

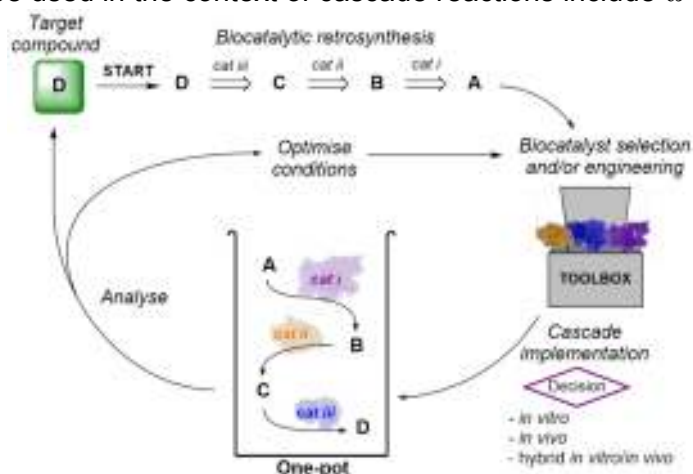
Design and Evolution of New Biocatalysts for Organic Synthesis

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This lecture will describe recent work from our laboratory aimed at developing new biocatalysts for enantioselective organic synthesis, with a particular emphasis on the design of *in vitro* and *in vivo* cascade processes for generating chiral pharmaceutical building blocks. By applying the principles of 'biocatalytic retrosynthesis' we have shown that it is now increasingly possible to design new synthetic routes to target molecules in which biocatalysts are used in the key bond forming steps [1].

The integration of several biocatalytic transformations into multi-enzyme cascade systems, both *in vitro* and *in vivo*, will be addressed in the lecture. In this context monoamine oxidase (MAO-N) has been used in combination with other biocatalysts and chemocatalysts in order to complete a cascade of enzymatic reactions [2-4]. Other engineered biocatalysts that can be used in the context of cascade reactions include ω -transaminases [5], ammonia lyases [6], amine dehydrogenases [7], imine reductases [8], and artificial transfer hydrogenases [9]. We shall also present some very recent work regarding the discovery of a new biocatalyst for enantioselective reductive amination and show how these enzymes can be used to carry out redox neutral amination of alcohols via 'hydrogen borrowing' [10].



- [1] N.J. Turner and E. O'Reilly, *Nature Chem. Biol.*, **2013**, *9*, 285-288; M. Hönic, P. Sondermann, N.J. Turner and E.M. Carreira, *Angew. Chem. Int. Ed.*, **2017**, *56*, 8942-8973; [2] D. Ghislieri et al., *J. Am. Chem. Soc.*, **2013**, *135*, 10863-10869; [3] J.H. Schrittwieser et al., *Angew. Chem. Int. Ed.*, **2014**, *53*, 3731-3734; [4] N.J. Turner et al., *Angew. Chem. Int. Ed.*, **2014**, *53*, 2447-2450; [5] A. Green et al., *Angew. Chem. Int. Ed.*, **2014**, *53*, 10714-10717; P. Both, H. Busch, P.P. Kelly, F.G. Mutti, N.J. Turner and S.L. Flitsch, *Angew. Chem. Int. Ed.*, **2016**, *55*, 1511-1513; [6] S.L. Lovelock et al., *Angew. Chem. Int. Ed.*, **2014**, *53*, 4652-4656; F. Parmeggiani, S.L. Lovelock, N.J. Weise, S.T. Ahmed and N.J. Turner, *Angew. Chem. Int. Ed.*, **2015**, *54*, 4608-4611; N.J. Weise, F. Parmeggiani, S.T. Ahmed and N.J. Turner, *J. Am. Chem. Soc.*, **2015**, *137*, 12977-12983; [7] F.G. Mutti, T. Knaus, N.S. Scrutton, M. Breuer and N.J. Turner, *Science*, **2015**, *349*, 1525-1529; [8] R.S. Heath, M. Pontini, S. Hussain and N.J. Turner, *ChemCatChem*, **2016**, *8*, 117-120; S.P. France, S. Hussain, A.M. Hill, L.J. Hepworth, R.M. Howard, K.R. Mulholland, S.L. Flitsch and N.J. Turner, *ACS Catal.*, **2016**, *6*, 3753-3759; [9] V. Koehler et al., *Nature Chem.*, **2013**, *5*, 93-99; [10] G.A. Aleku, S.P. France, J. Mangas-Sanchez, S.L. Montgomery, F. Leipold, S. Hussain, H. Man, M. Sharma and G. Grogan and N.J. Turner, *Nature Chem.*, **2017**, *9*, 961-969; G.A. Aleku, J. Mangas-Sanchez, J. Citoler, S.P. France, S.L. Montgomery, R.S. Heath, M.P. Thompson and N.J. Turner, *ChemCatChem*, **2018**, *10*, 515-519.