Fraunhofer IME

Fraunhofer Institute for Molecular Biology and Applied Ecology IME

Director
Prof. Dr. Stefan Schillberg

Division Molecular Biotechnology

Forckenbeckstraße 6
52074 Aachen
Germany

Dr. Henrik Nausch
Head of Department Bioprocess Engineering
Phone +49 241 6085-35112 | Fax -6085-1000
Henrik.nausch@ime.fraunhofer.de
www.ime.fraunhofer.de

Fraunhofer IME | Forckenbeckstraße 6 | 52074 Aachen

Bachelor-/Master thesis at the Fraunhofer IME
Department Bioprocess Engineering

To interested students in
Biology and Biotechnology

Aachen, 12.03.2025

Design and production of recombinant immunotoxins in plants

Abstract Current cancer therapies are based on antibody drug conjugates (ADCs) which consist of a monoclonal antibody (mAb) and a synthetic toxin, which are produced separately and then coupled in vitro. However, the complex production leads to high production costs, ranging from \$150,000 g^{-1} for widespread cancer types like breast cancer to \$1,000,000,000 g^{-1} for rare diseases like acute myeloid leukemia (AML). One alternative to ADCs might be recombinant immunotoxins (RITs), where a mAb is combined with a proteinogenic toxin and which can be produced in one step as fusion protein, reducing the production costs below \$30,000 g^{-1}. While the RITs interfere with the host metabolism in mammalian cell lines and thus are produced at low accumulation levels of less than 10 mg L^{-1}, plants proofed to be suitable for their production, since they can express the RIT in the vacuole, where it does not impact the metabolism, yielding up to 300 mg kg^{-1} of the RIT. Moreover, plants can be efficiently transiently transformed, and thus can be produce relevant amounts within 1-3 months, while mammalian cells need to be stably transformed which takes 6-12 months. Hence, plants can be used for the fast and economic production of RITs in particular for rare diseases like AML. This was demonstrated for the RIT VisA-H22 with an accumulation level of 40 mg kg^{-1} by using the plant cell pack (PCP) technology for screening. For further information see the following review DOI: 10.1016/j.biotechadv.2020.107683 and paper DOI: 10.1080/21655979.2023.2244235.
Task: The aim of the thesis is to develop novel RITs against AML, i.e. the anti-CD64 antibody H22 should be coupled with the proteinogenic toxins Melittin, Abrin, Bryodin, and Diphtheria toxin, expressed in plant cells via the PCP technology and tested for their cytotoxicity at the cell lines MonoMac-1, THP-1 and HL-60. This comprises i) the cloning of RIT expression cassettes and vectors, the transient transformation of plant cells and analysis of the RIT accumulation, ii) the production of selected RIT candidates in whole plants to produce sufficient quantities, and iii) the affinity and activity screening of RITs at MonoMac-1, THP-1 and HL-60 cells.
Duration: The time for the completion of the above-mentioned project will initially be set to 6 months. During the course of the project, progress will be documented using an electronic lab-book and communicated at least on a weekly basis with the supervisors as well as monthly progress reports. The overall progress will be monitored via Gantt chart. An internship is offered in advance to the thesis for orientation and familiarization with the upcoming tasks and equipment.
Requirements: The student successfully applying for this project has good basic knowledge in molecular biotechnology and bioengineering. S/He is skilled in written and spoken English to familiarize her/himself with the relevant protocols and to fluently communicate within the international atmosphere of the Fraunhofer IME.
Contact: For further questions and applications, please contact Monique Schulze (monique.schulze@ime.fraunhofer.de).