Heinrich Heine Universität Düsseldorf

3 PhD positions (3 Doktoranden-Stellen) (m/f/d), 50% TV-L E13

Three PhD positions are available at the Institute of Biochemistry, **Chair Biochemistry II** at the Heinrich Heine University Düsseldorf. The positions are for **3 years** and start by **March 2024**.

1. PhD position 1 (PhD 1)

The semi-synthetic lignan derivatives etoposide and teniposide are chemotherapeutic compounds of great clinical importance. Their natural precursors (-)-deoxypodophyllotoxin and (-)-podophyllotoxin are conventionally isolated from the roots and rhizomes of *Podophyllum hexandrum*, which is now endangered by overexploitation and environmental damage. In order to meet the high demand, individual parts of the (-)-deoxypodophyllotoxin biosynthetic pathway were reconstituted in *E. coli* in earlier work in our group.

The tasks of the PhD student in this project:

(i) Optimization of a toolbox for CRISPR/Cas-assisted chromosomal gene integration in *E. coli*.

(ii) Integration of the complete lignan pathway into the genome of *E. coli*.

(iii) Optimization of the biosynthetic pathway by fine-tuning gene expression.

(iv) Scaling up from shake flask to 5L bioreactor scale.

2. PhD position 2 (PhD 2)

Cellulose fibres are widely used in the textile, material reinforcement and paper industries. They are produced in complex processes that are energetically costly and can require large amounts of water, which has a direct impact on their sustainability. To address the complexity of the lignocellulosic substrate while controlling the properties of the final product, an alternative biotechnological approach will be developed in this multidisciplinary project with five partner groups. The tasks of the PhD student in this project:

(i) Identification of enzymes for degumming, bleaching and modifying the properties of cellulosic fibres.

(ii) Cloning and expression of the enzymes that degrade hemicellulose and pectic polysaccharides in *E. coli* or *Pichia pastoris* at a scale of up to 5 L.

(iii) Purification and characterization of the enzymes with regard to their catalytic properties, possible inhibitors and pH and solvent stability.

(iv) Site-directed mutagenesis to construct tailored enzyme variants that will be applied individually or in combination for fibre modification.

3. PhD position 3 (PhD 3)

Site-specific derivatization of complex plant-derived natural products is a challenging task for synthetic chemistry. In this respect, oxygenases like cytochromes P450 (P450s) and unspecific peroxygenases (UPOs) are attractive candidates for this purpose, because these enzymes are capable of late-stage oxidation of non-activated C-H-bonds. Protein engineering can be applied to extend their substrate spectrum and increase their activity and selectivity. The tasks of the PhD-candidate will be located in enzyme engineering of selected oxygenases to achieve selective oxyfunctionalization of natural products:

(i) Screening of in-house libraries of oxygenases.

(ii) Protein engineering of P450s and UPOs.

(iii) Biochemical characterization of selected optimized enzyme variants, e.g. with regard to thermo- and process stability, and determination of kinetic parameters.

(iv) Upscaling the biotransformation reactions.

Requirements

- Master degree or equivalent qualification in biochemistry, chemistry, biology, biotechnology or related disciplines
- Experience in gene cloning, heterologous protein production and protein engineering
- Additional experience in analytical methods (HPLC, GC/MS. LC/MS) or bioinformatics (e.g., Yasara, BLAST) is beneficial
- Proficient English in written and spoken form
- Interest in interdisciplinary work
- Communication skills and team spirit

Heinrich Heine University Düsseldorf aims at increasing the percentage of employed women. Applications from women will therefore be given preference in cases of equal aptitude, ability and professional achievements unless there are exceptional reasons for choosing another applicant. Applications from persons with severe disabilities or those of equal status according to Book IX of the German Social Code (SGB – Soziales Gesetzbuch) are encouraged.

Please submit your application documents (CV, degree certificates as well as an overview of achievements, letter of motivation (max. 1 page), contact details of two possible references) by 31 January 2024 in a single PDF document by e-mail to Prof. Vlada B. Urlacher vlada.urlacher@hhu.de with “PhD 1”, “PhD 2”, or “PhD 3” as subject.