CEITEC news

EXTERNAL NEWSLETTER No. 4/2012

External electronic Newsletter, December 2012

Dear CEITEC friends,

This is an exciting time for science. The CEITEC building sites are now going full steam ahead, and laboratories are filling up with new state-of-the-art equipment. We have had a number of the CEITEC investigators winning prizes for their scientific work. Additionally, we have many new international scientists joining CEITEC. As suggested by our International Scientific Advisory Board, we are starting to plan experiments that cross disciplines which will help stimulate new ways of approaching important scientific questions. Through all of these activities, CEITEC will continue to play a more important role not just for our scientific community, but for the region as a whole. Recently, CEITEC was represented in the Brno Days in New York which featured the many great aspects of living and working in Brno. An important theme coming out from this event was that the future of the city and region will be underscored by an economy based on knowledge. CEITEC will be positioned to play a pivotal role in realizing these goals.

For 2013, we look forward to another great year of growth, but more importantly that great scientific discoveries continue to be made. For the future, CEITEC will continue to foster an environment where creative ideas and corresponding results are supported and valued.

Best wishes for the close of 2012, and the coming New Year.

Markus Dettenhofer, Executive Director

Markus Dettenhofer studied microbiology and immunology at the renowned University of California at Berkley and gained his PhD in molecular microbiology and immunology at Johns Hopkins University. He undertook post-doctoral studies in genetics at Harvard Medical School. Before joining CEITEC he led research projects in the company Crucell (Johnson & Johnson) focussing for example on the search for viral vaccines and antibodies. He has worked in both the academic environment and in the biotechnology industry, gaining significant experience in running international scientific projects, as well as the transfer of technologies and marketing. He is also the author of a range of peer-reviewed publications.

More information can be found **HERE**.

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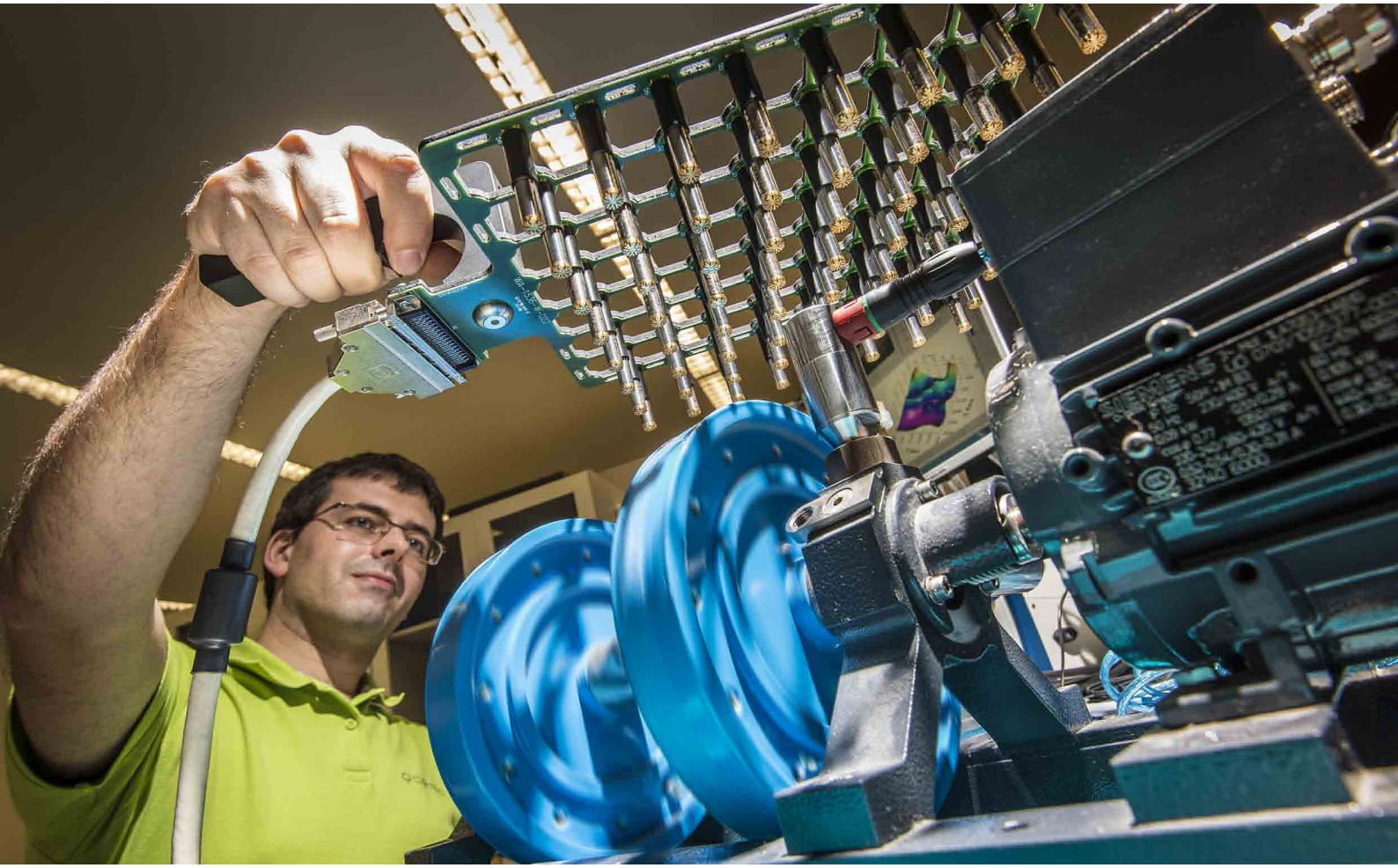


Scientists from CEITEC BUT granted patents for a unique holographic microscope

The Experimental Biophotonics group, led by Prof. Radim Chmelík, have been awarded European and Czech patents for a multimodal holographic microscope, which allows the observation of living cells under normal light. Patents are also pending in the US, China and Japan.

What's unique about this holographic microscope is that it allows a contrasted display of living cells, which are not normally easy to see in ordinary microscopes in their natural environment without the application of contrast materials.

The original scientific group from the Faculty of Mechanical Engineering at BUT got together with biologists from the Institute of Molecular Genetics at the Czech Academy of Science thanks to the CEITEC project. They then attempted to develop a microscope that was adapted to the needs of biological and medical research. The awarding of Czech and International patents is one of many great results of this cooperation between the scientific teams in Experimental Biophotonics from the Advanced Nanotechnology and Microtechnology research programme at CEITEC BUT. •●

Prof. Radimír Vrba receives award from the City of Brno

CEITEC's Scientific Director for Material Sciences Prof. Radimír Vrba received the 2012 award for activities in the field of technological development.

The City of Brno has gave Prof. Vrba the award for a significant contribution to a project which brings Brno new jobs, supports cooperation with industrial businesses in Brno and the region, contributes to technological development and enriches the international standing of the city. Radimír Vrba has participated in the CEITEC project since 2009.

As an academic, Prof. Vrba works in the field of applied electronics and sensors and as a principal investigator has received dozens of domestic and international research grants, the results of which have found real world industrial applications. Prof. Vrba will receive the award from the Mayor of Brno on the 22 January 2013 at a special ceremony in the council chambers of the town hall in Brno. •●

Prof. Josef Jančář given award for exceptional research results

On 29 November 2012, the Awards of the Minister of Education, Youth and Sports were awarded in Prague for exceptional results of research, development and innovation. One of the laureates was a CEITEC scientist, Prof. Josef Jančář. He received the award for the exceptional results of his research in the field of the physics of heterogeneous polymer systems, in particular for his inventions of a unique procedure of preparation of completely new heterogeneous polymer materials and polymer nanostructures, which led to the preparation of applications in lightweight extremely resistant materials that can be used in a wide range of areas, such as the tissue engineering of bones and cartilage or in the automobile industry.

More information in Czech can be found **HERE**. •●

Lukáš Trantírek receives a prestigious EMBO Installation Grant 2012

CEITEC MU scientist Lukáš Trantírek has received an EMBO Installation Grant and he is the only Czech scientist who received this grant in 2012. EMBO – the European Molecular Biology Organisation, awards these grants once a year to ten young scientists from the Czech Republic, Estonia, Poland, Portugal and Turkey. The EMBO Installation Grant allows talented researchers to relocate and set up their own research group in their country of origin.

The awarded scientists receive an amount of EUR 50,000 per year for three to five years from their host states. This makes it easier for them to establish their research groups and themselves in the scientific community. The ten grantees will also enter the prestigious network of EMBO Young Investigators, which helps them to integrate themselves and their laboratories into the European scientific community. 58 researchers have been funded by EMBO Installation Grants since the inception of the programme in 2006.

More information can be found **HERE**.

Huygens Image Contest 2012

Students from the Genetics and Reproduction Department, Martin Šodek and Thuraya Awadová from the Martin Anger laboratory (CEITEC VRI) participated in the competition Huygens Image Contest 2012 organized by the company SVI.

In this competition they were awarded first prize for a confocal microscopic image deconvolved and visualised by Huygens software used for 3D deconvolution and analysis.

The image represents a mouse oocyte arrested by a mitotic inhibitor (Taxol). Chromosomes (blue) are visualised by DAPI, kinetochores (red) by CREST antiserum, and spindle (green) by an antibody recognizing alpha tubulin. The confocal image (NA 1.3, 40x) was deconvolved and visualized with Huygens Essential.

More information can be found **HERE**.

Czech membership of EMBL approved

The European Molecular Biology Laboratory (EMBL), with its head office in Heidelberg, Germany, is one of the top research institutions in the life sciences. The great news for the Czech life sciences community is that after long years of discussions, Czech membership of EMBL was approved by the government on 5 December 2012. There is still rather a long process of formal accession ahead, but it is expected that by 2014 the Czech Republic will be a full member of EMBL. It will open up many opportunities for the Czech life sciences research community in staff exchanges, the possibility of PhD studentships, the use of EMBL core facilities and much more.

CEITEC and EMBL have established a close strategic partnership, which resulted in March 2012 in the signing of a Memorandum of Understanding between the two institutions. Preparations for a second CEITEC – EMBL research cooperation workshop as well a road show on the opportunities offered by EMBL to the Czech research community are underway.

CEITEC is part of ELIXIR

New technologies such as next-generation sequencing mean that data about DNA, proteins and other molecules' structure (i.e. bioinformatics data) is doubling every few months. The data are very useful and valuable, but such a volume of information cannot be handled by one institute or one country. For this reason, the European Strategy Forum on Research and Innovation (ESFRI) initiated the establishment of the pan-European bioinformatics infrastructure ELIXIR.

So far, ELIXIR's leadership body has been set up and 13 countries have joined ELIXIR. The Czech Republic has also joined ELIXIR – on 3 September 2012. As a next step, ELIXIR has announced a call for proposals of its national parts (so-called national nodes). The formation of the national ELIXIR nodes is a very important and strategic task for the bioinformatics community of each country. In Czech Republic, CEITEC together with UOCHB (a Czech ELIXIR coordinator) and five other Czech life science and IT organizations have accepted this challenge. Together they have established a Czech ELIXIR node as distributed infrastructure, focused on the handling of Czech bioinformatic data and software tools. CEITEC, together with cooperating institutions, completed the Czech ELIXIR node proposal on 15 October and submitted it to the European ELIXIR board.

More information about ELIXIR can be found **HERE**.

CEITEC mission to Canada

The representatives of CEITEC have successfully completed their negotiations concerning the cooperation with a number of research and government institutions in Ottawa, Toronto and Montreal, which were organized under the auspices of the Canadian Embassy in Prague and the Czech Embassy in Ottawa. The aim of the mission was to establish cooperation in the fields of neurosciences and cancer research.

Milan Brázdil from the research programme Brain and Mind Research succeeded in establishing cooperation with Tomáš Paus from the Rotman Centre on the preparation of intergenerational research project of health prevention in the new field of population neuroscience. There are also other possibilities of cooperation on offer with the experts from the Tanz Centre for neurodegenerative diseases in the fields of research of Parkinson´s and Alzheimer´s diseases.

Also the Coordinator of the research programme Molecular Medicine Šárka Pospíšilová and Michael Doubek regard the visit of the top Canadian workplaces as successful. A discussion with Pavel Hamet, Professor of Medicine at the University of Montreal, has resulted in finding topics for joint projects which can save expenses on treatment of chronic diseases, mainly cancer and heart and circulatory diseases.

More information can be found **HERE**.

Anniversary Mendel Lectures

World famous scientists from the field of genetics and cell and molecular biology came to Brno to give their lectures at the Anniversary Mendel Lectures to celebrate this year's 190th anniversary of birth of the founder of genetics, Gregor Johann Mendel. The lectures were given in the premises of the Mendel Museum, which also participated in the organisation, together with CEITEC.

Both students and the expert public could look forward to lectures from laureates of many prestigious awards, Gary Ruvkun and Günter Blobel (Nobel Prize in 1999), as well from the renowned Czech scientists Josef Jiřičný and Jiří Lukáš. The lecture cycle was closed by the CEITEC scientist Jiří Friml, one of the most successful of today's young Czech scientists.

More information can be found **HERE**.

Nobel Prize laureate Günter Blobel

Researchers' Night

CEITEC actively participated in another year of Researchers' Night, an event with the goal making science and research, both in the Czech Republic and throughout the European Union, popular in an attractive manner, to allow the general public access to the world of knowledge and present the scientists as rounded people with many different hobbies and activities. The employees and students of CEITEC also prepared a programme full of experience and education for all ages.

The scientists of CEITEC MU presented to the visitors the attractive issue of the development and functioning of painkillers. Visitors could also attend a lecture at the Brno Observatory entitled "How painkillers work". A truly practical part took place in the mathematics pavilion of the Faculty of Natural Sciences of MU, at the stand "Painkillers under the magnifying glass". Visitors could try, for example, visualisation of medications, proteins and their joint interaction, production of their own medication and computer simulation, as well as modelling medication molecules.

CEITEC BUT opened the doors of the laboratories of the research group Submicron Systems and Nanodevices, headed by Jaromír Hubálek. There was a programme for children and excursions to the research laboratories where visitors could become acquainted, for example, with the fundamental methods used in criminology, such as dactyloscopy, use of the microscope or revealing blood traces. Visitors also got an explanation of the basic principles of molecular-biological, physico-chemical and bioanalytical techniques.

More information can be found **HERE**.

Week of Science and Technology

Once again, CEITEC presented itself this year at the 12th year of the Week of Science and Technology, the most extensive and largest festival of science in the Czech Republic. The programme of the Week of Science and Technology this year offered more than 400 events, from lectures, through exhibitions and excursions, to the showing of documentaries, and representatives of CEITEC were present both in Brno and in Prague.

In Prague, Dr. Radka Svobodová Vařeková of CEITEC MU, presented life science in CEITEC; her lecture was entitled "From atoms to healthcare treatment, from viruses and bacteria to humans". Another extraordinarily successful lecture was that of Petr Dvořák of CEITEC BUT, entitled "The use of nanotechnologies in practice". He presented the field of nanotechnologies and plasmonics and the audience was captured to such an extent that they spent another hour after the lecture asking supplementary questions.

In Brno, CEITEC participated on the occasion of the Open Day of the Institute of Physics of Materials of the ASCR. The visitors could see the laboratories with the latest state-of-the-art equipment and each laboratory presented their devices together with typical outputs or the characteristics and scientific results obtained with their assistance.

More information can be found **HERE**.

Industry Meets Academia

At the end of November, an important conference took place under the name "Industry Meets Academia", prepared by the Association of Innovative Pharmaceutical Industry in co-operation with the Senate of the Parliament of the Czech Republic and the Association of Biotechnological Companies in the Czech Republic, CzechBio. The assembly hall of the Senate hosted representatives of Association of Innovative Pharmaceutical Industry member companies from the Czech Republic and other EU countries, smaller and medium-sized companies operating in the field of the manufacture and development of pharmaceuticals or their components, foreign experts and representatives of Czech scientific centres. Representatives of CEITEC were also present.

Norman Eisen, Ambassador of the United States to the Czech Republic

The main outcome of the conference was support for co-operation in the field of the research and development of new efficient pharmaceuticals between their manufacturers, academic research centres and small and medium-sized companies. The conference also provided a chance to establish of contacts between experts from the academic and the private sectors and the determination of conditions for the establishment and development of professional partnerships in the field of innovative treatment. The conference also emphasised the contributions and particular outcomes of the co-operation across the industry in the research and development of new innovative pharmaceuticals, including (but not limited to) those used in the treatment of oncological, cardiovascular, neurological or dermatological diseases, as well as a number of other, still incurable, diseases.

More information in Czech can be found **HERE**.

Brno New York Days

CEITEC took part in New York Brno Days on 1-2 October 2012. The event introduced the exceptional cultural and architectural genius loci of Brno and also its business, research and development potential. Day 1 was dedicated to the famous UNESCO-listed unique functionalist monument – the Villa Tugendhat, Day 2 introduced the business, research and development potential of the city with a conference "Brno – Knowledge Economy City". CEITEC was represented there by Executive Director Markus Dettenhofer. The aim of the event was to strengthen existing ties with American business partners in New York and to establish new contacts with potential new investors.

More information can be found **HERE**.

Czech Days for European Research

The preparation for the next EU framework programme for research, development and innovation that will run under the name Horizon 2020 (H2020) in the years 2014 – 2020 was discussed at the conference entitled "The 10th Czech Days for European Research". The draft programme H2020, prepared by the European Commission, assumes a budget of EUR 80 billion. The programme H2020 will be based on three pillars: scientific excellence, the leading role of industry and major social challenges. The budget allocated to scientific excellence will be managed, as now, by the European Research Council (ERC), which allocates grants not only to European researchers, but also to significant world investigators who want to work on their research projects at sites within the EU.

A part of the conference was a colloquium focused on the issues of research infrastructure, attended by the representatives of the European Molecular Biology Laboratory, CERN, and the Elettra and Soleil synchrotrons. The participants were informed of the current state of infrastructure development and top managers of infrastructure already operating in the "old" EU member states shared their experience with the management of these facilities. As a part of the programme, projects being developed in the Czech Republic were introduced, such as the laser ELI or the supercomputer IT4Innovations. CEITEC was represented for this purpose by Martin Bareš and Ondřej Hradil.

More information in Czech can be found **HERE**.

CEITEC Conference about Technologies

At the beginning of December, all CEITEC BUT research groups got together at a Technology Conference held at CEITEC to present the progress of their research activities. All day, 22 speakers from 16 research groups presented the results of their work in the CEITEC project to their colleagues and to the academic community. The event opened with an introductory word from Markus Dettenhofer, the new executive director of CEITEC. During the conference, a poster session was held in the foyer of hall Q at the Faculty of Mechanical Engineering, providing basic information about each research group.

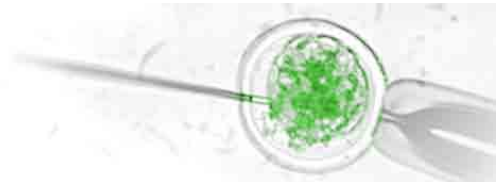
More information can be found **HERE**.

Interview with CEITEC scientist

MVDr. Boris Tichý

CEITEC Masaryk University

Head of the Core Facility - Genomics
Research Programme – Molecular Medicine



Scientists from the CEITEC Molecular Medicine research programme under the leadership of MVDr. Boris Tichý have invented a new method that will help reveal relapses of malignant lymphatic tissue tumours at an early stage. With this method, they can even detect relapsing cancer several months before it would be detected by current methods. Thus, the researchers have doubled the number of patients with this disease who can be examined. Doctors at the Internal Clinic of Haematology and Oncology of the Faculty of Medicine of Masaryk University and the Faculty Hospital of Brno have been using this method in practice for a year and a half now. The research team has had this method patented.

Your team's invention is helping in the treatment of lymphatic tissue cancer. For which patients can it be used?

This method can only be used for patients whose tumour has already been diagnosed and who have undergone treatment. The disease can return however, and we are capable, thanks to the high sensitivity of this method, of detecting a relapse at an earlier stage, accelerating subsequent treatment. Our method is an extension of an older procedure and it is not purely diagnostic, which means that it does not serve for revealing the tumour as such, but only for its monitoring. It applies to patients suffering from a specific type of lymphatic tumour, so-called mantle zone lymphoma, which is one of the subcategories of non-Hodgkin lymphomas. This type has a less successful prognosis, which is why it is especially important to monitor the course of the disease. In summary, the basis of our method is monitoring the residual population of tumour cells after treatment.

How long has this research project been used in practice? And what does the patient examination look like?

We have been using this method at the Centre of Molecular Biology and Gene Therapy of the Internal Clinic of Haematology and Oncology of the Faculty of Medicine of Masaryk University and the Faculty Hospital Brno for a year and a half now. Based on our results, the doctors choose a treatment for their patients. We have ten to twelve new patients each year, and we are still monitoring some thirty-five existing patients. We examine the patient and determine whether we can find and characterise the necessary genetic marker in him/her. Then, we take blood samples every three months and monitor whether tumour cells are still present and if so in what numbers. It is a minimally invasive method for the patient; it only takes a blood sample because in this type of lymphoma the tumour cells often circulate directly in the blood.

> *WE CAN DETECT THE DISEASE'S RELAPSE AT AN EARLIER STAGE, WHICH GIVES US AN OPPORTUNITY TO START TREATMENT MORE EFFICIENTLY AND WITH FEWER ADVERSE EFFECTS.*

How specifically can this research help patients suffering from lymphatic cancer?

The main thing is that we can detect the disease's relapse at an early stage, which gives us an opportunity to start treatment more efficiently and with fewer adverse effects. When the patient starts treatment earlier we can apply a more gentle form of treatment. Typically, doctors apply immuno-chemotherapy, but with the use of our method, they only use immunotherapy, which is much kinder to the human body. In most cases, there are several relapse and immunotherapy cycles, but it is highly individual – for some immunotherapy can be repeated, while for others it can't. We also use chemo-immunotherapy, which is a combination of chemotherapy and therapy using targeted antidotes aimed at lymphocytes, which is quite gentle compared to classical chemotherapy, because it is more targeted. Unfortunately, there are also certain adverse effects, but since the antibodies can be targeted to a certain type of cell, not all the cells in the body are affected as is commonly the case with classical chemotherapy. Our method is also used for monitoring patients after undergoing a transplant. entific work abroad.

What is the principle of your method? How can you detect a tumour of lymphatic tissue that is still invisible?

Each tumour is specific, as it affects a different tissue, and each tumour proliferation is preceded by a certain change in the human genome, the genetic information, that results in the loss of the body's ability to control the cells. Our method is based on the attempt to detect one of these changes and characterize it, as precisely as possible, at the level of DNA. We try to isolate DNA from blood samples, trying to find out whether there is a changed piece of DNA indicating the continuing presence of tumour cells in the blood. In this type of lymphatic cancer, the DNA change can be very well characterized and this change occurs in more than 95% of these tumours. We are capable of identifying one diseased cell among a hundred thousand healthy ones, which is a very good sensitivity. Thus, our method is quite fast and highly specific. Not only is the marker very specific for this type of tumour, since it can be found in no other cells, but it is also very detailed, because it is essentially different for each individual patient. This allows us to detect tumour cells very precisely.

How have you developed this method? Were you intending to find something that would identify this particular disease?

The marker we detect has been known for some time, but we have developed a method that enables detection of the sought after marker in a much greater number of patients, so that we have practically doubled the number of patients who can be examined. Since current diagnostic methods are quite problematic, we wanted to extend the use of chromosomal translocation as a marker. So we prepared a slightly different method of finding the translocation, capable of covering quite a significant part of the DNA on chromosome 11, thus increasing the possibility of examination of an additional 35% of patients. When we put together this new method with the older one, we can examine up to 80% of patients for whom we can use the sequence of translocation fracture point 11;14 as the marker. The remaining part of the examinations are covered by a more complex method of sequencing clonal immunoglobulin (antibody), which means that we are now capable of monitoring more than 90% of patients suffering from this disease.

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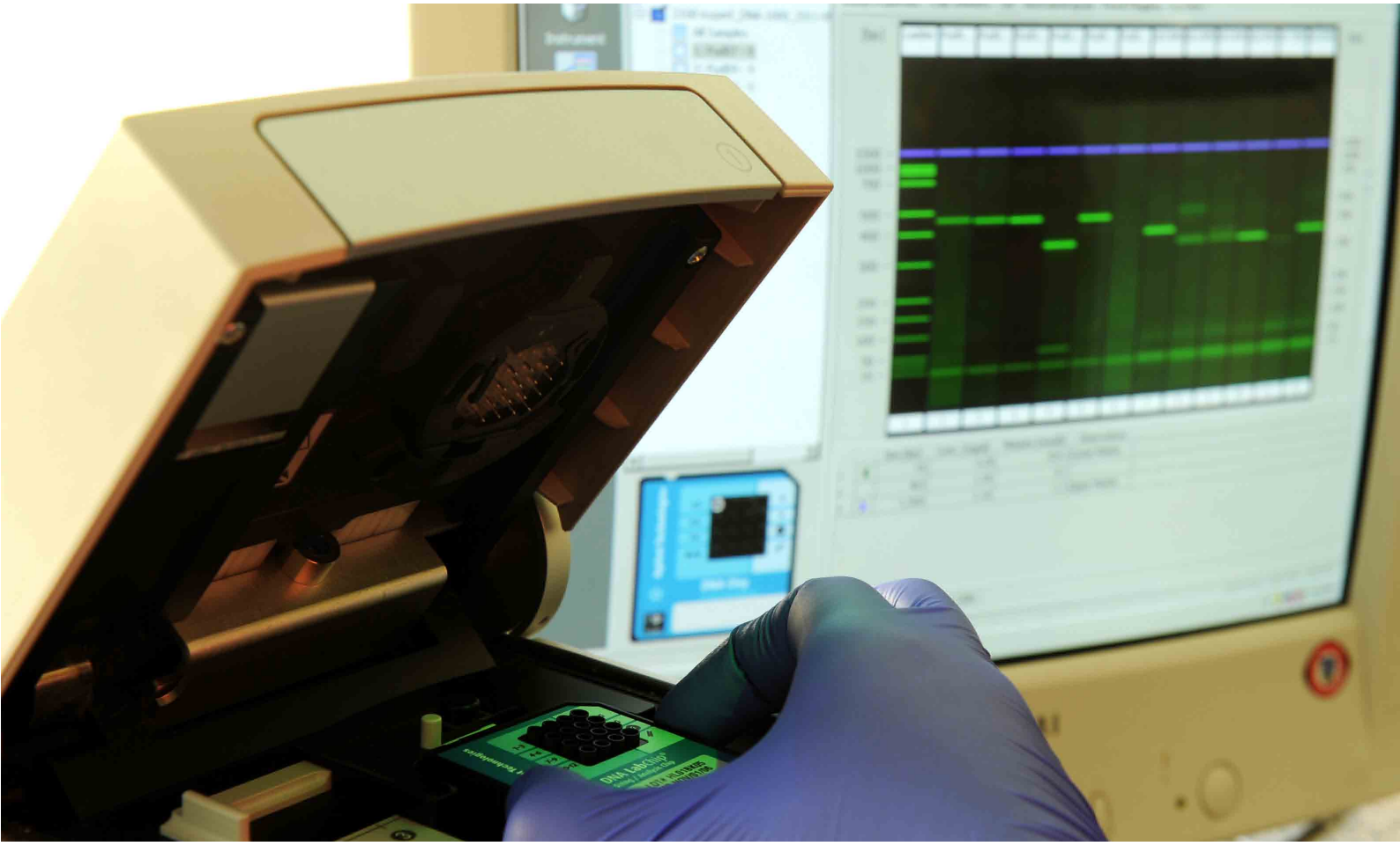
You have had this method patented in the Czech Republic. Have you been contacted by any of your colleagues interested in co-operation?

Yes, some laboratories are interested; we expect to receive response from other countries in time as well. The advantage is that our method is not extremely expensive, it is comparable with other techniques for determining residual tumours in tumour diseases, and it is definitely less expensive than therapy. We have not yet published the method, but we are preparing an article since we already have quite an extensive amount of the necessary data.

The scope of your research is much wider, however. What else have you been working on?

At the Centre of Molecular Biology and Gene Therapy of the Department of Internal Medicine – Haematology and Oncology of the Faculty of Medicine of Masaryk University and the University Hospital Brno, we focus on oncology, and in particular blood cell diseases. Primarily, we focus on diagnostics and research into the widest possible range of neoplastic diseases of lymphoid and myeloid cells. I personally specialise in tumour diseases of lymphocytes, which are special leukocytes responsible for the specific defensive power of the body against viruses and bacteria and which are often prone to tumour proliferation.



You were also the head of the team that has recently obtained the renowned Discovery Award for progress achieved in the diagnostics of chronic lymphocytic leukaemia.

Yes, this award is the result of the extensive work of the large team of the Centre of Molecular Biology and Gene Therapy of the Department of Internal Medicine – Haematology and Oncology of the Faculty of Medicine of Masaryk University and the University Hospital Brno and of the CEITEC Centre of Molecular Medicine. This team has been working on the investigation of genetic changes in tumour cells in patients suffering from chronic lymphocytic leukaemia for ten years now. Chronic lymphocytic leukaemia, i.e. a tumour disease of the lymphocytes, where the primary affected sites are lymph nodes and bone marrow, is the most frequent type of leukaemia in the adult western population. Again, we are not focusing directly on primary diagnostics, but primarily on being able to estimate the future course of the disease and to determine whether it is less or more aggressive. We are trying to estimate the prognosis of the disease as early as possible, ideally already during the course of the first diagnosis, and to determine whether the patient will need therapy.

This team has managed to get implemented an important recommendation for a new procedure of determining the prognosis of chronic lymphocytic leukaemia. What precisely is the basis of this discovery?

My colleagues have been investigating the mutation of tumour suppressor TP53 that encodes the protein protecting cells against their possible transformation into tumour cells. And they have managed to confirm that the changes in this particular gene are of tremendous importance. For example, changes in this gene can occur also in the period after diagnosis, after two or three or more years. And this finding can direct the doctors to assess the possibility of therapy for their patients and to determine which of the therapeutic methods will be most suitable.

> *RENOWNED DISCOVERY AWARD FOR PROGRESS ACHIEVED IN THE DIAGNOSTICS OF CHRONIC LYMPHOCYTIC LEUKAEMIA*

Let's get back to you for a while. Originally, you graduated from the University of Veterinary and Pharmaceutical Sciences in Brno. Why and when did you decide to change the specialisation of your research?

During my studies, I found out that I am more interested in laboratory work and research than clinical work. After I graduated, I wanted to continue my scientific career and I felt close to the fields of molecular biology or immunology and oncology. So in the end, I chose a doctoral programme in oncology at Masaryk University.

What attracted you to research?

The vision of a Nobel Prize (laughs). But I have changed my mind after a realistic re-assessment. I enjoyed playing, inventing and modifying new methods and after some time, I started spending more time on methodology research which was much more appealing to me than basic research. For example, with chronic lymphocytic leukaemia, I wasn't so interested in why the translocation occurs, but in how to detect it. My work in CEITEC is also more focused on methodology application, rather than pure biological research.

Within CEITEC, you work as the head of the research group "Core Facility – Genomics". Who do you co-operate with most?

Naturally, we most frequently co-operate with the groups of the Molecular Medicine programme, but we are also planning close co-operation with the groups of the Molecular Veterinary Medicine programme and the Genomics and Proteomics of Plant Systems programme. Our primary goal is the shared use of the devices, equipment and procedures, in particular with programmes focused on genomics, and also in general in all fields focusing on DNA analysis.

What is the idea of the shared laboratories or "Core Facilities"?

The idea of Core Facilities is to avoid duplication of resources, i.e. to ensure 100% utilisation of equipment and devices that are very costly and specialised, by enabling several groups and individuals to use them. The CEITEC project has envisioned this form of co-operation since the very start, which is why the acquisition of individual devices was planned in advance, jointly, by several groups. Core Facilities will enable multiple groups and individuals to access the devices and know-how in order to share, to the maximum extent possible, the results of our research, so that the methods and measurements that have already been performed by someone can be shared by the others without having to be repeated. For example, in the research into chronic lymphocytic leukaemia, we've had an opportunity to test a sequencing device and the same methodology could also be used by our colleagues from a different research team.

Will these Core Facilities also be open to your colleagues from other institutions and to commercial entities?

Yes, one of the main contributions of CEITEC is the possibility to rent out equipment that is quite costly and in some cases absolutely unique within the Czech Republic to other researchers and private companies, both from the Czech Republic and other countries. In the autumn we acquired the first devices, so we will be able to start offering to rent them out in the near future. Our short-term plans include, for example, co-operation with industry in the field of commercial diagnostics. The devices in our Core Facility will be used by laboratories in co-operation with a foreign company that is developing new diagnostic sets allowing for the technical processing of specialised examinations. I believe that this form of co-operation will also be interesting for other private laboratories in the Czech Republic.

Selected CEITEC Publications

International Journal of Electrochemical Science

Electrochemical behaviour of apoferritin encapsulating of silver(I) ions and its application for treatment of *Staphylococcus aureus*

Dospivová, D.; Hynek, D.; Kopel, P.; Bezděková, A.; Sochor, J.; Křížková, S.; Adam, V.; Trnková, L.; Hubálek, J.; Babula, P.; Provazník, I.; Vrba, R.; Kizek, R.

CEITEC Research Group: Submicron Systems and Nanodevices
Research Programme 1: Advanced Nanotechnologies and Microtechnologies

Summary

Methicillin-resistant *Staphylococcus aureus* (MRSA) is responsible for several difficult-to-treat infections in humans. Therefore, it is not surprising that other ways how to treat these bacteria are looked for. Silver(I) ions and silver nanoparticles exhibited the highest antimicrobial activity against MRSA but their transporting to the place of needs and in situ determination is an issue. The aim of this work was electrochemical determination of silver(I) ions using four types of modified carbon paste electrodes (CPEs) with different content of carbon nanoparticles. CPE made from expanded carbon was the most sensitive one. Therefore, we optimized the experimental conditions as time of accumulation 60 s, deposition potential 0.5 V and 0.2 M acetate buffer, pH = 5.0 to obtain detection limit (3 S/N) of 5 nM for silver(I) ions. Further, we studied the encapsulation of silver(I) ions into apoferritin as a possible way for transportation of these ions. Primarily we optimized the encapsulation conditions to prepare the most stable complex, which was subsequently utilized for treatment of S. aureus. Based on the results obtained it can be concluded that silver(I) ions remain enclosed in the apoferritin structure until decomposition of apoferritin by bacterial enzymatic apparatus occurs.

Spectrochimica Acta Part B

Application of laser-induced breakdown spectroscopy to the analysis of algal biomass for industrial biotechnology

Pořízka, P.; Prochazka, D.; Pilát, Z.; Krajcarová, L.; Kaiser, J.; Malina, R.; Novotný, J.; Zemánek, P.; Ježek, J.; Šerý, M.; Bernatová, S.; Krzyžánek, V.; Dobranská, K.; Novotný, K.; Trtílek, M.; Samek, O.

CEITEC Research Group: X-ray Micro CT and Nano CT
Research Programme 1: Advanced Nanotechnologies and Microtechnologies

Summary

We report on the application of laser-induced breakdown spectroscopy (LIBS) to the determination of elements distinctive in terms of their biological significance (such as potassium, magnesium, calcium, and sodium) and to the monitoring of accumulation of potentially toxic heavy metal ions in living microorganisms (algae), in order to trace e.g. the influence of environmental exposure and other cultivation and biological factors having an impact on them. Algae cells were suspended in liquid media or presented in a form of adherent cell mass on a surface (biofilm) and, consequently, characterized using their spectra. In our feasibility study we used three different experimental arrangements employing double-pulse LIBS technique in order to improve on analytical selectivity and sensitivity for potential industrial biotechnology applications, e.g. for monitoring of mass production of commercial biofuels, utilization in the food industry and control of the removal of heavy metal ions from industrial waste waters.

Journal of the American Ceramic Society

Optimization of Fine Alumina Gelcasting Using In Situ Dynamic Rheology

Bera, O.; Trunec, M.

CEITEC Research Group: Advanced Ceramics Materials
Research Programme 2: Advanced Materials

Summary

In situ dynamic rheology was used to investigate the polymerization process of gelcasting suspensions based on fine alumina and water solution of methacrylamide and methylene bisacrylamide monomers. Small-strain oscillatory shear measurements were able to detect the progress of the whole gelation process from the liquid suspension to the elastic gel. The parameters describing the gelation kinetics and final gel properties such as idle time, total gelation time, and equilibrium complex viskosity were correlated with the initiator/accelerator concentration, linear to cross-linking monomer ratio, polymerization temperature, and alumina loading. A strong catalytic effect of fine alumina particles on the decomposition of ammonium persulfáte into free radicals was established. The catalytic activity of alumina powder was controlled by ions adsorbed on the partije surface. The catalytic effect of alumina in the presence of the Dolapix CE 64 dispersant made the polymerization process independent of the accelerator concentration and enabled the gelation of concentrated ceramic suspensions at and below room temperature without any accelerator. The variations of the polymerization process in the range of investigated gel compositions did not affect the particle packing in green bodls and the densities of sintered ceramic bodies were similar.

Journal of Physics: Condensed Matter

Dynamic stability of fcc crystals under isotropic loading from first principles

Řehák, P.; Černý, M.; Pokluda, J.

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

Summary

Lattice dynamics and stability of four fcc crystals (Al, Ir, Pt and Au) under isotropic (hydrostatic) tensile loading are studied from first principles using the linear response method and the harmonic approximation. The results reveal that, contrary to former expectations, strengths of all the studied crystals are limited by instabilities related to soft phonons with finite or vanishing wavevectors. The critical strains associated with such instabilities are remarkably lower than those related to the volumetric instability. On the other hand, the corresponding reduction of the tensile strength is by 20% at the most. An analysis of elastic stability conditions is also performed and the results obtained by means of both approaches are compared.

Nucleic Acids Research

Polymorphism of human telomeric quadruplex structure controlled by DNA concentration: A Raman study

Palacky, J.; Vorlickova, M.; Kejnovska, I.; Mojzes, P.
CEITEC Research Group: Spectroscopy of Nucleic Acids and Proteins
Research Programme 3: Structural Biology

Summary

DNA concentration has been recently suggested to be the reason why different arrangements are revealed for K+-stabilized human telomere quadruplexes by experimental methods requiring DNA concentrations differing by orders of magnitude. As Raman spectroscopy can be applied to DNA samples ranging from those accessible by absorption and CD spectroscopies up to extremely concentrated solutions, gels and even crystals; it has been used here to clarify polymorphism of a core human telomeric sequence G3(TTAG3)3 in the presence of K+ and Na+ ions throughout wide range of DNA concentrations. We demonstrate that the K+-structure of G3(TTAG3)3 at low DNA concentration is close to the antiparallel fold of Na+-stabilized quadruplex. On the increase of G3(TTAG3)3 concentration, a gradual transition from antiparallel to intramolecular parallel arrangement was observed, but only for thermodynamically equilibrated K+-stabilized samples. The transition is synergically supported by increased K+ concentration. However, even for extremely high G3(TTAG3)3 and K+ concentrations, an intramolecular antiparallel quadruplex is spontaneously formed from desalted non-quadruplex single-strand after addition of K+ ions. Thermal destabilization or long dwell time are necessary to induce interquadruplex transition. On the contrary, Na+ stabilized G3(TTAG3)3 retains its antiparallel folding regardless of the extremely high DNA and/or Na+ concentrations, thermal destabilization or annealing.

PLoS Computational Biology

Charge Profile Analysis Reveals That Activation of Pro-apoptotic Regulators Bax and Bak Relies on Charge Transfer Mediated Allosteric Regulation

Ionescu, C.M.; Svobodova Varekova, R.; Prehn, J.H.M.; Huber, H.J.; Koca J.
CEITEC Research Group: **Computational Chemistry**
Research Programme 3: **Structural Biology**

Summary

Apoptosis is a physiological form of cell death that is fundamental for development, growth and homeostasis in multi-cellular organisms. Deviations in the apoptosis machinery are known to be involved in cancer, neurodegenerative disorders, and autoimmune diseases. The proteins Bax and
Bak are essential for executing apoptosis, yet the mechanism of their activation is not properly understood at the structural level. In order to understand this mechanism, we developed a straightforward and accessible methodology based on the estimation of atomic partial charges and subsequently inter- and intra-molecular charge transfer. This methodology allows to identify the key residues involved in the fast activation of proteins during signal transduction. We thus were able to identify the specific interactions responsible for the exposure of the functional sites of Bax upon binding of an activator peptide. These sites are present also in Bak, and represent potential drug targets.

Taxon

Whole-genome triplication and species radiation in the southern African tribe Heliophileae (Brassicaceae)

Mandáková, T.; Mummenhoff, K.; Al-Shehbaz, I.A.; Mucina, L.; Mühlhausen, A.; Lysak, M.A.
CEITEC Research Group: **Plant Cytogenomics**
Research Programme 4: **Genomics and Proteomics of Plant Systems**

Summary

The unigeneric tribe Heliophileae includes ca. 90 *Heliophila* species, all endemic to southern Africa. The tribe is morphologically the most diverse crucifer lineage in every aspect of habit, foliage, flower and fruit morphology. Despite this diversity, virtually nothing was known about its origin and genome evolution. Comparative chromosome painting analyses in several species with different chromosome number revealed that all *Heliophila* species, and probably the entire tribe Heliophileae, experienced an ancient whole-genome triplication (WGT) event. The WGT has been followed by chromosome rearrangements resulting in species-specific reduction of chromosome numbers towards extant quasi-diploid genomes (diploidization process). The WGT might have contributed to diversification and species radiation in Heliophileae. To our knowledge, this is the first study to document polyploidy as a potential major mechanism for the radiation of a Cape plant lineage.

Plant Cell

Spatiotemporal Regulation of Lateral Root Organogenesis in Arabidopsis by Cytokinin

Bielach, A.; Podlešáková, K.; Marhavý, P., Duclercq, J.; Cuesta, C.; Müller B.; Grunewald, W.; Tarkowski, P.; Benková, E.
CEITEC Research Group: **Hormonal Crosstalk in Plant Development**
Research Programme 4: **Genomics and Proteomics of Plant systems**

Summary

The architecture of a plant's root system, established postembryonically, results from both coordinated root growth and lateral root branching. The plant hormones auxin and cytokinin are central endogenous signaling molecules that regulate lateral root organogenesis positively and negatively, respectively. Tight control and mutual balance of their antagonistic activities are particularly important during the early phases of lateral root organogenesis to ensure continuous lateral root initiation (LRI) and proper development of lateral root primordia (LRP). Here, we show that the early phases of lateral root organogenesis, including priming and initiation, take place in root zones with a repressed cytokinin response. Accordingly, ectopic overproduction of cytokinin in the root basal meristem most efficiently inhibits LRI. Enhanced cytokinin responses in pericycle cells between existing LRP might restrict LRI near existing LRP and, when compromised, ectopic LRI occurs.

Experimental Hematology

Gene expression profiling of acute graft-vs-host disease after hematopoietic stem cell transplantation

Verner, J.; Kabathova, J.; Tomancova, A.; Pavlova, S.; Tichy, B.; Mraz, M.; Brychtova, Y.; Krejci, M.; Zdrahal, Z.; Trbusek, M.; Volejnikova, J.; Sedlacek, P.; Doubek, M.; Mayer, J., Pospisilova, S.

CEITEC Research Group: **Medical Genomics**
Research Programme 5: **Molecular Medicine**

Summary

Acute graft-vs-host disease (aGVHD) is a frequent, life-threating complication after allogeneic hematopoietic stem cell transplantation (allo-HSCT). Despite that, there are no reliable molecular markers reflecting the onset or clinical course of aGVHD. We performed a pilot study on gene expression profiling in peripheral blood mononuclear cells taken from 15 patients with haematological malignancies who underwent allo-HSCT and developed aGVHD. Based on survival rates after aGVHD, patients were divided into two groups – favourable (all patients alive; median follow-up 40 months) vs unfavourable group (all patients died; median survival 2 months). Two-hundred and eighty genes differentially expressed between these two groups were identified; among them, genes responsible for cytokine signalling, inflammatory response, and regulation of cell cycle were over-represented; *interleukin-8, G0S2, ANXA3*, and *NR4A2* were upregulated in the unfavourable group, CDKN1C was downregulated in the same group. Interestingly, the same genes were also described as overexpressed in connection with autoimmune diseases. This indicates an involvement of similar immune regulatory pathways also in aGVHD. Our data support use of gene expression profiling at aGVHD onset for a prediction of its outcomes.

Cell Division

Cyclin K goes with Cdk12 and Cdk13

Kohoutek, J.; Blazek, D.
CEITEC Research Group: Inherited Diseases II – Transcriptional Regulation
Research Programme 5: Molecular Medicine

Summary

The cyclin-dependent kinases (Cdks) regulate many cellular processes, including the cell cycle, neuronal development, transcription, and posttranscriptional processing. To perform their functions, Cdks bind to specific cyclin subunits to form a functional and active cyclin/Cdk complex. This review is focused on Cyclin K, which was originally considered an alternative subunit of Cdk9, and on its newly identified partners, Cdk12 and Cdk13. We briefly summarize research devoted to each of these proteins. We also discuss the proteins' functions in the regulation of gene expression via the phosphorylation of serine 2 in the C-terminal domain of RNA polymerase II, contributions to the maintenance of genome stability, and roles in the onset of human disease and embryo development.

The International Journal of Neuropsychopharmacology

The effects of methamphetamine self-administration on behavioural sensitization in the olfactory bulbectomy rat model of depression

Kucerova, J.; Pistovcakova, J.; Vrskova, D.; Dusek, L.; Sulcova, A.
CEITEC Research Group: Experimental and Applied Neuropsychopharmacology
Research Programme 6: Brain and Mind Research

Summary

In this study the effect of repeated administration of methamphetamine on i.v. drug self-administration in an olfactory bulbectomy model of depression in rats was investigated in order to propose and validate a rat model of comorbid depression and addiction.

Exp Brain Res - Experimental Brain Research

The role of the right dorsolateral prefrontal cortex in the Tower of London task performance: repetitive transcranial magnetic stimulation study in patients with Parkinson's disease.

Srovnalova, H., Marecek, R.; Kubikova, R.; Rektorova, I.
CEITEC Research Group: Applied Neuroscience
Research Programme 5: Brain and Mind Research

Summary

Using repetitive transcranial stimulation (rTMS), the authors demonstrated the causal role of the right dorsolateral prefrontal cortex in solving the Tower of London task, i.e. the cognitive task that evaluates spatial-planning, attention, and executive functions.

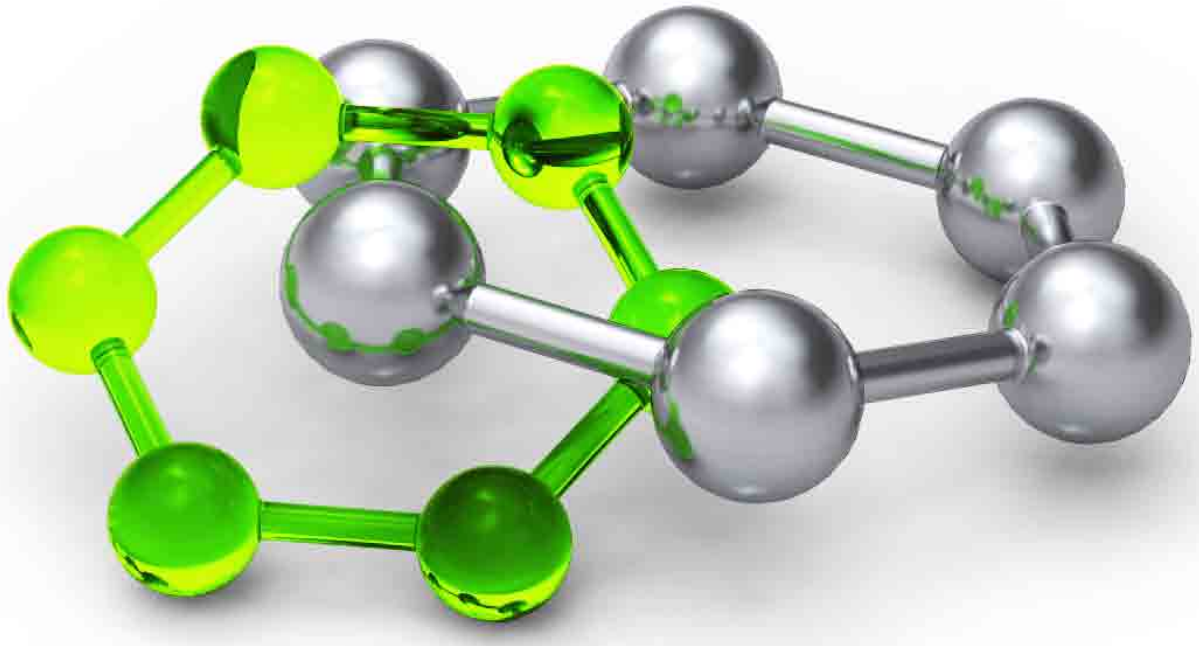
Antimicrobial Agents and Chemotherapy

Dogs of Nomadic Pastoralists in Northern Kenya Are Reservoirs of Plasmid-Mediated Cephalosporin- and Quinolone-Resistant *Escherichia coli*, Including Pandemic Clone B2-O25-ST131.

Albrechtova, K.; Dolejska, M.; Cizek, A.; Tausova, D.; Bebora, L.; Literak, I.
CEITEC Research Group: Molecular Bacteriology
Research Programme 6: Molecular Veterinary Medicine

Summary

Resistance in *Escherichia coli* isolates colonizing gastrointestinal tracts of dogs, cats, and their owners in Northern Kenya was investigated with an emphasis on extended-spectrum beta-lactamases (ESBLs). Totals of 47 (22%, *n* = 216), 2 (4%, *n* = 50), and 4 (17%, *n* = 23) CTX-M-15-producing *E. coli* isolates were obtained from dogs, cats, and humans, respectively. CTX-M-15-producing *E. coli* isolates with identical PFGE profiles were detected in animals and humans living in the same area.



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