CEITEC news

EXTERNAL NEWSLETTER 02/2012

External electronic Newsletter, June 2012

Dear friends of CEITEC,

We have just concluded our first official CEITEC Common Evaluation of Scientific Excellence. The outcomes are indeed encouraging; all the teams have the potential to be among the best teams in their fields. In fact, some are already there and many others are very close. It is a promising start. The evaluation had yet one other purpose – to show that it is not the friendship with whomever is in charge but it is rather the quality of research, capability to attract competitive international grants and appropriate attention to the future generation of scientists that matters and will matter in CEITEC. •●

Tomáš Hruda, Executive Director

CEITEC Common Evaluation of Scientific Excellence - Prof. Knoll final speech

Content

CEITEC Common Evaluation of Scientific Excellence

More than twenty top experts from leading scientific institutes from around the world have arrived in Brno in order to evaluate the work results of over 400 scientists from CEITEC. CEITEC organized evaluations of scientists solely by foreign experts. The aim was to obtain results on the basis of which concrete impacts on individual research groups of CEITEC would be achieved. The evaluation was taking place on the level of 53 research groups that operate within CEITEC's 7 research programmes. The proceedings took place from 7th – 8th June and 11th – 12th June.

CEITEC Common Evaluation of Scientific Excellence

CEITEC uses the ERC classification, i.e. a scale from A (excellent) to D (unsatisfactory). In addition, group A has 3 subcategories (A1, A2 and A3).

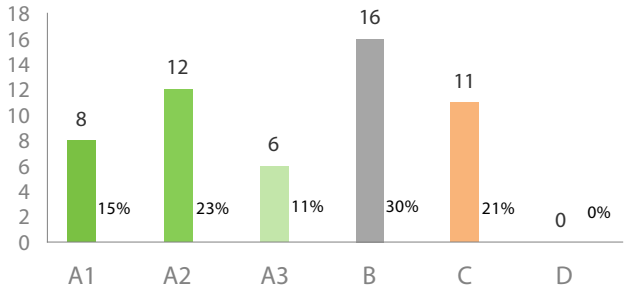
A	excellent	A1
		A2
		A3
B	good	
C	satisfactory	
D	unsatisfactory	

EVALUATION | **2012**

CEITEC

Overview of outcomes

	Number of RGs	Percentage
A1	8	15%
A2	12	23%
A3	6	11%
B	16	30%
C	11	21%
D	0	0%
Total	53	100%



Evaluators Facebook can be downloaded **HERE**.

Interdisciplinary PhD projects

The call aimed to support interdisciplinary research in CEITEC through direct support of the best proposals in interdisciplinary research to be conducted by PhD students. The selected projects will obtain funding for participating PhD students for up to 3 years.

Selected projects

Project name	Project leader	Project partner
Preparation and testing of quantum dots-protein complex as a label for *in vitro* and *in vivo* imaging of prions	Jaromír Hubálek/René Kizek (RP1)	Petr Dubový/Vladimír Pekařík/Michal Masařík (RP6)
Application of magnetizable particles in analysis of molecular mechanisms of zinc ions in prostate tumor cells	Jaromír Hubálek/René Kizek (RP1)	Petr Dubový/Vladimír Pekařík/Michal Masařík (RP6)
Advanced Immunosensors	Petr Skládal (RP3)	Jaromír Hubálek (RP1)
Measurement of ultra-weak affinities in bio-molecular systems	Richard Štefl (RP3)	Josef Humlíček (RP1)

CEITEC representatives met their counterparts at ETH Zürich

Representatives of Central European Institute of Technology from the areas of Grant Support, Technology Transfer, Financial Management, Public Relations and Core Facilities visited their counterparts at ETH Zurich. The main aim of the visit was to share experiences and transfer best practices from ETH Zurich to CEITEC in these areas. There will be a second visit to Zurich with the participation of researchers representing all CEITEC research programmes. The main objective of this visit, which will take place in the middle of July, is to promote scientific cooperation between CEITEC researchers and their counterparts in Zürich. All the activities are coordinated by CEITEC central Grant Office and EU GrantsAccess (common grant office shared between ETH Zurich and University of Zurich) as a part of the common project financed by the Swiss-Czech Cooperation Programme. More information can be found **HERE**.

CEITEC and ETH Representatives, University of Zurich , May 2012

SynBIOsis final conference in Brussels

CEITEC as a project partner took part in the Final Conference of the SynBIOsis project (funded by FP7) which was held in the Committee of the Regions in Brussels on 29th May 2012. Scope of the conference was to present the process outlined during the project execution that has allowed the progressive creation of solid cooperation between universities, research driven clusters and businesses in the fields covering the intersections of biotechnology, nanotechnology and ICT. These good practices, already tested in South Moravia and Friuli Venezia Giulia regions and highly replicable in other European backgrounds, could likely contribute to the optimization of the utilization of the European Structural Funds earmarked for research and innovation. More information can be found **HERE**.

SynBIOsis final conference in Brussels, May 2012

CEITEC also took part in the CZELO (Czech Liaison Office for R&D) 7-year anniversary celebration on the premises of the Czech Permanent Representation to the EU on 30 May 2012. More information can be found **HERE**. •●

Japan-Czech Technology Days 2012 & Nanofibers 2012

CEITEC participated at Japan-Czech Technology Days 2012 & Nanofibers 2012. In addition to meetings taking place as part of Nanofibers 2012, individual meetings have been organized with Riken and Tokyo Institute of Technology. The broad scope of research areas, multidisciplinary nature of these institutions and their advanced PhD and Postdoc programmes make them very attractive for future cooperation with CEITEC. •●

Oeda Kenji, Executive Director, RIKEN
Tomáš Hruda, Executive Director, CEITEC
Jan Ostřížek, Grant Office Manager, CEITEC BUT
Reiji Nagashima, Senior Manager, RIKEN

RIKEN - Institute of Physical and Chemical Research, Japan

Interview with CEITEC scientist

Prof. MUDr. Milan Brázdil, Ph.D.

CEITEC Masaryk University, Brno, Czech Republic

Brain and Mind Research Programme Coordinator
Group Leader, Behavioural and Social Neuroscience Research Group

The mystery of déjà vu unveiled

Prof. Milan Brázdil with his team and other colleagues have recently made a significant discovery in their field of specialisation. They are first in the world to prove that the déjà vu phenomenon in healthy humans is associated with certain structures in the brain, which clearly supports a neurological origin of this phenomenon. The results of their research were published in April by a reputable scientific magazine in the field of neuroscience, Cortex (Impact Factor 7.25). To this date, no specific piece of evidence has been offered by anyone explaining the déjà vu phenomenon in healthy humans. Scientists from the Central European Institute of Technology at Masaryk University (CEITEC MU) and of the Faculty of Medicine of Masaryk University, together with their colleagues from the University of Exeter in Britain are the first ones in the world to prove such interconnection. This is a significant contribution to unveiling the mystery of this phenomenon.

Professor, you and your team have reached a point that most researchers probably dream about. You have proven something that no one else in the world has been able to prove. How do you feel about being first?

I think that it is the goal of each scientist to discover something completely new, and most scientists do succeed to do so in a certain form. At the same time, however, it is always about the degree of invention, true originality and actual impacts of such discovery. In this perspective, our proof of morphologic differences in the human brain associated with the déjà vu phenomenon is something that kind of stands out of the long line of other publications. As such, it naturally represents a great satisfaction and joy for us.

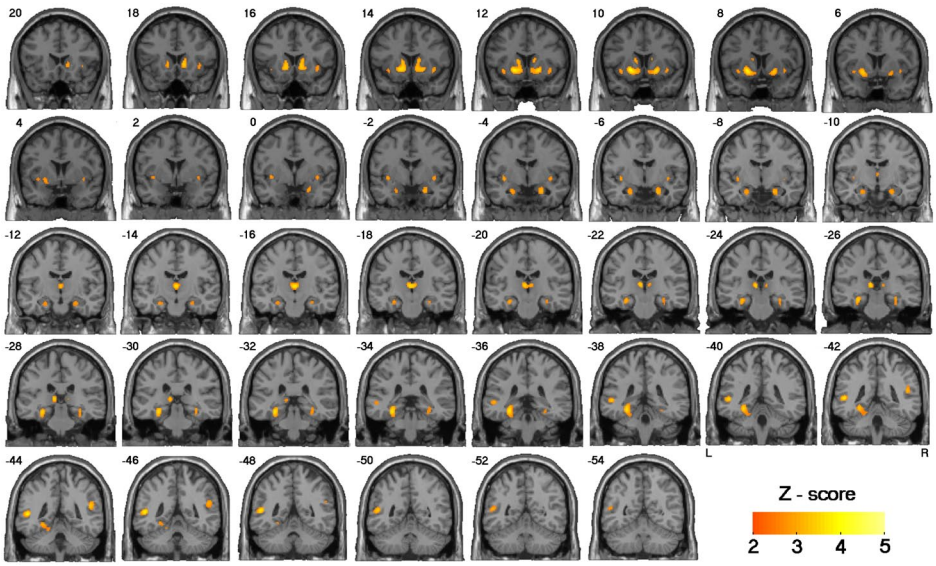
> *Occasional occurrence of déjà vu is observed in 60 – 85% of healthy individuals*

Can you describe how specifically is the déjà vu phenomenon associated with the structures in the human brain?

By means of an imaging examination of the brain of 133 healthy subjects – volunteers - by magnetic resonance, we have proven that the fascinating experience of déjà vu is affected by certain brain structures. We compared the sizes of individual brain areas of persons who do experience déja vu from time to time and those who have never experienced this phenomenon. The morphologic analysis did prove certain minor, but statistically significant differences in the amount of grey matter in some regions of the brain, with a maximum of findings in the differences in hippocampal regions - small structures within the medial temporal lobes that play a major role in memory functions. These structures were significantly smaller in individuals with the occurrence of déjà vu than in individuals who have not experienced déjà vu. Moreover, we have discovered that the more often déjà vu occurred in the examined individuals, the smaller these brain structures were. This discovery was enabled by a type of recently developed sophisticated mathematic analysis (among other things), capable of revealing in the magnetic resonance images even differences so small that they could not be detected by the methods used in the past.

It has already been proven in the past that déjà vu occurs quite often as a sign of the beginning of an epileptic seizure in patients suffering from temporal lobe epilepsy. And that it is even possible to artificially cause this condition by means of electric stimulation. Have you relied on these presumptions?

Yes, past research has repeatedly proven a general interconnection between déjà vu and certain regions of the brain, primarily the hippocampus, and other parts of the temporal lobes. As you have mentioned, diagnostic electric stimulation of these particular brain structures performed in epileptic patients through EEG electrodes in the brain does provoke the occurrence of déja vu in a number of these patients. However, this was only observed in patients suffering from uncontrollable epilepsy of temporal lobes. In a large number of these individuals (perhaps up to one third) déja vu occurs in the form of the so-called aura, i.e. the first subjective symptom of an upcoming epileptic seizure. In this case, we speak of a certain pathological form of déja vu, the pathogenesis of which need not be identical with the origin of the déja vu phenomenon occurring in healthy individuals. On the other hand, this experience has similar clinical features both in healthy individuals and in epileptics. This was why we focused on the potential relationship between déja vu and the hippocampus in healthy individuals. By discovering structural differences in these regions in healthy individuals who do and who don't have any experience of déja vu, we have clearly proven that common déjà vu is directly associated with the functioning of these particular brain structures. At the moment, we still do not know what exactly is the trigger of this non-pathologic déja vu, but we believe that in principle, there may be similar processes going on in the brain as those occurring during epilepsy. It is probably a certain "system error" associated with higher excitability of the hippocampuses. This, together with the smaller size of the hippocampuses, could be the result of changes in these most sensitive regions of the brain originating probably in the course of the neural system development.

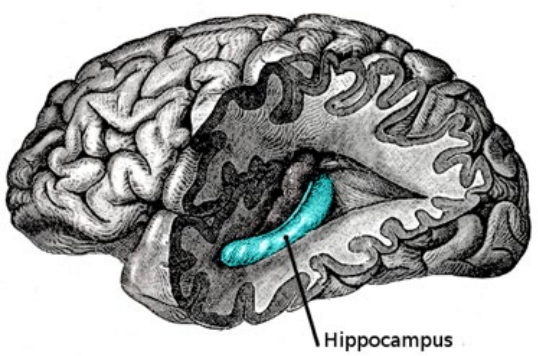


The results of your research prove that there is probably a causal link between the hippocampus and common déja vu that, according to the literature, occurs more often in younger individuals and in individuals with higher education level. You have also mentioned the relationship between the hippocampus and memory. How are these aspects interconnected?

Yes, the hippocampus is an extremely plastic neural structure, in which neurogenesis (birth of new neurons) takes place exclusively for the entire life. However, as such, it is extremely sensitive to various external impacts, either pathological, such as inflammations, insufficient perfusion or seizures, or physiological, such as psycho-social stress or sleep deprivation, primarily if these occur in early childhood. All these factors, together with genetic impacts (as was proven by a current study recently published in one of the most reputable scientific magazines, Nature Genetics, in which participated also Richard Barteček of our research group), may result in a smaller volume of the adult hippocampus, thus increasing its neuronal excitability. Consequently, common accidental excitation of neurons in weakened hippocampuses may become false memories - déjà vu. At the same time, it must be noted that although hippocampus is very important in the process of creating memory tracks, for which reason it might seem that its size would negatively affect the memory functions, the truth is much more complex. There is definitely no reciprocal proportion between the level of intelligence and the occurrence of the déja vu phenomenon.

Are you planning to continue in this line of research and try to discover what exactly is the trigger of déjà vu?

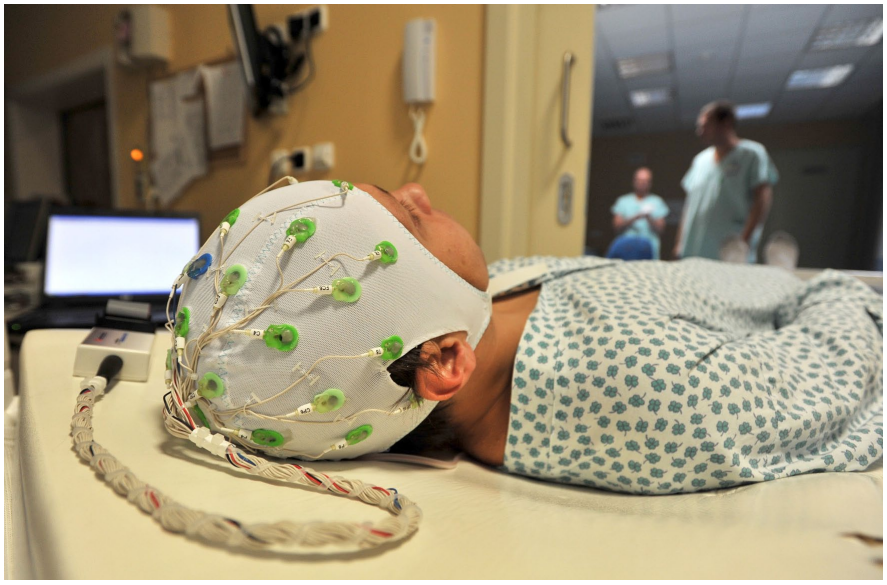
Definitely. For example, at the moment we are preparing a joint project of CEITEC and ICRC, the subject of which is detailed research of hippocampal metabolism in individuals with déjà vu. For this research, we need a magnetic resonance device with a higher field (min. 3 Tesla), allowing the completion of sophisticated spectroscopic analyses. Such a device is already available at ICRC. We expect that the spectroscopic analyses might shortly bring us material information regarding the distribution of the main inhibition and excitation of neurotransmitters in specific areas of the hippocampuses or other brain structures that are relevant. Their proportions reflect the excitability of any specific brain region, which means that they can assist in confirming or refuting our working hypotheses regarding the role of spontaneous excitation of neurons in weakened hippocampuses.



What was the response of your colleagues to your research? Have you received any requests for co-operation?

Yes, basically immediately after the publication of our results, we noticed positive responses from our colleagues, not only from the Czech Republic, but also from other countries. We have been asked, for example, to give a lecture at the European conference on cognitive and affective neurosciences in Marseille that took place a month ago and where we attended a specialised symposium focused for the first time ever on the topic of déjà vu. Now we are going to another conference in Beijing and we have other lectures ahead, for example at the Faculty of Psychology of Vienna University. Other new contacts keep appearing also because the déjà vu phenomenon is a very attractive topic. And we also have a number of other ideas for projects relating to déjà vu. With our colleagues – psychologists of the Faculty of Social Studies or Masaryk University and of the Institute of Psychology of the Czech Academy of Science – we are preparing an extensive questionnaire research relating to potential relationship between the non-pathological déjà vu and the so-called emotional connection. There are obvious analogies between both these phenomena, such as the fact that exposition to stress in early childhood results in abnormal development of emotional connection in adulthood, with the hippocampus volume in individuals with abnormal emotional connections being reduced in a similar way. The interesting aspect is that we will use social networks for the administration of the prepared questionnaire. We expect a large number of respondents, Facebook and other social networks are used mainly by younger people who tend to be more open and who experience déjà vu more often. Sociologists are already using this form of questionnaire research and it has proven effective several times in practice. We want to continue our déjà vu research also in co-operation with our colleagues from the Exeter University in Britain.

And what are your further ambitions in the field of neurosciences within CEITEC?



Other research plans are related to our behavioural and social neurosciences research group. We are gradually moving from the study of the most simple cognitive functions, such as attention, movement timing or detection of scarce stimuli, to the more complex functions – detection of one's own errors, complex decision-making or functioning of human brain in the context of what is happening around and what social interactions are going on. We are more and more aware of how significant the impact of social influences is on the activities in various regions of the brain or their functional interconnection and how significantly these aspects modify the behaviour of human brain.

Generally speaking, system neuroscientists were until recently researching mainly what regions of the brain are activated in the course of working on any specific task, but in recent years they have started to focus more and more on the interactions and relations between various activated areas, i.e. the functional connectivity or functional integration. And this brings an extremely complex, complicated, yet fascinating look into the brain. For example, it turns out that a very simple scarce visual stimulus results in a dramatic increase of interconnections between the number of brain areas that can be compared to an increased number of current "phone calls" within the brain. And individual interconnected areas can communicate simultaneously on different frequencies!

Within CEITEC, brain research is carried out in co-operation between various theoretic, experimental and clinical fields, starting from molecular level, up to the cognitive and behavioural level. What specific tasks are you currently working on?

All our projects are extremely interdisciplinary. At the moment, for example, we are finalising a joint study with the Transport Research Centre and the Institute of Psychology of the Czech Academy of Science, focused on the importance of empathy and motivation in road users. During functional magnetic resonance examination, we were showing healthy individuals various sequences of the popular educational campaign for drivers by the director Filip Renč entitled "Not thinking? You will pay!" that were broadcasted on Czech TV some time ago. These short spots always contain information regarding dangerous behaviour of specific participants of the road traffic and their ending is catastrophic. As control stimuli, we used similar video sequences that did not contain the dangerous behaviour and the dramatic ending. It was interesting, that watching the traffic campaign spot (as compared to the control spots) caused a statistically significantly higher activation in the brain of the examined individuals on the outside surface of both temporal lobes, corresponding anatomically to the location of sulcus temporalis superior. It is known that this area may play a significant role with respect to empathy. Accordingly, the aforementioned areas were statistically significantly more activated in individuals with a higher empathy level. The first results of a subsequent examination of problematic drivers reveal a different level of activation in these areas of the brain compared to common drivers in the course of watching the spots of the "Not thinking? You will pay!" campaign. Thus, we have proven a relationship between the level of empathy and the dangerousness of behaviour and we have also relativised the potential impacts of the aforementioned campaign on the target group of problematic drivers.

Who do you plan to co-operate with in CEITEC?

Within CEITEC, we are preparing intensive co-operation with our colleagues from the research program of advanced nano- and micro-technologies. We are planning to use the magnetic nano-particles produced by them and detected on magnetic resonance devices with a high magnetic field (7 and 9.4 Tesla) for sophisticated diagnostics of certain neurologic and psychiatric diseases, or even for their treatment. Specifically, we are planning to start animal experiments by the end of this year focused on the behaviour of magnetic nano-particles transported into the brain by a strong magnetic field and their role in detection of functional epileptic stratum.

What are the benefits of CEITEC for your program? And where do you see the future of your field within CEITEC?

In the not very far future, CEITEC should offer us an excellent infrastructure and modern, well equipped labs for the growing neurosciences teams. At the moment, the possibilities of high-quality research in our field are quite limited in our region. For example, magnetic resonance devices are only available for scientific and research purposes to a very limited extent, the existing devices are located in hospitals and are, naturally, used mainly for clinical purposes, i.e. for diagnostics of individual patients. In the entire region, there is still no specialised device for a widely defined neurosciences research. As a part of the currently developed central molecular and functional imaging laboratory (MAFIL), our neurosciences program will acquire unique magnetic resonance devices with the capacity of 3 and 7 Tesla. These will enable us to perform much more detailed and precise examinations, significantly extending the possibilities of our research. CEITEC currently offers a major help with solving the issue of insufficient space that has been currently burdening us. In the past decade, neurosciences have gone through an intensive growth in all their fields, which has resulted in a significant progress of their quality. At the same time, however, we have reached our limit in terms of laboratory and office space, which poses enormous problems for enrolling new colleagues in our programs, including graduate students.

Finally, I would like to mention that the activities in CEITEC fill me with a positive feeling. I believe that everyone who is participating in this project is really serious about it and that CEITEC will truly be about excellent research. In the Czech Republic, we have unfortunately too often seen research carried out just for the sake of research and not everyone perceives the recently completed international evaluation of CEITEC as positive. However, I believe that an independent evaluation by foreign experts is a step in the right direction and I trust that its results will be used in the right way.

Selected CEITEC publications

Journal of the American Chemical Society

Highly Adaptable Two-Dimensional Metal–Organic Coordination Networks on Metal Surfaces

Kley, S. Ch.; Čechal, J.; Kumagai, T.; Schramm, F.; Ruben, M.; Stepanow, S.; Kern, K.

CEITEC Research Group: **Fabrication and Characterisation of Nanostructures**
Research Programme 1: **Advanced Nanotechnologies and Microtechnologies**

Summary

The formation of extended two-dimensional metal–organic coordination networks (2D-MOCNs) showing high adaptability to surface step edges and structural defects is revealed by scanning tunneling microscopy. Rod-like 4,4'-di-(1,4-buta-1,3-diynyl)-benzoic acid (BDBA) and iron atoms assemble into extended 2D-MOCNs on Au(111) and Ag(100) surfaces. Independent from the chosen substrate and its surface symmetry the MOCN grows continuously over multiple surface terraces through mutual inphase structure adaptation of network domains at step edges as well as on terraces. The adaptability of the MOCNs is mainly ascribed to the high degree of conformational flexibility of the butadiynyl functionality of the ligand. Despite their flexibility, the MOCNs exhibit considerable robustness against annealing at high temperatures. The findings show that mesoscale self-assembled functional architectures with a high degree of substrate error tolerance can be realized with metal coordination networks.

International Journal of Fatigue

Casting defects and high temperature fatigue life of IN 713LC superalloy

Kunz, L.; Lukáš, P.; Konečná, R.; Fintová, S.

CEITEC Research Group: **Advanced Metallic Materials and Metal Based Composited**
Research Programme 2: **Advanced Materials**

Summary

High-cycle high temperature fatigue life of a superalloy IN 713LC in as cast state and after hot isostatic pressing was experimentally determined for symmetrical cycling and cycling with tensile mean stress of 300 MPa. Fatigue tests were conducted at 800 °C in laboratory air. It has been found that the hot isostatic pressing improves the fatigue life. Large casting defects are sites of fatigue crack initiation in both states of the alloy. The hot isostatic pressing reduces the size of casting defects, however the broad scatter band of the lifetime data remains. Determination of casting defects size by optical microscopy on metallographic sections and an analysis of the size distribution by extreme value statistics indicates two types of defects: (i) small isolated defects and (ii) defect clusters consisting of complicated interconnected shrinkages in the three-dimensional space. The size distribution of both types of defects follows the extreme value statistics. This enables to estimate the maximum size of a defect likely to occur in a defined volume. The predicted maximum defect size in a volume of a fatigue specimen reasonable corresponds to the size of defect observed on the fracture surface of failed specimen.

Journal of Chemical Information and Modeling

SiteBinder: An Improved Approach for Comparing Multiple Protein Structural Motifs

Sehnal, D.; Varekova; Svobodova, R.S.; Huber, H. J .; Geidl, S.; Ionescu, C. M.; Wimmerova, M.; Koca, J.

CEITEC Research Group: Computational Chemistry
Research Programme 3: Structural Biology

Summary

There is a paramount need to develop new techniques and tools that will extract as much information as possible from the ever growing repository of protein 3D structures. We report here on the development of a software tool for the multiple superimposition of large sets of protein structural motifs. Our superimposition methodology performs a systematic search for the atom pairing that provides the best fit. During this search, the RMSD values for all chemically relevant pairings are calculated by quaternion algebra. The number of evaluated pairings is markedly decreased by using PDB annotations for atoms. This approach guarantees that the best: fit will be found and can be applied even when sequence similarity is low or does not exist at all. We have implemented this methodology in the Web application SiteBinder, which is able to process up to thousands of protein structural motifs in a very short time, and which provides an intuitive and user-friendly interface. Our benchmarking analysis has shown the robustness, efficiency, and versatility of our methodology and its implementation by the successful superimposition of 1000 experimentally determined structures for each of 32 eukaryotic linear motifs. We also demonstrate the applicability of SiteBinder using three case studies. We first compared the structures of 61 PA-ILL sugar binding sites containing nine different sugars, and we found that the sugar binding sites of PA-IIL and its mutants have a conserved structure despite their binding different sugars. We then superimposed. over 300 zinc finger central motifs and revealed that the molecular structure in the vicinity of the Zn atom is highly conserved. Finally, we superimposed 12 BH3 domains from pro-apoptotic proteins. Our findings come to support the hypothesis that there is a structural basis for the functional segregation of BH3-only proteins into activators and enablers.

PLoS One

Analysis of the Nse3/MAGE-binding Domain of the Nse4/EID Family Proteins

Guerineau M.; Kriz Z.; Bednarova K.; Kozakova L.; Janos P.; Palecek J.

CEITEC Research Group: Chromatin Molecular Complexes
Research Programme 4: Genomics and Proteomics of Plant Systems

Summary

The SMC (structural maintenance of chromosomes) complexes are conserved in all eukaryotes and play crucial roles in chromosome maintenance. The SMC5-6 complex is comprised of 6 subunits assembled into two sub-complexes. The Nse1, Nse3 and Nse4 subunits interact with each other and form one of the SMC5-6 sub-complexes. Interestingly, Nse3/MAGEG1 is the founding member of the MAGE (melanoma-associated antigen) mammalian protein family and Nse4 is related to the EID (E1A-like inhibitor of differentiation) family of proteins. We have shown that human MAGE proteins can interact with NSE4/EID proteins through their characteristic conserved hydrophobic pocket. Using mutagenesis and protein-protein interaction analyses, we have identified a conserved Nse3/MAGE-binding domain of the Nse4/EID proteins. In addition, docking and molecular dynamic simulations enabled us to generate a structure model for EID-MAGE heterodimer. The conservation of the interacting surfaces suggest tight co-evolution of both Nse4/EID and Nse3/MAGE protein families.

Journal of Experimental Botany

Developmetal silencing of the AtTERT gene is associated with increased H3K27me3 loading and maintenance of its euchromatic environment

Ogrocká, A.; Sýkorová, E.; Fajkus, J.; Fojtová, M.

CEITEC Research Group: Chromatin Molecular Complexes
Research Programme 4: Genomics and Proteomics of Plant Systems

Summary

Telomerase is an enzyme responsible for the maintenance of telomeres, specialized nucleoprotein structures at the ends of linear chromosomes, and its activity is precisely regulated during development. In animal model organisms, involvement of epigenetic mechanisms (DNA methylation and histone modifications determining chromatin structure) in the complex process of regulation of telomerase activity has been reported. In this work, telomerase activity and transcription in plant tissues was correlated to the epigenetic state of telomerase promoter. Our discovery that (i) DNA methylation is not involved in developmental regulation of telomerase promoter and (ii) euchromatic nature of the AtTERT chromatin is maintained even in telomerase-negative tissues may reflect the totipotency, unique attribute of plants, and represents another interesting difference in plant and animal telomere biology.

Chromosoma

HMGB1 gene knockout in mouse embryonic fibroblasts results in reduced telomerase activity and telomere dysfunction

Polanská, E.; Dobšáková, Z.; Dvořáčková, M.; Fajkus, J; Štros, M.

CEITEC Research Group: Chromatin Molecular Complexes
Research Programme 4: Genomics and Proteomics of Plant Systems

Summary

Telomere DNA repeats are added onto chromosome ends by telomerase, consisting of two main components: a catalytic protein subunit (telomerase reverse trancriptase, TERT), and an RNA subunit (telomerase RNA, TR). We found HMGB1 (a chromatin-associated protein acting as a DNA chaperone in transcription, replication, recombination, and repair) can modulate cellular activity of telomerase. Knockout of the HMGB1 gene (HMGB1 KO) in mouse embryonic fibroblasts (MEFs) results in chromosomal abnormalities, emerging DNA damage signals at telomeres, and telomere shortening. HMGB1 KO MEFs also exhibit much lower telomerase activity than the wild-type MEFs. orrespondingly, enhanced telomerase activity is observed upon overexpression of HMGB1 in MEFs. HMGB1 physically interacts with both TERT and TR, as well as with active telomerase complex in vitro. However, direct interaction of HMGB1 with telomerase is most likely not accountable for the observed higher telomerase activity in HMGB1-containing cells, as revealed from the inability of purified HMGB1 protein to stimulate telomerase activity in vitro. While no transcriptional silencing of TERT is observed in HMGB1 KO MEFs, levels of TR are diminished (~3-fold), providing possible explanation for the observed lower telomerase activity in HMGB1 KO cells. Interestingly, knockout of the related HMGB2 gene elevates telomerase activity (~3-fold) in MEFs, suggesting that the two closely related proteins of the HMGB family, HMGB1 and HMGB2, have opposite effects on telomerase activity in the cell. The ability of HMGB1 to modulate cellular activity of telomerase and to maintain telomere integrity can help to understand some aspects of the protein involvement in chromosome stability and cancer.

Neurological Sciences

Iowa Gambling Task in patients with early-onset Parkinson's disease: strategy analysis

Gescheidt, T.; Czekoova, K.; Urbanek, T.; Marecek, R.; Mikl, M.; Kubıkova, R.; Telecka, S.; Andrlova, H.; Husarova, I.; Bares, M.

CEITEC Research Group: Behavioural and Social Neuroscience
Research Programme 6: Brain and Mind Research

Summary

The aim of our study was to analyse decision making in early-onset Parkinson's disease (PD) patients performing the Iowa Gambling Task (IGT). We compared 19 patients with early-onset PD (B45 years) on dopaminergic medication (no evidence of depression, dementia, executive dysfunction according to the Tower of London test and the Stroop test, or pathological gambling) with 20 age-matched controls. A computer version of the IGT was employed. The PD patients achieved slightly lower IGT scores than the control group. A detailed analysis based on 'shift frequencies' between the individual decks showed that the patients tended to change their preferences for the decks more frequently, with a higher preference for the 'disadvantageous' deck B. Control subjects seemed to develop a more effective strategy. These differences could be caused by the poorer ability of the patients to develop any strategy at all. We observed changes in decision making during IGT performance in patients with earlyonset PD, although they had no executive dysfunction as measured by established neuropsychological tests. The more detailed analysis employed in the present study could lead to a more accurate study of IGT performance and application of IGT in clinical practice.

Cortex

Unveiling the mystery of de´ja` vu: The structural anatomy of de´ja` vu

Brazdil, M.; Marecek, R.; Urbanek, T.; Kasparek, T.; Mikl, M.; Rektor, I.; Zeman, A.

CEITEC Research Group: Behavioural and Social Neuroscience
Research Programme 6: Brain and Mind Research

Summary

De´ ja` vu (DV) is a widespread, fascinating and mysterious human experience. It occurs both in health and in disease, notably as an aura of temporal lobe epilepsy. This feeling of inappropriate familiarity has attracted interest from psychologists and neuroscientists for over a century, but still there is no widely agreed explanation for the phenomenon of non-pathological DV. Here we investigated differences in brain morphology between healthy subjects with and without DV using a novel multivariate neuroimaging technique, Source-Based Morphometry. The analysis revealed a set of cortical (predominantly mesiotemporal) and subcortical regions in which there was significantly less gray matter in subjects reporting DV. In these regions gray matter volume was inversely correlated with the frequency of DV. Our results demonstrate a structural correlate of DV in healthy individuals for the first time and support a neurological explanation for the phenomenon. We hypothesis that the observed local gray matter decrease in subjects experiencing DV reflects an alteration of hippocampal function and postnatal neurogenesis with resulting changes of volume in remote brain regions.

Pharmacology, Biochemistry and Behavior

Differential effects of modafinil, methamphetamine, and MDMA on agonistic behavior in male mice

Machalova, A.; Slais, K.; Vrskova, D.; Sulcova, A.

CEITEC Research Group: Experimental and Applied Neuropsychopharmacology
Research Programme 6: Brain and Mind Research

Summary

The results of this study present behavioral profiles of acute effects of modafinil, methamphetamine, and MDMA (ecstasy) in male mice that differ in some parameters of agonistic behavior. The model allowed us to observe different responses to administered drugs, apparent especially in categories of affective behavioral activities (sociable, timid, aggressive) and in locomotor behavior, which varied between predominantly aggressive and timid mice. Agonistic behavior was not affected by modafinil as markedly as by MET and MDMA treatment; however, it was the only drug tested that increased aggression in timid mice. This should be taken into account in the individualized set up of neuroscience experiments, regarding the individual behavioral and neurochemical background of tested subjects. Such an approach may contribute substantially to translation of our knowledge from animal to individualized human treatment.

Critical Care Medicine

Poststroke delirium incidence and outcomes: Validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

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Research Programme 6: Brain and Mind Research

Summary

We evaluated epidemiology of poststroke delirium and validated a tool for delirium assessment: the Czech version of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). An episode of delirium based on reference Diagnostic and Statistical Manual assessment was detected in 55 patients with stroke (42.6%). The CAM-ICU demonstrated a sensitivity of 76% (95% confidence interval [CI] 55% to 91%), a specificity of 98% (95% CI 93% to 100%), an overall accuracy of 94% (95% CI 88% to 97%), and high interrater reliability (κ = 0.94; 95% CI 0.83-1.0).

Neurodegenerative Diseases

Default Mode Network and Extrastriate Visual Resting State Network in Patients with Parkinson's Disease Dementia

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CEITEC Research Group: Applied Neuroscience
Research Programme 6: Brain and Mind Research

Summary

Aims: Using fMRI, we evaluated the default mode network (DMN) and the extrastriate visual resting state network (ESVRSN) in 14 patients with Parkinson's disease dementia (PDD) as compared with 18 patients with Parkinson's disease (PD) without dementia and 18 healthy controls (HC). *Methods*: We analyzed the seed-based functional connectivity of both resting state data and deactivations during a visual complex scene-encoding task. *Results*: Using the posterior cingulate cortex/precuneus as a seed for the DMN analysis, we observed significant decreases of connectivity in the right inferior frontal gyrus in PDD as compared to PD and HC. Using the caudate nucleus as a seed for the ESV-RSN analysis, we found significant decreases of connectivity in the left and right inferior occipital gyrus in PDD as compared to HC. **Conclusion**: Differences in functional connectivity patterns between PDD and PD/HC were observed in areas known to be engaged in stimulus-driven reorienting of attention and in visual processing.

PLOS one

Aneuploidy Detection in Pigs Using Comparative Genomic Hybridization: From the Oocytes to Blastocysts

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CEITEC Research Group: **Animal Cytogenomics**
Research Programme 7: **Molecular Veterinary Medicine**

Summary

Data on the frequency of aneuploidy in farm animals are lacking and there is the need for a reliable technique which is capable of detecting all chromosomes simultaneously in a single cell. With the employment of comparative genomic hybridization coupled with the whole genome amplification technique, this study brings new information regarding the aneuploidy of individual chromosomes in pigs. Focus is directed on in vivo porcine blastocysts and late morulas, 4.7% of which were found to carry chromosomal abnormality. Further, ploidy abnormalities were examined using FISH in a sample of porcine embryos. True polyploidy was relatively rare (1.6%), whilst mixoploidy was presented in 46.8% of embryos, however it was restricted to only a small number of cells per embryo. The combined data indicates that aneuploidy is not a prevalent cause of embryo mortality in pigs.

Journal of Antimicrobial Chemotherapy

Escherichia coli with extended-spectrum beta-lactamase and plasmid-mediated quinolone resistance genes in great cormorants and mallards in Central Europe

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CEITEC Research Group: **Molecular Bacteriology**
Research Programme 7: **Molecular Veterinary Medicine**

Summary

The emergence of multidrug-resistant bacteria in the natural environment constitutes a serious risk to domestic animal and human health. It can be presumed that resistant bacteria colonizing wild cormorants and mallards originated in aquatic environment. Faecal *Escherichia coli* strains were isolated from great cormorants and mallards, which are commonly occurring waterbirds in Europe, and studied for resistance to cephalosporins and fluoroquinolones. Ten ESBL (extended spectrum beta-lactamase)-producing E. coli with the *bla*$_{CTX-M-15}$ or *bla*$_{CTX-M-27}$ gene were isolated from eight great cormorants (1.6%, n=499). The blaCTX-M genes were harboured by plasmids of F and I1 incompatibility groups. CTX-M-27-producing isolates were identified as the epidemiologically important B2-O25b-ST131 clone which has high virulence potential all over the world and represents a great public health problem. This is the first detection of a CTX-M-27 ESBL type in an O25b-ST131 isolate in Europe. Eight *E. coli* isolates with plasmid-mediated quinolone resistance (PMQR) genes [six *aac(6')-Ib-cr*, and two *qnrS1*] were detected in six great cormorants (1.2%). Seventeen strains with qnrS1 were detected in 17 mallards (6%, n=305). The PMQR genes were located on plasmids of incompatibility groups F, N or X2. ESBL and PMQR genes were found on conjugative plasmids, enabling the horizontal spread of resistance. Both great cormorants and mallards can spread epidemiologically important antimicrobial resistant E. coli isolates to water bodies throughout Europe.