DEVELOPMENT AND APPLICATION OF NOVEL ENGINEERED TRANSAMINASE PANELS ASSISTED BY IN-SILICO RATIONAL DESIGN FOR THE PRODUCTION OF CHIRAL AMINES

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There is a high demand for the synthesis of chiral amines as building blocks for a large number of industrially valuable compounds. Transaminases (TAm) offer an enzymatic route for the synthesis of chiral amines that avoids complex chemical synthesis [1]. However, their catalytic efficiency towards bulky ketone substrates is greatly limited by steric hinderance [2]. This poster highlights a rational design strategy of combining in silico and in vitro methods to engineer the transaminase enzyme with a minimal number of mutations, achieving high catalytic activity and high enantioselectivity. The wildtype TAm showed no detectable activity towards the ketone 2-acetylbiphenyl but upon introduction of two mutations detectable enzyme activity was observed. The reaction rate was improved a further 1716-fold with the rationally designed variant, that contained a further 5 mutations, producing the corresponding enantiomeric pure (S)-amine (enantiomeric excess (ee) value of >99%)[3].
In addition, screening of in silico designed (R)-TAm mutant panels in resolution mode offered an attractive and efficient route for the preparation of problematic (S)-amines. A mutant was identified from the panels that gave complete resolution of the racemic amine (high substrate loading) to leave the desired enantiomer at a low enzyme loading fit for process development towards an economically viable scale up process.

[1] R. C. Simon, et al, ACS Catal. 2014, 4(1)
[2] F. Steffen-Munsberg, et al, ChemCatChem 2013, 5, (1)
[3]D.F.A.R.Dourado et al, ACS Catal. 2016, 6 (11)