

CeBiTec – Quarterly

Spring 2018

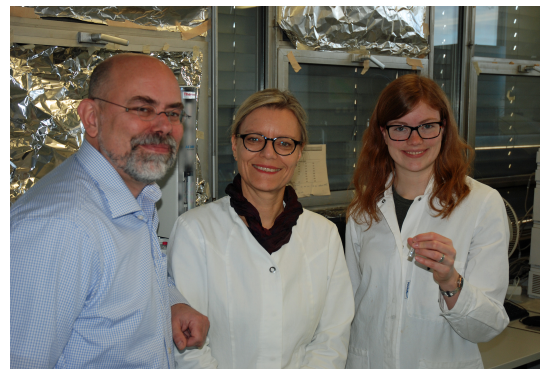
In this Issue

- INDIE – International Collaborative Research Project will develop sustainable production of the flavoring compound indole
- Further eighteen months for DiDy
- CeBiTec researchers searching for “silver bullets”
- The successful 12th CeBiTec Symposium on Big Data in Medicine and Biotechnology
- The 8th International CeBiTec Research Conference/Biocascades Symposium – Reaction Concepts for Industrial Biocatalysis
- CeBiTec Advisory Board Meeting 2018
- Upcoming Events

INDIE – International Collaborative Research Project will develop sustainable production of the flavoring compound indole

Prof. Dr. Volker F. Wendisch (CeBiTec and Faculty of Biology) is principle investigator in the ERA CoBioTech funded project INDIE in which academic and industrial partners from three European countries collaborate to develop sustainable production of high-value chemicals by fermentation. INDIE is one of the 22 projects funded in ERA CoBioTech's first call “Biotechnology for a sustainable bio economy”, with a total budget of 31 M€. The academic collaboration partners Prof. Dr. Dirk Bosch (Wageningen Plant Research, Netherlands), who is coordinating the project, Prof. Dr. Kristina Gruden (National Institute of Biology, Slovenia), Prof. Dr. Vitor Martins dos Santos (Wageningen University, Netherlands), the industrial partner Dr. Peter van der Schaft (Axxence GmbH, Germany) and Prof. Wendisch are working on a synthetic and systems biological approach on the principle of design-build-test-learn-cycle for the biotechnological production of indole. Indole is an important flavoring compound, which finds applications in dairy, tea drinks and fine fragrances. The market for indole is shared by synthetic indole, which is derived from coal tar, and by natural indole, which is prepared by a high-cost soft chemistry. Since INDIE is aiming at the replacement of hardly sustainable processes at a competitive price, the GRAS organism *Corynebacterium glutamicum* was chosen as production host. This bacterium is a well-developed platform technology for the efficient production of several amino acids and aromatic compounds and has been used safely in food and feed biotechnology for decades. The work of Prof. Wendisch, Dr. Petra Peters-Wendisch, Tatjana Walter (s. photo) and a further PhD student will focus on the engineering of metabolic pathways to indole, identification of indole resistance mechanism(s), implementation of synthetic pathways to access alternative feedstocks, generation and analysis of transcriptomic data and indole production in lab scale fermenters.

www.cobiotech.eu/call-information#collapse428



Further eighteen months for DiDy

After a successful first funding period, the International Research Training Group GRK 1906 “Computational Methods for the Analysis of the Diversity and Dynamics of Genomes – DiDy” receives additional funding from the German Research Foundation (DFG) to continue the program until September 2019. This will allow all current doctoral students to complete their three-year PhD studies without interruption and with full salaries.

Despite the discontinuation of funding on the Vancouver side in 2016 and thus the loss of a symmetrical international partner program – integral part of the DFG funding format *International Research Training Groups* –, Bielefeld principal investigators worked out a plan for a second round of DiDy. National partners in Gießen and Marburg should act as a bridge to human biology and medicine in central Hesse, e.g., the *Universitätsklinikum Gießen und Marburg*, the German Center for Lung Research and the German Center for Infection Research, to complement expertise of the CeBiTec and to compensate Vancouver’s former strong translational role in the program for immediate access to data and research questions.

Both switching the funding format from international to national, and applying for a bi-local program seemed to be venturous at the beginning, but made absolute sense – also to the review board that visited Bielefeld University in September last year. Finally, everyone was convinced that not only the first funding phase in collaboration with the Canadian partners has been a clear success, but also that the continuation with additional partners in central Hesse would have great potential.

However, barely comprehensible small doubts in the final decision process overruled pages of notably positive approval by the reviewers, and DiDy has not been granted a complete second funding phase. Still, more than half a million Euros will not only allow the remaining five doctoral students to finish their three years in the program. It also includes adequate travel funding such that, in addition to usual conference travels, also the last cohort of PhD students can experience a six-months research stay in Vancouver – hosted by colleagues whose collaboration outlives funding.



CeBiTec researchers searching for “silver bullets”

Multiple antibiotic-resistant bacterial pathogens are one of the serious threats in today's medicine. Infections with such strains, e.g. methicillin-resistant *Staphylococcus aureus* (MRSA) or multi-resistant Gram-negative strains (MRGN) are on the rise and frequently appearing. The number of antibiotics remaining for therapy of these infections is constantly decreasing and the “antibiotics of last resort” should only administered in very special cases. Therefore, there is an urgent need to find novel substances with antibiotic action that can be developed to broaden the arsenal of modern clinical infection therapies, so-called silver bullets.

Almost all antibiotics in clinical use were derivatives of natural substances from the class of secondary metabolites, meaning that they are not part of the (primary) metabolism that is essential for cell growth, but are extras with which microorganisms protect themselves and their ecological niches. New antibiotics are looked for by mining strains from genera of microorganisms that are known to produce many secondary metabolites. The most famous among these is the genus *Streptomyces*. Streptomyces are environmental bacteria and producers of around 70% of the today's clinically used antibiotics from natural sources. Besides the antibiotics that are produced by these organisms at standard laboratory conditions, their genomes contain the genetic repertoire for many more, but produced at mostly unknown circumstances. The advent of high-throughput sequencing of microbial genomes has advanced these searches dramatically, and therefore, genome mining has efficiently complemented the standard microbiological approaches.

In a recent study, researchers from Bochum University together with CeBiTec scientists have explored the genome and the secondary metabolite-production potential of *Streptomyces chartreusis*. It turned out, that the genome con-

tains 128 gene clusters for synthesis of secondary metabolites and more than 1 000 substances were detected to be produced in different growth media. The study represents an important contribution to the understanding of bacterial secondary metabolite synthesis in a genomic context and was published in the journal PNAS [2].

Most bacterial species on earth are not yet cultivated and the number of uncultivated species probably exceeds the cultivated species by a factor of 1 000 or more. Since these microorganisms also are prospective producers, research has turned to isolating single cells of such bacteria for genome analysis, to identify the gene clusters and assign them to the product spectrum observed in the original environment and later to clone and express those clusters in cultivatable hosts for specific studies on these antibiotics. A specific environment where antibiotics-producing uncultivated bacteria are found are marine sponges. It appears that sponges have evolved to provide specific bacteria with beneficial living conditions and in return, these bacteria protect the sponge against predatory animals and microorganisms by producing cytotoxic or antibiotic chemicals. The Indo-Pacific sponge species *Theonella swinhoei* can display different chemotypes, differing in their repertoire of secondary metabolites according to the isolation site.

It was already known from metagenome sequencing of one chemotype (Japan), the bacterial producer is from the genus *Endotheonella*, a phylum without a single cultivated species [3]. In a recent study published in the journal PNAS [1] researchers from ETH Zürich, together with colleagues at CeBiTec and different research institutions in Japan and Israel, have compared the producers of these chemotypes by single-cell genome sequencing and found very similar bacteria but with different repertoires of gene clusters responsible for the production of these chemicals, many of these previously unknown (Figure). The data validate *Endotheonella* as a rich and varied producer taxon with considerable biotechnological potential.

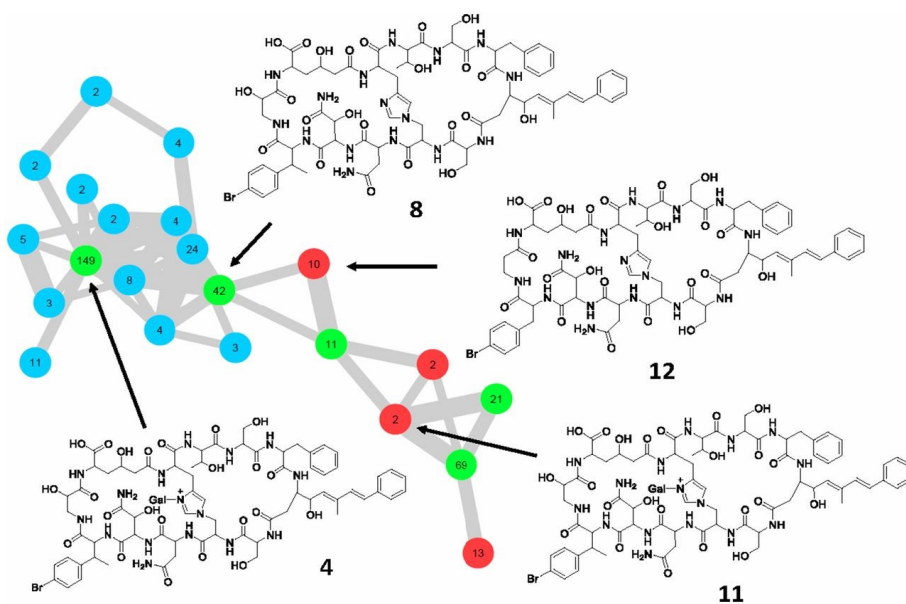


Figure: Molecular network analysis of theonellamides produced by *Endotheonella* sp. Nodes are color-coded according to the sponge sample from which the data were obtained: blue, TSWA (Japan); red, TSWB (Israel); green, metabolites present in both sponges. Numbers within each node indicate the number of MS² spectra obtained for each metabolite as a proxy for their relative abundance. The edge line width indicates the relatedness between two metabolites (cosine 0.7). (Figure 3 from [1])

1. Mori T, Cahn JKB, Wilson MC, Meoded RA, Wiebach V, Martinez AFC, Helfrich EJN, Albersmeier A, Wibberg D, Dätwyler S, Keren R, Lavy A, Rückert C, Ilan M, Kalinowski J, Matsunaga S, Takeyama H, Piel J. (2018) Single-bacterial genomics validates rich and varied specialized metabolism of uncultivated *Endotheonella* sponge symbionts. *Proc Natl Acad Sci U S A.* 115(8):1718–1723. doi:10.1073/pnas.1715496115. Epub 2018 Feb 8.
2. Senges CHR, Al-Dilaimi A, Marchbank DH, Wibberg D, Winkler A, Haltli B, Nowrousian M, Kalinowski J, Kerr RG, Bandow JE. (2018) The secreted metabolome of *Streptomyces chartreusis* and implications for bacterial chemistry. *Proc Natl Acad Sci U S A.* 2018 Feb 20. pii: 201715713. doi: 10.1073/pnas.1715713115. [Epub ahead of print]
3. Wilson MC, Mori T, Rückert C, Uria AR, Helf MJ, Takada K, Gernert C, Steffens UA, Heycke N, Schmitt S, Rinke C, Helfrich EJ, Brachmann AO, Gurgui C, Wakimoto T, Kracht M, Crüsemann M, Hentschel U, Abe I, Matsunaga S, Kalinowski J, Takeyama H, Piel J. (2014) An environmental bacterial taxon with a large and distinct metabolic repertoire. *Nature.* 506(7486):58–62.

The successful 12th CeBiTec Symposium on Big Data in Medicine and Biotechnology

The 12th CeBiTec Symposium belongs to a series of symposia started in the year 2006. The CeBiTec symposia are organized to address specific research fields playing a dominant role at the CeBiTec. The 12th CeBiTec Symposium took place from 19 to 21 March 2018 at the Center for Interdisciplinary Research (ZiF) of Bielefeld University and was focused on “Big Data in Medicine and Biotechnology”. The program was composed of 30 speakers, most of them from abroad. For the symposium, more than 130 participants registered. In particular, more than 40 researchers and PhD candidates affiliated with the CeBiTec followed the presentations.

The symposium was collaboratively organized by the CeBiTec, the Bielefeld Center for Data Science (BiCDaS) and the German Network for Bioinformatics Infrastructure (de.NBI). Welcome addresses were presented by the *Rektor* of Bielefeld University, Prof. Dr. Gerhard Sagerer, and the Director of the CeBiTec, Prof. Dr. Olaf Kruse. The CeBiTec specifically organized sessions focused on the use of big data in medicine and biotechnology. The de.NBI network was responsible for the organization of the second day dedicated to use cases discussed currently in the ELIXIR organization. Finally, BiCDaS initiated the final round table discussion on ethical and legal aspects concerning medical data. The highlight of the symposium was without doubt the distinguished symposium lecture at the end of the second day where Prof. Dr. Eva Winkler, Heidelberg, informed on ethical and Prof. Dr. Kai Cornelius, Regensburg, on legal considerations of collecting and processing medical big data.



The 8th International CeBiTec Research Conference/Biocascades Symposium – Reaction Concepts for Industrial Biocatalysis

In the Center for Interdisciplinary Research (Zentrum für interdisziplinäre Forschung, ZiF) at Bielefeld University the 8th International CeBiTec Research Conference/Biocascades Symposium on “Reaction Concepts for Industrial Biocatalysis – Process Catalysts, Process Development, Cascades and New Products” was held from April 9 to 11, 2018. This meeting was jointly organized by members of the EU-MSCA-ITN-network project Biocascades and the Chair of Organic Chemistry I at Bielefeld University. On this occasion, more than 80 researchers from academia and industry exchanged their views and information on current developments in the field of enzyme catalysis for the synthesis of organic molecules. The focus of this symposium was on the development of tailor-made biocatalysts, process development of biotransformations and cascade reactions in the presence of enzymes as well as applications of biocatalysis in industry, particularly in the pharmaceutical industry. The lecture programme consisted of 23 lectures, comprising the keynote lectures given by Prof. Dr. Jun Ogawa (Kyoto University), Prof. Dr. Marko Mihovilovic (Vienna University of Technology) and Dr. Birgit Kosjek (Merck Sharp & Dohme),



and was complemented by poster sessions with 34 poster contributions. In addition, the following young scientists were awarded: Laura Leemans (Viazym BV) received the Biocascades Scholarship Award, Frederica Ruggieri (Saromics Biostructures AB) was awarded the Biocascades Award Talk, and the poster prizes sponsored by the scientific journals Bioengineering and Molecular Catalysis, respectively, were given to Christian Schnepel (Bielefeld University), Sabrina Höhenreich (Philipps-Universität Marburg) and Jana Löwe (Bielefeld University).

CeBiTec Advisory Board Meeting 2018

The Advisory Board of the CeBiTec gathered for its 2018 meeting from April 11 to 13, 2018, at Evonik Industries AG in Halle/Westfalen. The representatives of the Board used this meeting to intensively discuss recent achievements as well as future activities and strategies of the CeBiTec together with members of the rectorate as well as with the principal investigators of the CeBiTec. A special focus within the strategy discussions was set on activities in the fields of bioinformatics and medical research in the frame of the establishment of a new Medical Faculty at Bielefeld University. Furthermore, the Advisory Board highlighted positively on recent success by members of the CeBiTec in collaborative grant applications and strongly supported attempts for intensive activities in the research field of chemical biocatalysis. 'This was again a very supportive and fruitful meeting of the CeBiTec Advisory Board, clearly underlining the overall importance of this Board for our work at the CeBiTec', the Scientific Director of the CeBiTec, Prof. Dr. Olaf Kruse, resumed at the end of the meeting.



Upcoming Events

- August 20 – 24, 2018 | CeBiTec, Bielefeld University
[7th CeBiTec Students Academy Synthetic Biology/Biotechnology](#)
- September 10–11, 2018 | Landwirtschaftszentrum Haus Düsse, Bad Sassendorf
[4th CeBiTec Retreat](#)
- September 24, 2018 | Center for Interdisciplinary Research (ZiF), Bielefeld University
20 Years Anniversary of CeBiTec
- October 15–19, 2018 | CeBiTec, Bielefeld University
[3rd teutolab-Academy Systems Biology](#)
- November 26, 2018, 17 c.t. | Center for Interdisciplinary Research (ZiF), Bielefeld University
[CeBiTec Distinguished Lecture – Dr. Tobias Erb \(Max Planck Institut für terrestrische Mikrobiologie, Marburg\)](#)
- further events are announced on the [CeBiTec web page](#)