

# CeBiTec – Quarterly

## Summer 2016

### In this Issue

- Distinguished Lecture by Peter Gresshoff, Centre for Integrative Legume Research, Brisbane, Australia
- A new DFG-funded project addressing the regulation of photosynthetic light harvesting in green cell factories
- Gene identification by mapping-by-sequencing without a mapping population
- Putting two pieces together – combination of biocatalytic halogenation with chemocatalytic cross-coupling reactions
- Brainstorming workshop on the installation of a de.NBI specific cloud
- Upcoming Events

### Distinguished Lecture by Peter Gresshoff, Centre for Integrative Legume Research, Brisbane, Australia



On the invitation of Prof. Dr. Olaf Kruse and Prof. Dr. Alfred Pühler, Prof. Dr. Peter Gresshoff, Director of the Centre for Integrative Legume Research, The University of Queensland, Brisbane, Australia, visited the CeBiTec on April 11, 2016. Prof. Gresshoff gave a talk in the CeBiTec Distinguished Lecture Series entitled “Benefits of symbiotic nitrogen fixation and legume nodulation for food, feed and fuel production”. In the plenary hall of the Center for Interdisciplinary Research (ZiF) of Bielefeld University he reported about the huge scientific advances made in the last two decades in the understanding of the key mechanisms involved in this symbiosis between plants of the legume family and soil bacteria broadly called rhizobia. Prof. Gresshoff’s talk also touched an interesting applied aspect of his legume research work which can be used for mitigation of climate change and provision of feedstock for biofuels and biorefineries. Particularly, the investigation of a universal legume process called Autoregulation of Nodulation (AON) was presented in his very well attended talk.

### A new DFG-funded project addressing the regulation of photosynthetic light harvesting in green cell factories

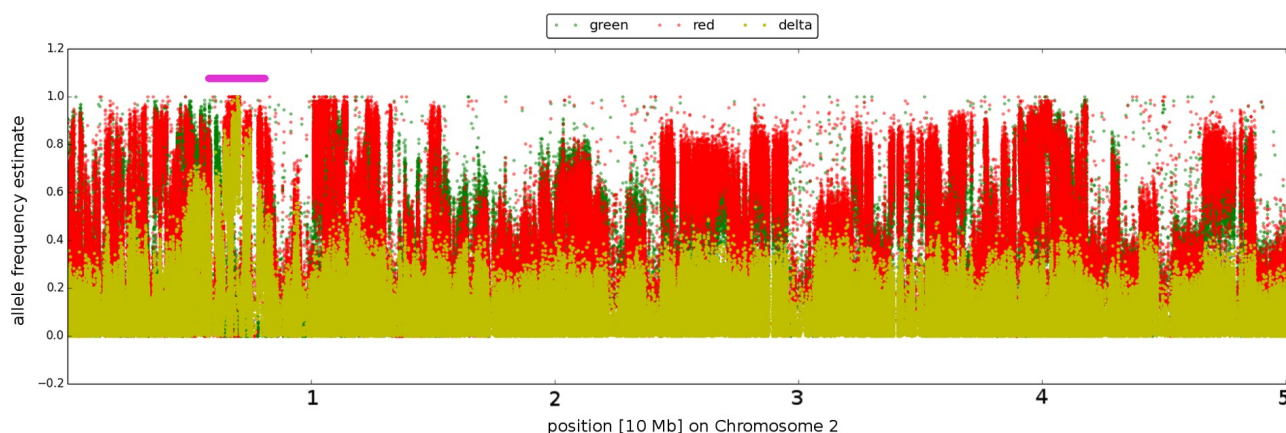
The German Research Foundation (DFG) funds a three year project dedicated to the analysis of the network that controls light acclimation in the phototrophic microbe *Chlamydomonas reinhardtii*, with Prof. Dr. Olaf Kruse as the principal investigator. Work in the project will be done at the CeBiTec in collaboration with Dr. Stephane Lemaire (CNRS Paris). Olaf Kruse’s group identified the translation repressor NAB1 as a key factor implicated in light acclimation responses which determine the size of the light-harvesting antenna in *C. reinhardtii*. Work of the past years led to a detailed functional knowledge of the NAB1-containing regulatory hub. Therefore, this protein will be used as a tool to create a blueprint, depicting the regulatory network that determines antenna size in microalgal cells. This blueprint

will provide the basis for future engineering approaches, aiming at the design of microalgal cells which convert light energy more efficiently into biomass or high value products.

## Gene identification by mapping-by-sequencing without a mapping population

Mapping-by-sequencing (MBS) is a method for rapid and simultaneous mapping as well as identification of genes underlying a phenotype [1]. MBS combines the identification of genomic loci linked to a phenotype by Bulk Segregant Analysis (BSA) with high-resolution and genome-wide discovery of allele frequencies using whole genome sequencing. By building DNA pools based on the phenotypes of F<sub>2</sub> individuals, loci that cause the phenotype studied can be localized in the genome with base-pair resolution. No prior knowledge about the causal gene is required. As a prerequisite, a mapping population is needed which segregates progeny with the phenotype of interest. Depending on the generation time of the species analysed, setting up a F<sub>2</sub> population can be quite time consuming.

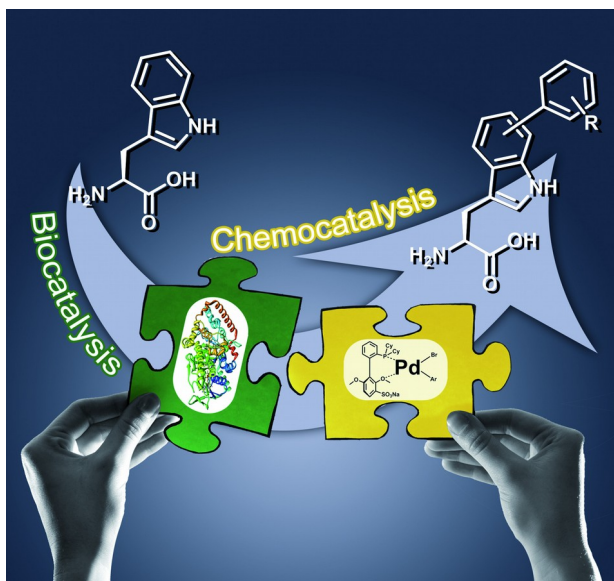
By modifying the published MBS approach, a team of researchers from the CeBiTec in cooperation with breeding companies demonstrated the applicability of MBS without the need to generate a mapping population. The example studied was the *R* locus which controls red hypocotyl color in sugar beet (*Beta vulgaris*) [2]. The team compared the genome-wide distribution of allele frequencies within pooled DNA of two times 180 homozygous beets distinguished by the ability to produce the red pigment betalain. The two pools of beets were selected directly from preexisting breeding panels, and thus a mapping population was not needed. Allele frequency analysis pointed at the locus causing the phenotype within a 30 kbp interval, which was in concordance with the location of the published *RED* gene. Further research will aim at the identification of quantitative traits.



1. Schneeberger K, Ossowski S, Lanz C, Juul T, Petersen AH, Nielsen KL, Jorgensen JE, Weigel D, Andersen SU. (2009) SHOREmap: simultaneous mapping and mutation identification by deep sequencing. *Nat. Methods* 6:550–551
2. Ries D, Holtgräwe D, Viehöver P, Weisshaar B. (2016) Rapid gene identification in sugar beet using deep sequencing of DNA from phenotypic pools selected from breeding panels. *BMC Genomics* 17:236

## Putting two pieces together – combination of biocatalytic halogenation with chemocatalytic cross-coupling reactions

Halogenation of organic compounds is a common strategy in chemical synthesis. Due to a facile modification by nucleophilic attack or metal-catalyzed cross-coupling reactions, aryl halides are known as important intermediates in the chemical, agrochemical and pharmaceutical industry. The chemical introduction of halogen substituents requires hazardous chemicals and harsh reaction conditions with only limited control over regioselectivity. In contrast, nature has evolved enzymatic strategies to halogenate organic metabolites regioselectively under much milder conditions, making use of benign halide salts and oxygen at 25 °C and pH 7. The workgroup *Organic and Bioorganic Chemistry*, headed by



Prof. Dr. Norbert Sewald, explores new biocatalytic approaches for the halogenation of aromatic compounds using highly regioselective FAD-dependent tryptophan halogenases, one of the major enzyme classes responsible for halogenated secondary metabolites in nature.

Very recently, the group of Prof. Sewald published results about the combination of enzymatic halogenation of L-tryptophan with subsequent chemocatalytic Suzuki–Miyaura cross-coupling reactions [1]. By combining biocatalysis and metal catalysis, this modular synthesis leads to an array of C<sub>5</sub>, C<sub>6</sub>, or C<sub>7</sub> aryl-substituted tryptophan derivatives. In a three-step one-pot reaction, the bromo substituent is initially incorporated regioselectively by immobilized tryptophan 5-, 6-, or 7-halogenases, respectively, with concomitant cofactor regeneration. The halogenation proceeds in

aqueous media at room temperature in the presence of NaBr and O<sub>2</sub>. After separation of the biocatalyst by filtration, a palladium catalyst, a base, and an aromatic boronic acid are added to the aryl halide formed in situ to effect direct Suzuki–Miyaura cross-coupling reactions followed by *tert*-butoxycarbonyl (Boc) protection. After a single purification step, different Boc-protected aryl tryptophan derivatives are obtained that may, for example, be used for peptide or peptidomimetic synthesis.

1. Frese M, Schnepel C, Minges H, Voß H, Feiner R, Sewald N (2016). Modular combination of enzymatic halogenation of tryptophan with Suzuki–Miyaura cross-coupling reactions. *ChemCatChem*. DOI: 10.1002/cctc.201600317

## Brainstorming workshop on the installation of a de.NBI specific cloud



The eight service centers of de.NBI, the German network for Bioinformatics Infrastructure, are confronted with the problem, not to be equipped with sufficient compute power necessary for the analysis of all the data produced by German life science groups. In order to develop the compute power within the network there is the plan to build a de.NBI specific cloud, which should be installed at service centers already involved in developing the soft- and hardware structure important for cloud computing. For this reason a brainstorming meeting dealing with these aspects took place at the CeBiTec on May 30, 2016. The workshop attended by delegates of different de.NBI service centers first reviewed the more medically oriented white paper entitled “The Applied and Translational Genomics Cloud (ATGC)” (<http://www.applied-translational-genomics-cloud.de/joomla/index.php/en/>) developed by three organizations, namely Heidelberg University, DKFZ and EMBL. As a further highlight, Dr. Alexander Sczyrba from the BiGi service center for microbial bioinformatics reported on the topic “Cloud computing meets de.NBI – scaling out bioinformatics workloads of the German Network for bioinformatics infrastructure”. It became evident that the work on cloud computing carried out at the CeBiTec represents a format for the installation of a de.NBI cloud. In a first estimate, around 5 Mio. Euro were considered to be necessary for building such a cloud. Establishing a de.NBI cloud, of course, depends on the availability of the resources mentioned. The de.NBI coordinator Prof. Dr. Alfred Pühler and, the head of the de.NBI office Prof. Dr. Andreas Tauch, are involved in discussions with representatives of the Federal Ministry of Education and Research (BMBF) to solve the financial aspect.

[www.denbi.de](http://www.denbi.de)

## Upcoming Events

- July 04–06, 2016 | Center for interdisciplinary Research (ZiF), Bielefeld University  
11<sup>th</sup> CeBiTec Symposium – Microbial Genomics and Metabolomics in Human Health and Disease
- July 11–15, 2016 | CeBiTec building  
5<sup>th</sup> CeBiTec Students Academy – Synthetic Biology/Biotechnology
- August 29–30, 2016 | Evangelische Akademie Loccum  
3<sup>rd</sup> CeBiTec Retreat
- September 25–28, 2016 | Center for interdisciplinary Research (ZiF), Bielefeld University  
6<sup>th</sup> International CeBiTec Research Conference – Advances in Industrial Biotechnology
- November 21, 2016 | Center for interdisciplinary Research (ZiF), Bielefeld University  
CeBiTec Distinguished Lecture – Prof. Dr. Birger Lindberg Møller (University of Copenhagen, Denmark)
- further events are announced on the CeBiTec web page