

CeBiTec – Quarterly

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11th CeBiTec Symposium – Microbial Genomics and Metagenomics in Human Health and Disease

The CeBiTec organizes symposia which are held on an annual basis. These conferences cover a wide range of topics reflecting the various foci of the CeBiTec's research groups. The 11th CeBiTec Symposium entitled 'Microbial Genomics and Metagenomics in Human Health and Disease' was held at the Center for Interdisciplinary Research (ZiF) of Bielefeld University from July 4 to 6, 2016. The conference was aimed at highlighting the impact of the genomics revolution on medical microbiology. Members of the Medical Faculty of Münster University who contributed the medical expertise, co-organized the meeting. The format of the symposium included a satellite meeting organized by the office of the German Network for Bioinformatics Infrastructure (de.NBI) located at Bielefeld University. The de.NBI mini symposium focused on Bioinformatics for Metagenome Analysis. Some 90 participants attended the conference, most of them affiliated with German universities.

The conference was opened by Prof. Dr. Olaf Kruse, scientific director of the CeBiTec and Prof. Dr. Jörn Kalinowski, the chair of the organizing committee. The first session entitled 'Genomics of Major Bacterial Human Pathogens' addressed important aspects of the pathogenicity of human pathogens such as *Legionella pneumophila*, *Clostridium difficile* or *Escherichia coli*, respectively. The second session focused on 'Microbial Population Genetics and Genomics Nomenclature'. Talks in this session emphasized the importance of next-generation sequencing (NGS) technologies for the evaluation of the population structure of human pathogens, i.e. in the context of tracking pathogen outbreaks. The third session 'Host-Pathogen Interactions Assessed by Transcriptomics Approaches' focused on the analysis of host-pathogen interactions at the level of transcriptomics, i.e. the Dual RNA-seq method which analyses the transcriptomes of host and pathogen simultaneously. The first day of the Symposium concluded with a Distinguished Lecture presented by the President of the German Science Academy Leopoldina, Prof. Dr. Jörg Hacker. After the welcome and introduction by Prof. Dr. Martin Egelhaaf, Vice Rector of Bielefeld University, Prof. Hacker reported in his talk entitled



'Antibiotics and Antibiotic Resistances: Scientific and Social Implications' about current efforts to cope with the global threat posed by antibiotic resistant pathogens.

The second day of the Symposium started with two sessions focussing on the 'Epidemiology and Surveillance of Pathogenic Microorganisms'. NGS was considered as a ground-breaking technology in today's clinical microbiology due to its obvious advantages in epidemiological studies and the simultaneous detection of pathogenicity and antibiotic resistance traits. The session 'Novel Sequencing Technologies as a Tool in Human Medicine' presented the current status of sequencing technologies offered by Pacific Biosciences, Illumina Inc. as well as Oxford Nanopore. Although the various technologies are fundamentally different, they occupy specific niches when applied in a medical context. The last session of the day was reserved for young scientists whose talks were selected among poster presenters. A total of six talks addressed a wide range of topics such as the use of next generation sequencing for the typing of pathogens or the development of software for metagenomics analyses. The second day concluded with another Distinguished Lecture presented by Prof. Dr. Peer Bork of the EMBL Heidelberg. The talk entitled 'My Gut Microbes and Me: A long-Term yet Fragile Relationship' summarized the current understanding of the human microbiome. Due to the complexity of the habitat, research into the human microbiome is at an early stage. However, associations between several human diseases and the composition of microbial gut communities were reported.

Finally, the last day of the conference was reserved for the de.NBI mini symposium 'Bioinformatics for Metagenome Analysis'. The first session entitled 'Bioinformatics Tools for Analyzing Metagenome Sequences' addressed the challenges of computational analyses of metagenome sequences. These challenges refer, e.g. to the difficulties encountered when processing enormous data sets or the comparability of results obtained with different bioinformatics tools employed for the evaluation of metagenomics data. The last session 'Human Microbiomes in Health and Disease' linked metabolites with specific human diseases. For instance, the human gut microbiome was shown to impact the serum metabolome, thus contributing to insulin resistance in humans. In conclusion, the 11th CeBiTec Symposium was a timely event to demonstrate the impact of the genomics revolution on medical microbiology. The conference was topped off by two outstanding Distinguished Lectures.

Algae make perfume from light and CO₂

The Algae Biotechnology and Bioenergy group of Prof. Dr. Olaf Kruse has, for the first time, demonstrated that heterologous terpenoid product can be produced from the eukaryotic microalgae *Chlamydomonas reinhardtii*. The research was led by Dr. Kyle J. Lauersen in the group of Prof. Kruse in the CeBiTec. The team succeeded in producing the terpene product patchoulol from the microalga. Patchoulol is the natural chemical known for the distinct musky aroma of patchouli perfume.

Terpenoids are one of the largest groups of natural products and are also known as terpenes or isoprenoids. There are thousands of known and characterized terpenoid molecules which have natural roles in photosynthesis, membrane fluidity, protein functionalization, pigmentation, electron transport, defense, and signalling. Numerous natural terpenes are currently used as key ingredients in cosmetics, fragrances, foods, and medicines.

The advent of synthetic biology has allowed the transfer of modular terpenoid pathways from their native organisms into biotechnologically tractable microbial hosts. This has two practical benefits: 1. microbial cultivation is reliable and can be conducted in a standardized manner, allowing consistent product yields. 2. for rare or low-abundant terpene products, such as those found in medicinal plant extracts, the target bio-active molecule can be produced to desirable amounts without disturbing the natural environment of the organism.

The desire to use a microalga as a production platform stems from the capacity for containable photosynthetic growth using sunlight energy and carbon dioxide as culture inputs. Eukaryotic microalgae are notoriously difficult to



genetically engineer. In this work, the team used their advanced knowledge of microalgal genetic regulation to adapt gene expression cassettes to the algal host with completely synthetic DNA sequences, a process heavily used in the growing field of synthetic biology. The team succeeded not only in re-routing the host metabolism to produce the perfume compound patchoulol, they were able to express the largest heterologous protein sequence ever in a eukaryotic microalgae, 223.9 kDa!

This work has demonstrated that photosynthetic eukaryotic microalgae can be used as hosts for sustainable bio-production of high value natural products. The work has broad implications for microalgal biotechnology and greatly expands the range of possibilities for sustainable bio-production using this photosynthetic host, with possible applications for medicines, cosmetics, and biofuels.

1. Lauenstein K J, Baier T, Wichmann J, Wördenweber R, Hübner W, Huser T, Kruse O (2016). Efficient phototrophic production of a high-value sesquiterpenoid from the eukaryotic microalga *Chlamydomonas reinhardtii*. *Metabolic Engineering* doi:10.1016/j.ymben.2016.07.013.

A long lasting scientific collaboration of 25 years in molecular biology between Bielefeld University and the National University of La Plata

The German-Argentinean collaboration was started 25 years ago in 1991 between Prof. Dr. Alfred Pühler (Bielefeld University; right) and Prof. Dr. Antonio Lagares (National University of La Plata, UNLP; left), when the Argentinean partner visited the Chair for Genetics at Bielefeld University supported by a postdoctoral fellowship from the Alexander von Humboldt Foundation. Since that time both groups sustained a continuous scientific cooperation supported by crossed scientific visits of young PhD students and senior researchers. The Institute for Biotechnology and Molecular Biology at the UNLP was repeatedly visited by Prof. Dr. Alfred Pühler, Prof. Dr. Karsten Niehaus, and Prof. Dr. Jörn Kalinowski, all current scientists at the CeBiTec. The participation of Dr. Andreas Schlüter in the International Conference on Plasmid Biology (ICPB) in Bariloche, organized by the Argentinean group in 2010, also contributed to consolidate the current collaboration between both groups in the research area of bacterial plasmid mobilomes and the evolution of bacterial genomes. The exchange of PhD students from Germany to Argentina (Dr. Caren Wegener, Dr. Bodo Kohring, Dr. Steven Watt) and from Argentina to Germany (Dr. Florencia Del Papa, Dr. Mariano Pistorio, Dr. Walter Draghi, Dr. Gonzalo Torres Tejerizo and Dr. Carla Martini) over the years served as a central support to the fruitful collaboration between both groups. Students were supported by agencies like the German Academic Exchange Service (DAAD), Alexander von Humboldt Foundation, and the Argentinean Ministry of Science and Technology (MinCyT), with their research financed with local grants and by EC-multicentric collaborative projects. The joint research resulted in the publication of more than 17 papers in peer reviewed scientific journals. The strong collaborative interaction between both groups continues in the area of biochemical and genomic adaptation of bacteria to different environments, with two recent papers published in Scientific Reports from Nature Publishing Group. Dr. Gonzalo Torres Tejerizo is currently working at the CeBiTec until 2017 supported by an Alexander von Humboldt postdoctoral fellowship. In an increasing scientific exchange with German groups, Prof. Lagares has also running projects that include former members of the CeBiTec, now with their own groups at the Philips University of Marburg (Prof. Dr. Anke Becker), and at the Justus-Liebig University of Giessen (Prof. Dr. Alexander Goesmann). Evidently, the collaboration between Bielefeld University and the National University of La Plata is still very successful and will be continued in the coming year.



1. Draghi WO, Del Papa MF, Hellweg C, Watt SA, Watt TF, Barsch A, Lozano MJ, Lagares A, J, Salas ME, Lopez JL, Albicoro FJ, Nilsson JF, Torres Tejerizo GA, Luna MF, Pistorio M, Boiardi JL, Pühler A, Weidner S, Niehaus K, Lagares A (2016). A consolidated analysis of the physiologic and molecular responses induced under acid stress in the legume-symbiont model-soil bacterium *Sinorhizobium meliloti*. *Sci Rep.* 6: 29278. doi:10.1038/srep29278.

2. Martini MC, Wibberg D, Lozano M, Torres Tejerizo G, Albicoro FJ, Jaenicke S, van Elsas JD, Petroni A, Pilar Garcillan-Barcia M, de la Cruz F, Schlüter A, Pühler A, Pistorio M, Lagares A, Del Papa MF (2016). Genomics of high molecular weight plasmids isolated from an on-farm biopurification system. *Sci Rep.* 6: 28284. doi:10.1038/srep28284.

The German ELIXIR Node is coordinated by CeBiTec



In August 2016 Germany became the latest country to join the European life sciences infrastructure initiative ELIXIR, following the ratification of the ELIXIR Consortium Agreement by the Federal Ministry for Education and Research (BMBF). ELIXIR was nominated by the G7 Science Ministers as a world-leading infrastructure, vital for enabling the life sciences to derive maximum knowledge and understanding from biological, medical and environmental 'Big Data'. ELIXIR's membership now stands at 20; 19 European countries and EMBL as an intergovernmental organisation.

The national ELIXIR Node will be run by the German Network for Bioinformatics Infrastructure (de.NBI), which has been established to provide comprehensive bioinformatics services and training to users in basic and applied life sciences research across Germany. de.NBI was officially launched on March 1, 2015 and is financially supported by the BMBF. The network is bringing together eight German Service Centers that specialize in processing bioinformatics data from the life sciences. The coordinator of the programme is Prof. Dr. Alfred Pühler from CeBiTec, the Administration Office of de.NBI is managed by Prof. Dr. Andreas Tauch from CeBiTec, who is also the vice-coordinator of the network. In future, both CeBiTec scientists will be coordinating the German ELIXIR Node. The German membership in ELIXIR allows de.NBI to build on initial collaboration with ELIXIR in the area of tool registries and to expand it to other areas of interest such as user training, research clouds, proteomics, crop sciences, and industrial biotechnology.

www.denbi.de

www.elixir-europe.org



5th CeBiTec Students Academy – Synthetic Biology/Biotechnology

The 5th CeBiTec Students Academy 'Synthetic Biology/Biotechnology' was held at the CeBiTec from July 11 to 15, 2016. The Students Academy is a joint project of the CeBiTec, the District Council Detmold as well as the Familie-Osthushenrich-Stiftung which provides the essential financial support. The academy is organized by Honorary Prof. Dr. Walter Arnold, Prof. Dr. Alfred Pühler and Dr. Werner Selbitschka. The one-week course is directed towards gifted and talented students living in Ostwestfalen-Lippe of Northrhine-Westfalia who will finish their Abitur in one-years time, the general qualification for university entrance.



From a total of more than 40 applications, 20 participants were accepted to the academy. All of the attendees had excellent grades in natural sciences. It is worth noting that 15 of the 20 participants had A+ grades in at least two of the four school subjects Biology, Chemistry, Mathematics and Physics. As observed for the last years' courses, more than half of the attendees were female. Lectures which were held by members of the Faculty of Biology and the Technical Faculty addressed various aspects of modern biotechnology. Relevant subjects were (i) industrial biotechnology, (ii) modern plant breeding, (iii) industrial production of pharmaceuticals, as well as (iv) synthetic biology. Moreover, an invited talk entitled 'Communication of New Technologies Using the Examples Biotechnology and Synthetic Biology' was contributed by Marc-Denis Weitze, Head of the Technology Communication of the acatec – The National Academy of Science and Engineering. The CRISPR/CAS technique was also presented to the students.

The experimental part was organized by members of the CeBiTec and dealt with the isolation, amplification as well as the sequencing of DNA. In addition, the proteomics experiment newly introduced into the last year's course was

repeated. The knowledge acquired by the students was used for the (i) taxonomic identification of bacterial communities employing bioinformatics tools, (ii) MALDI-TOF based identification of *Xanthomonas campestris* pv. *campestris* proteins, and finally (iii) for the analysis of regulatory networks constructed by synthetic biology approaches. Evonik Industries AG in Halle-Künsebeck was this year's destination of the excursion within the framework of the Students Academy. It is worth noting that the CEO of the Familie-Osthushenrich-Stiftung, Dr. Burghard Lehmann, has promised the organizers the continuation of the Students Academy after the end of the current funding period. For this purpose, the format of the course will be newly designed.

CeBiTec celebrated Summer Party on the 25th of August

Although 'Walking on Sunshine' would have been perfect, DJ D.W. put on 'Smells Like Teen Spirit' (Nirvana) and actually, with this record encouraged people to dance, by the way, for the first time on the occasion of a CeBiTec Summer Party. CeBiTec staff and guests enjoyed the hottest day of this year's summer having a beer or two ..., grilled steaks, a bratwurst and of course inspiring discussions, this time all organized by GRIM (Research Group Genome Research of Industrial Microorganisms) and de.NBI (German Network for Bioinformatics Infrastructure) members. Light and music were powered off late at night and the pictures shown, nicely reflect the enthusiastic atmosphere of that summer evening.



Miscellaneous

From August 29 to 30, 2016, the 3rd CeBiTec Retreat was held in the Evangelische Akademie Loccum. During the two days 17 scientific talks representing different research topics of the CeBiTec were given by MSc and PhD students, postdocs, and professors. Additionally, a special lecture about Microfluidic Single-Cell Cultivation was held by Dipl. Ing. A. Grünberger (Forschungszentrum Jülich).

Upcoming Events

- November 11, 2016 | CeBiTec building
5th CeBiTec full day education for high school teachers in Synthetic Biology/Biotechnology
- November 21, 2016 | Center for interdisciplinary Research (ZiF), Bielefeld University
CeBiTec Distinguished Lecture – Prof. Dr. Birger Lindberg Møller (University of Copenhagen, Denmark)
- September 11–12, 2017 | Landwirtschaftszentrum Haus Düsse, Bad Sassendorf
4th CeBiTec Retreat
- further events are announced on the CeBiTec web page

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