration in the scientific community of CEITEC through the SoMoPro (South Moravian Programme for Distinguished Researchers) initiative, jointly funded by the European Commission and the region of South Moravia. With a total of twelve projects being financed, results of this last SoMoPro call clearly confirmed the role of CEITEC as a regional leader in scientific excellence and a pioneer of scientific internationalization in South Moravia. SoMoPro grants will allow the beneficiaries to establish their independent research agenda at CEITEC while they will bring along their knowledge, experience, and contact networks from (often multiple) prestigious institutions from around the world – countries such as Austria, Belgium, Germany, Russia, South Korea, the United Kingdom, or the United States.

The supported scientific projects cover most of the CEITEC Research Programmes – 2 of them are implemented in Genomics and Proteomics of Plant Systems, 1 in Advanced Nanotechnologies and Microtechnologies, 1 in Advanced Materials, 1 in Molecular Medicine, and 1 in Brain and Mind Research.

CEITEC launches new web pages!

We have prepared a new web site for you, which should be more user-friendly and intuitive. Whether it is information about CEITEC in general that you are looking for, you are interested in Research Groups, or you would like to know about planned events and lectures, you can find all faster and well arranged in one place. We believe that you will like the new web site and you will be glad to keep coming back to it.

Selected CEITEC publications

Nature Nanotechnology

Dynamic switching of the spin circulation in tapered magnetic nanodisks

Uhlíř, V.; Urbánek, M.; Hladík, L.; Spousta, J.; Im, M-Y.; Fisher, P.; Eibagi, N.; Kan, J.; Fullerton, E.; Šikola, T.

CEITEC Research Group: Fabrication and Characterisation of Nanostructures
Research Programme: Advanced Nanotechnologies and Microtechnologies

Summary

Magnetic vortices are characterized by the sense of in-plane magnetization circulation and by the polarity of the vortex core. With each having two possible states, there are four possible stable magnetization configurations that can be utilized for a multibit memory cell. Dynamic control of vortex core polarity has been demonstrated using both alternating and pulsed magnetic fields and currents. Here, we show controlled dynamic switching of spin circulation in vortices using nanosecond field pulses by imaging the process with full-field soft X-ray transmission microscopy. The dynamic reversal process is controlled by far-from-equilibrium gyrotropic precession of the vortex core, and the reversal is achieved at significantly reduced field amplitudes when compared with static switching. We further show that both the field pulse amplitude and duration required for efficient circulation reversal can be controlled by appropriate selection of the disk geometry.

Composites Science and Technology

The shear adhesion strength between the FRC substructure and denture base resin: Effects of FRC architecture, adhesive composition and hydrolytic degradation

Poláček, P.; Salajková, M.; Jančář, J.

CEITEC Research Group: Advanced Polymers and Composites
Research Programme: Advanced Materials

Summary

The adhesion strength between fiber reinforced composite (FRC) members and denture-base resin is pivotal for enhancing removable denture long lasting performance and patient comfort. FRC reinforcing rods based on glass fibers impregnated with light curing resin were used to model the FRC substructure. The influence of fiber architecture and adhesive layer composition on the shear adhesion strength, τ_a, between the FRC and denture-base resin was investigated both dry and in moist environment to assess the stability of the adhesive bond in the oral cavity. The obtained results suggest that for a given fiber architecture, adhesive composition and test conditions, the wetting of the FRC surface was the primary variable affecting the τ_a. In the case of good wetting and formation of adhesive bond between the substrates, interlaminar shear strength of the unidirectional FRC substrate was the limiting factor. In multidirectional FRC substrate, the shear strength of the outer resin rich layer was limiting factor for the maximum adhesion strength.

JCTC – Journal of Chemical Theory and Computation

Toward Reproducing Sequence Trends in Phosphorus Chemical Shifts for Nucleic Acids by MD/DFT Calculations

Přecechtělová, J.; Munzarová, M.L.; Vaara, J.; Novotný, J.; Dračínský, M.; Sklenář, V.

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

Summary

This work addresses the question of the ability of the molecular dynamics–density functional theory (MD/DFT) approach to reproduce sequence trend in ^{31}P chemical shifts (δP) in the backbone of nucleic acids. δP for $[d(CGCGAATTCGCG)]_2$, a canonical B-DNA, have been computed using density functional theory calculations on model compounds with geometries cut out of snapshots of classical molecular dynamics (MD) simulations. The values of ^{31}P chemical shifts for two distinct B-DNA subfamilies BI and BII, δP/BI and δP/BII, have been determined as averages over the BI and BII subparts of the MD trajectory. This has been done for various samplings of MD trajectory and for two sizes of both the model and the solvent embedding. For all of the combinations of trajectory sampling, model size, and embedding size, sequence dependence of δP/BI in the order of 0.4–0.5 ppm has been obtained. Weighted averages for individual ^{31}P nuclei in the studied DNA double-helix have been calculated from δP/BI and δP/BII using BI and BII percentages from free MD simulations as well as from approaches employing NMR structural restraints. A good qualitative agreement is found between experimental sequence trends in δP and theoretical δP employing short (24 ns) MD run and BI, BII percentages determined by Hartmann et al. or via MD with the inclusion of NMR structural restraints. Theoretical δP exhibit a systematic offset of ca. 11 ppm and overestimation of trends by a factor of ca. 1.7. When scaled accordingly, theoretical δP/BI and δP/BII can be used to determine the expected percentage of BII to match the experimental value of δP. As evidenced by the calculations on snapshots from Car–Parrinello molecular dynamics, the systematic offsets of the theoretical δP obtained by MD/DFT approach result primarily from the unrealistic bond lengths employed by classical MD. The findings made in this work provide structure–δP relationships for possible use as NMR restraints and suggest that NMR calculations on MD snapshots can be in the future employed for the validation of newly developed force fields.

Chemistry – A European Journal

A QM/MM Investigation of the Catalytic Mechanism of Metal-Ion-Independent Core 2 β1,6-*N*-Acetylglucosaminyltransferase

Tvaroška, I.; Kozmon, S.; Wimmerová, M.; Koča, J.

CEITEC Research Group: **Glycobiochemistry & Computational Chemistry**
Research Programme: **Structural Biology**

Summary

β1,6-GlcNAc-transferase (C2GnT) is an important controlling factor of biological functions for many glycoproteins and its activity has been found to be altered in breast, colon, and lung cancer cells, in leukemia cells, in the lymhomonocytes of multiple sclerosis patients, leukocytes from diabetes patients, and in conditions causing an immune deficiency. The result of the action of C2GnT is the core 2 structure that is essential for the further elongation of the carbohydrate chains of *O*-glycans. The catalytic mechanism of this metal-ion-independent glycosyltransferase is of paramount importance and is investigated here by using quantum mechanical (QM) (density functional theory (DFT))/molecular modeling (MM) methods with different levels of theory. The structural model of the reaction site used in this report is based on the crystal structures of C2GnT. The entire enzyme–substrate system was subdivided into two different subsystems: the QM subsystem containing 206 atoms and the MM region containing 5914 atoms. Three predefined reaction coordinates were employed to investigate the catalytic mechanism. The calculated potential energy surfaces discovered the existence of a concerted S_N2-like mechanism. In this mechanism, a nucleophilic attack by O6 facilitated by proton transfer to the catalytic base and the separation of the leaving group all occur almost simultaneously. The transition state for the proposed reaction mechanism at the M06-2X/6-31G** (with diffuse functions on the O1′, O5′, O_{Glu}, and O6 atoms) level was located at C1-O6=1.74 Å and C1-O1=2.86 Å. The activation energy for this mechanism was estimated to be between 20 and 29 kcalmol^{-1}, depending on the method used. These calculations also identified a low-barrier hydrogen bond between the nucleophile O6H and the catalytic base Glu320, and a hydrogen bond between the N-acetamino group and the glycosidic oxygen of the donor in the TS. It is proposed that these interactions contribute to a stabilization of TS and participate in the catalytic mechanism.

The Plant Cell

Deciphering the Diploid Ancestral Genome of the Mesohexaploid Brassica rapa

Cheng, F.; Mandáková, T.; Wu, J.; Xie, Q.; Lysak, M.A.; Wang, X.

CEITEC Research Group: Plant Cytogenomics
Research Programme: Genomics and Proteomics of Plant Systems

Summary

The genus *Brassica* includes several important agricultural and horticultural crops. Their current genome structures were shaped by whole-genome triplication followed by extensive diploidization. The availability of several crucifer genome sequences, especially that of Chinese cabbage (*Brassica rapa*), enables study of the evolution of the mesohexaploid *Brassica* genomes from their diploid progenitors. We reconstructed three ancestral subgenomes of *B. rapa* ($n = 10$) by comparing its whole-genome sequence to ancestral and extant Brassicaceae genomes. All three *B. rapa* paleogenomes apparently consisted of seven chromosomes, similar to the ancestral translocation Proto-Calepineae Karyotype (tPCK; $n = 7$), which is the evolutionarily younger variant of the Proto-Calepineae Karyotype ($n = 7$). Based on comparative analysis of genome sequences or linkage maps of *Brassica oleracea*, *Brassica nigra*, *radish* (*Raphanus sativus*), and other closely related species, we propose a two-step merging of three tPCK-like genomes to form the hexaploid ancestor of the tribe Brassiceae with 42 chromosomes. Subsequent diversification of the Brassiceae was marked by extensive genome reshuffling and chromosome number reduction mediated by translocation events and followed by loss and/or inactivation of centromeres. Furthermore, via interspecies genome comparison, we refined intervals for seven of the genomic blocks of the Ancestral Crucifer Karyotype ($n = 8$), thus revising the key reference genome for evolutionary genomics of crucifers.

European Journal of Immunology

Pairing of T-cell receptor chains via emulsion PCR

Turchaninova, M.A.; Britanova, O.V.; Bolotin, D.A.; Shugay, M.; Putintseva, E.V.; Staroverov, D.B.; Sharonov, G.; Shcherbo, D.; Zvyagin, I.V.; Mamedov, I.Z.; Linnemann, C.; Schumacher, T.N.; Chudakov, D.M.

CEITEC Research Group: Adaptive Immunity Group
Research Programme: Molecular Medicine

Summary

Our ability to analyze adaptive immunity and engineer its activity has long been constrained by our limited ability to identify native pairs of heavy-light antibody chains and alpha-beta T-cell receptor (TCR) chains – both of which comprise coupled "halves of a key", collectively capable of recognizing specific antigens. Here we report a cell-based emulsion RT-PCR approach that allows the selective fusion of the native pairs of amplified TCR alpha and beta chain genes for complex samples. A new type of PCR suppression technique was developed that makes it possible to amplify the fused library with minimal noise for subsequent analysis by high-throughput paired end Illumina sequencing. With this technique, single analysis of a complex blood sample allows identification of multiple native TCR chain pairs. This approach may be extended to identify native antibody chain pairs and, more generally, pairs of mRNA molecules that are co-expressed in the same living cells.

Genome Biology and Evolution

Contrasting patterns of transposable element and satellite distribution on sex chromosomes (XY_1Y_2) in the dioecious plant *Rumex acetosa*

Steflova, P.; Tokan, V.; Vogel, I.; Lexa, M.; Macas, J.; Novak, P.; Hobza, R.; Vyskot, B.; Kejnovsky, E.

CEITEC Research Group: **Genome Dynamics**
Research Programme: **Molecular Medicine**

Summary

Rumex acetosa is a dioecious plant with the XY_1Y_2 sex chromosome system. Both Y chromosomes are heterochromatic and are thought to be degenerated. We performed low-pass 454 sequencing and similarity-based clustering of male and female genomic 454 reads in order to identify and characterize major groups of *R. acetosa* repetitive DNA. We found that Copia and Gypsy retrotransposons dominated, followed by DNA transposons and non-LTR retrotransposons. CRM and Tat/Ogre retrotransposons dominated the Gypsy superfamily while Maximus/Sireviruses were most abundant among Copia retrotransposons. Only one Gypsy subfamily had accumulated on Y_1 and Y_2 chromosomes while many retrotransposons were ubiquitous on autosomes and the X chromosome, but absent on Y_1 and Y_2 chromosomes, and others were depleted from the X chromosome. One group of CRM Gypsy was specifically localized to centromeres. We also found that majority of previously described satellites (RAYSI, RAYSII, RAYSIII, RAE180) are accumulated on the Y chromosomes where we identified Y chromosome-specific variant of RAE180. We discovered two novel satellites - RA160 satellite dominating on the X chromosome, and RA690 localized mostly on the Y_1 chromosome. The expression pattern obtained from Illumina RNA sequencing showed that the expression of transposable elements is similar in leaves of both sexes and that satellites are also expressed. Contrasting patterns of TEs and satellite localization on sex chromosomes in *R. acetosa*, where not only accumulation but also depletion of repetitive DNA was observed, suggesting that a plethora of evolutionary processes can shape sex chromosomes.

Pharmacology & Therapeutics

Endocannabinoid system and mood disorders: Priming a target for new therapies

Micale, V.; Di Marzo, V.; Sulcova, A.; Wotjak, C.T.; Drago, F.

CEITEC Research Group: **Experimental and Applied Neuropsychopharmacology**
Research Programme: **Brain and Mind Research**

Summary

The endocannabinoid system comprising the cannabinoid receptor systems and their endogenous ligands is strongly involved in neuropsychiatric disorders, particularly in affective disturbances such as anxiety and depression. There are discussed in this review article, scientific suggestions how synthetic molecules that interact with the activity the endocannabinoid system can open the way to new multi-target therapeutic strategies in mood disorders.

Human Brain Mapping

Brain functional connectivity of male patients in remission after the first episode of schizophrenia

Kasparek, T.; Prikryl, R.; Rehulova, J.; Marecek, R.; Mikl, M.; Prikrylova, H.; Vanicek, J.; Ceskova, E.
CEITEC Research Group: Behavioural and Social Neuroscience
Research Programme: Brain and Mind Research

Summary

Objectives: Abnormal task-related activation and connectivity is present in schizophrenia. The aim of this study was the analysis of functional networks in schizophrenia patients in remission after the first episode. *Experimental design*: Twenty-nine male patients in remission after the first episode of schizophrenia and 22 healthy controls underwent examination by functional magnetic resonance during verbal fluency tasks (VFT). The functional connectivity of brain networks was analyzed using independent component analysis. *Results*: The patients showed lower activation of the salience network during VFT. They also showed lower deactivation of the default mode network (DMN) during VFT processing. Spectral analysis of the component time courses showed decreased power in slow frequencies of signal fluctuations in the salience and DMNs and increased power in higher frequencies in the left frontoparietal cortex reflecting higher fluctuations of the network activity. Moreover, there was decreased similarity of component time courses in schizophrenia—the patients had smaller negative correlation between VFT activated and deactivated networks, and smaller positive correlations between DMN subcomponents. *Conclusions*: There is still an abnormal functional connectivity of several brain networks in remission after the first episode of schizophrenia. The effect of different treatment modalities on brain connectivity, together with temporal dynamics of this functional abnormality should be the objective of further studies to assess its potential as a marker of disease stabilization.

Plos Neglected Tropical Diseases

Novel insights into the genetic diversity of *Balantidium* and *Balantidium*-like cyst-forming ciliates

Pomajbíková, K.; Oborník, M.; Horák, A.; Petrželková, K.J.; Grim, J.N.; Levecke, B.; Todd, A.; Mulama, M.; Kiyang, J.; Modrý, D.
CEITEC Research Group: Parasitology
Research Programme: Molecular Veterinary Medicine

Summary

Balantidiasis is considered a neglected zoonotic disease with pigs serving as reservoir hosts. However, *Balantidium coli* has been recorded in many other mammalian species, including primates. Here, we evaluated the genetic diversity of *B. coli* in non-human primates using two gene markers (SSrDNA and ITS1-5.8SDNA-ITS2). We analyzed 49 isolates of ciliates from fecal samples originating from 11 species of captive and wild primates, domestic pigs and wild boar. The phylogenetic trees were computed using Bayesian inference and Maximum likelihood. *Balantidium entozoon* from edible frog and *Buxtonella sulcata* from cattle were included in the analyses as the closest relatives of *B. coli*, as well as reference sequences of vestibuliferids. The SSrDNA tree showed the same phylogenetic diversification of *B. coli* at genus level as the tree constructed based on the ITS region. Based on the polymorphism of SSrDNA sequences, the type species of the genus, namely *B. entozoon*, appeared to be phylogenetically distinct from *B. coli*. Thus, we propose a new genus Neobalantidium for the homeothermic clade. Moreover, several isolates from both captive and wild primates (excluding great apes) clustered with *B. sulcata* with high support, suggesting the existence of a new species within this genus. The cysts of *Buxtonella* and *Neobalantidium* are morphologically indistinguishable and the presence of *Buxtonella*-like ciliates in primates opens the question about possible occurrence of these pathogens in humans.

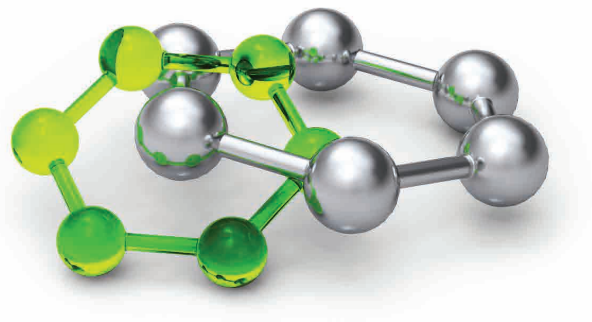
PLoS One

Natural Killer Cell Receptor Genes in the Family *Equidae*: Not only *Ly49*

Futas, J.; Horin, P.
CEITEC Research Group: **Animal Immunogenomic**
Research Programme: **Molecular Veterinary Medicine**

Summary

Natural killer (NK) cells have important functions in immunity. NK recognition in mammals can be mediated through killer cell immunoglobulin-like receptors (KIR) and/or killer cell lectin-like *Ly49* receptors. Genes encoding highly variable NK cell receptors (NKR) represent rapidly evolving genomic regions. No single conservative model of NKR genes was observed in mammals. Single-copy low polymorphic NKR genes present in one mammalian species may expand into highly polymorphic multigene families in other species. In contrast to other non-rodent mammals, multiple *Ly49*-like genes appear to exist in the horse, while no functional *KIR* genes were observed in this species. In this study, *Ly49* and *KIR* were sought and their evolution was characterized in the entire family Equidae. Genomic sequences retrieved showed the presence of at least five highly conserved polymorphic *Ly49* genes in horses, asses and zebras. These findings confirmed that the expansion of *Ly49* occurred in the entire family. Several *KIR*-like sequences were also identified in the genome of Equids. Besides a previously identified non-functional *KIR*-Immunoglobulin-like transcript fusion gene (*KIR-ILTA*) and two putative pseudogenes, a *KIR3DL*-like sequence was analyzed. In contrast to previous observations made in the horse, the *KIR3DL* sequence, genomic organization and mRNA expression suggest that all Equids might produce a functional *KIR* receptor protein molecule with a single non-mutated immune tyrosine-based inhibition motif (ITIM) domain. No evidence for positive selection in the *KIR3DL* gene was found. Phylogenetic analysis including rhinoceros and tapir genomic DNA and deduced amino acid *KIR*-related sequences showed differences between families and even between species within the order *Perissodactyla*. The results suggest that the order *Perissodactyla* and its family *Equidae* with expanded *Ly49* genes and with a potentially functional *KIR* gene may represent an interesting model for evolutionary biology of NKR genes.



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