UNIVERSITÄT BIELEFELD

CeBiTec Center for Biotechnology

CeBiTec – Quarterly

Summer 2022

- A. Pühler received the certificate as honorary senator during a regular senate meeting
- DFG-Funding for CeBiTec-research with Technical University of Hamburg towards a biocatalytic sustainable synthesis of pharma-related β-hydroxy α-amino acids
- Visiting Professorship at Osaka University awarded to Prof. Dr. Harald Gröger
- Microalgae as green cell factories

A. Pühler received the certificate as honorary senator during a regular senate meeting

In the last Senate meeting before the end of the summer semester, the appointment of Prof. Dr. Alfred Pühler as Honorary Senator of Bielefeld University was honored. The appointment as honorary senator was already made two years ago in the Senate meeting of July 8, 2020, but due to Corona restrictions, the presentation of the award could only be implemented now. The chair of the senate, Prof. Dr. Silke Schwandt, presented the certificate of appointment. Since Bielefeld University was founded, a total of 17 honorary senators have been appointed in the past 39 years. The honorary certificate justifies the appointment of A. Pühler as honorary senator. It was noted that as a respected, outstanding and visionary researcher, he has contributed significantly to establishing the subject "Genetics/Biotechnology". He also succeeded in establishing unique research infrastructures with the Center for Biotechnology and the German Network for Bioinformatics Infrastructure, through which Bielefeld University has gained international visibility.

Figure 1: Presentation of the honorary certificate at the last Senate meeting of the summer semester 2022. From left to right: Senate Chair Prof'in Dr. S. Schwandt, Honorary Senator Prof. Dr. A. Pühler, Rector Prof. Dr. G. Sagerer. (© Bielefeld University)

It was also pointed out that he has persevered and courageously pursued the involvement of his research field in scientific associations and academies as well as the dialogue with society and politics. Overall, it was emphasized that his work has represented Bielefeld University in an exemplary manner both nationally and internationally.

In his response to the Senate, A. Pühler emphasized that the development of the infrastructures would not have been possible without the incisive participation of Bielefeld University. In 1998, for example, to avert a call to the position of Scientific Director at the GBF, an Helmholtz Center in Braunschweig, he was enabled to establish a Center for Genome Research at Bielefeld University. This center played a dominant role in the decision to construct the research building of the Center for Biotechnology (CeBiTec).

Bielefeld University was also significantly involved in the establishment and especially in paving the way for sustainable continuation of the German Network for Bioinformatics Infrastructure (de.NBI). The de.NBI network, an association of leading bioinformatics groups in Germany, was funded by the German Federal Ministry of Education and Research starting in 2015. The BMBF appointed A. Pühler as coordinator of this de.NBI network. One of the coordinator's tasks was to find options for a sustainable continuation of the de.NBI network. For this purpose, the BMBF recommended to involve the political level, which is not an easy task for a scientifically oriented coordinator.

To organize a discussion at the political level, the Rector of Bielefeld University, Prof. Dr. G. Sagerer, participated and organized telephone calls. He made contact with the former chairman of the CDU/CSU parliamentary group in the Bundestag. Within a very short time, the problem of continuity was solved. The de.NBI network was integrated into the Helmholtz Association, in particular into the Forschungszentrum Jülich since January 2022. For this purpose, a new section was established at the Jülich Institute for Bio- and Geosciences. The de.NBI employees formerly working at Bielefeld University were taken over and continue to operate from Bielefeld. This became possible since Forschungszentrum Jülich plans to establish a branch at Bielefeld University. This development is particularly due to the negotiating skills of Bielefeld University, which succeeded in working out the common advantages of such a branch for both sides.

The coordinator activity of the de.NBI network of A. Pühler has ended since January 2022. However, he will remain within CeBiTec and lead, as Senior Research Professor, a research group with the topic "Genome Research of Industrial Microorganisms". Besides supervising two long-lasting industrial projects, he is mainly active in supervising PhD students.

(L. Wobbe)

DFG-Funding for CeBiTec-research with Technical University of Hamburg towards a biocatalytic sustainable synthesis of pharma-related β-hydroxy α-amino acids

Enantiomerically pure α-amino acids play an important role in today's pharmaceutical industry since these compounds serve as valuable chiral key building blocks for the synthesis of modern active pharmaceutical ingredients. Many of them are already produced by means of biocatalysis. However, the access to more complex, non-proteinogenic β-hydroxy substituted α-amino acids bearing two stereogenic centers, which are of interest for production of

a range of pharmaceuticals such as antibiotics, still represents a challenge and a biocatalytic approach to those molecules on large industrial scale has not been realized yet. This "white spot" on the "map of enzymatically produced amino acids" is now to be targeted jointly by the Institute of Technical Biocatalysis (ITB) at Hamburg University of Technology being headed by Professor Dr. Andreas Liese and the Chair of Industrial Organic Chemistry and Biotechnology (IOCB) at Bielefeld University headed by Prof. Dr. Harald Gröger as CeBiTec member in a research project funded by the German Research Foundation (DFG). The two research groups are collaborating intensively since more than a decade on various research topics in the field of biocatalysis and sustainable organic synthesis.

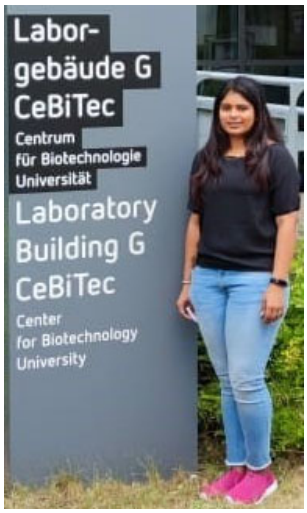

Figure 2: Doctoral course student Ms. Logia Jolly in front of the CeBiTec building.

From Bielefeld University side, the lab research will be conducted by Ms. Logia Jolly who very recently started her doctoral thesis work at the IOCB group.

In this interdisciplinary tandem project of ITB and IOCB combining expertises of bioprocess engineering and organic synthesis with enzymes, the aim is to develop a deep basic scientific understanding for efficient stereoselective synthetic processes using L-threonine aldolases as catalysts as well as the development of a process technology with these types of enzymes, thus laying the ground for production of pharmaceutically relevant β-hydroxy α-amino acids with this enzyme class on technical scale in the future.

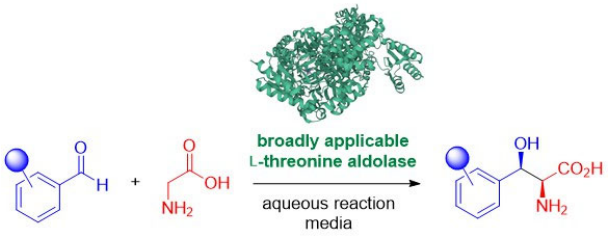

Figure 3: Target reaction based on the use of an L-threonine aldolase as biocatalyst.

What makes this biocatalytic approach attractive from a conceptual perspective is the direct generation of two stereogenic centers in one step within an aldol reaction without protecting groups and by using readily available and commercially attractive chemicals such as an aldehyde and glycine as starting materials. One of the scientific challenges in this research project is to achieve high diastereoselectivity in combination with high productivity.

(H. Gröger)

Visiting Professorship at Osaka University Awarded to Prof. Dr. Harald Gröger

The CeBiTec-member Prof. Dr. Harald Gröger from the Chair of Industrial Organic Chemistry and Biotechnology has been awarded a Visiting

Professorship at Osaka University, which will consist of two planned stays in Osaka during September/October 2022 and March 2023. A particular focus of this visiting professorship is the intensification of the research collaborations with various colleagues from Osaka University. Among research collaborations with colleagues from Osaka University are the long-standing collaborations with the research

group of Professor Dr. Hiroaki Sasai on vanadium catalysis as well as with the research group of Professor Dr. Shuji Akai on chemo-enzymatic synthesis. In this joint collaboration with the group of Prof. Akai, recently the first example of a dynamic kinetic resolution of a tertiary alcohol has been successfully demonstrated.

(H. Gröger)

Microalgae as green cell factories

Microalgae are playing an increasing role as sustainable green cell factories in biotechnology. The algae biotechnology group of Prof. Dr. Olaf Kruse at the CeBiTec now succeeded in engineering the microalga *Chlamydomonas reinhardtii* as a powerful green cell factory for robust efficient photoautotrophic diterpenoid production (Einhaus et al., 2022) as well as for polyamine production (Freudenberg et al., 2022a) (Figure 4). Both achievements represent a breakthrough in establishing a photosynthetic microorganism that converts CO_2 and sunlight into carbon-based products as a powerful green cell factory for the competitive use in industrial biotechnology.

By implementing state-of-the-art genetic engineering concepts into a systematic evaluation of novel metabolic engineering strategies, the heterologous production of valuable diterpenoids by *C. reinhardtii* was distinctly advanced. Rate-limiting steps in the MEP pathway, by which the isoprene building blocks for terpenoids are generated, could be identified and overcome. In combination with a high cell-density cultivation concept, robust photoautotrophic diterpenoid production is demonstrated. The diterpenoid sclareol, which is highly demanded for its application in the fragrance industry and for its potential use as a pharmaceutical, could be produced to titers of up to 656 mg L^{-1}, which displays the highest production of any heterologous compound ever achieved in *C. reinhardtii* (Einhaus et al., 2022).

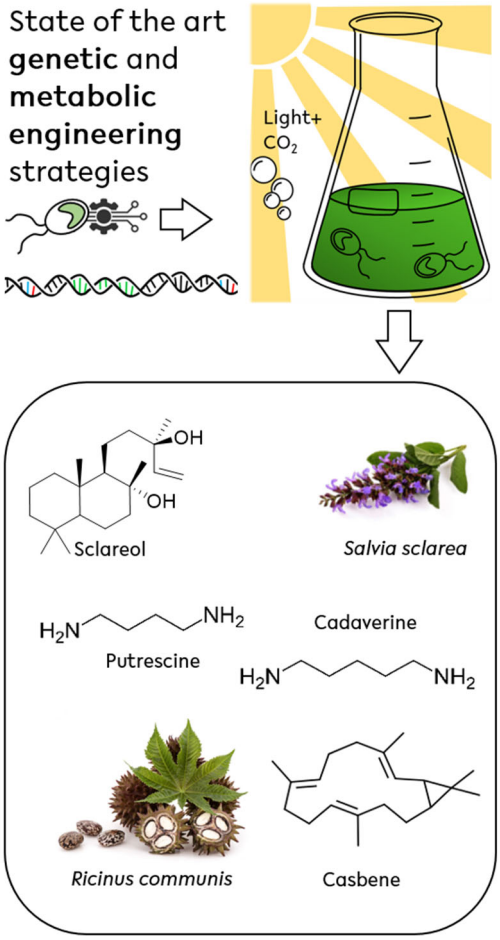

Figure 4: Carbon-based compounds that can be sustainably produced in the microalga *C. reinhardtii*.

In addition to producing high-value compounds, the algae biotechnology group has expanded its capabilities of bulk chemical manufacturing for use in the bio-polymer industry. The most recent achievement concerns overproduction of the native diamine putrescine, which acts as a monomer during bio-polyamide production similar to cadaverine. Utilizing sophisticated genome editing via CRISPR/Cas9 (Freudenberg et al., 2022b), the key putrescine degrading enzyme in *C. reinhardtii* was identified. Further modifying the endogenous put-

rescine metabolism by overexpression of key pathway enzymes, successfully raised production titers to 200 mg L^{-1} in a high cell density, phototrophic cultivation. Productivities are competitive with certain bacteria fermentations, which utilize pre-treated rice-straw feedstock as primary carbon source.

References

Einhaus, A., Steube, J., Freudenberg, R.A., Barczyk, J., Baier, T., Kruse, O., 2022. Engineering a powerful green cell factory for robust photoautotrophic diterpenoid production. Metab. Eng. 73, 82–90. https://doi.org/10.1016/j.ymben.2022.06.002

a) Freudenberg, R.A., Wittemeier, L., Einhaus, A., Baier, T., Kruse, O., 2022. Advanced pathway engineering for phototrophic putrescine production. Plant Biotechnol. J. 1–15. https://doi.org/10.1111/pbi.13879

b) Freudenberg, R.A., Wittemeier, L., Einhaus, A., Baier, T., Kruse, O., 2022. The Spermidine Synthase Gene SPD1: A Novel Auxotrophic Marker for Chlamydomonas reinhardtii Designed by Enhanced CRISPR/Cas9 Gene Editing. Cells 11, 837. https://doi.org/10.3390/cells11050837

(A. Einhaus & R. Freudenberg)

Impressum

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