Engineered Halogenases for the Late Stage Functionalization of Added-Value Chemicals

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Project Summary

Nature offers an enormous plethora of enzymes which catalyze chemical transformations also for reactions which are not easily performed by organic synthesis due to the lack of specificity or low yields. In addition, the implementation of biocatalytic steps in industrial processes is a powerful tool to increase sustainability of chemical productions.

Halogenation is a biocatalytic transformation which is not often explored for industrial processes. However, in the context of the discovery of a range of novel halogenases, this type of biotransformation is being reconsidered as a greener, more sustainable and more regio- and enantiospecific alternative to chemical halogenations. To tackle the challenge of harnessing halogenases for industrial processes, a collaboration between Novartis Pharma AG, Syngenta and the Competence Center of Biocatalysis (CCBIO) at the ZHAW was initiated with the aim to implement bio-halogenation processes for substrates of pharmaceutical and agrochemical interest.

Current halogenating enzymes very often suffer from instability and very narrow substrate scope. Within this call we will address those drawbacks by enzyme engineering and thus alter the selected enzymes' properties in order to prepare robust and broad-use biocatalysts for aliphatic and aromatic halogenations. Modern tools for enzyme discovery, combined with increasingly reliable strategies for protein engineering have expanded the range of enzymes with practical applications. We envisage to applying this proven technology to the design of novel halogenases for a regioselective green synthesis, addressing the shortcomings of chemical methods and providing Syngenta, Novartis and the wider academic and industrial community with access to high-value low-molecular-weight intermediates, APIs, or agrochemicals.

Success in this field will lead to a wider uptake of halogenating enzymes, and biocatalysis in general, and is highly aligned with the "Late Stage Functionalisation Initiatives" between Syngenta and Novartis. Having access to robust, regioselective and scalable halogenases will results in a significant time and cost savings in synthesis of novel drugs and agrochemicals and will allow the preparation of novel compounds not possible or difficult to manufacture with conventional chemical methods. Enzymatic halogenation would also contribute to the establishment of a greener and more sustainable way of producing pharmaceutical or agrochemical compounds and expand the biocatalytic toolbox through the development of tailored enzymes which offer access to novel chemistries.