McGill Chemical Society Seminar Series

Tuesday, 6 October, 2015, 1:00 PM

Otto Maass Chemistry Building, **Room 10**

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Design and Evolution of New Biocatalysts for Organic Synthesis

***T**his lecture will describe recent work from our laboratory aimed at developing new biocatalysts for enantioselective organic synthesis, with a particular emphasis on the application of engineered biocatalysts for sustainable synthesis. By applying the principles of 'biocatalytic retrosynthesis' it is possible to design new synthetic routes to target molecules in which biocatalysts are used in the key bond forming steps.[1]*

For example, monoamine oxidases (MAO-N) are a family of enzymes that catalyze the (S)-selective oxidation of amines to imines. MAO-N can be used as biocatalysts to obtain enantiomerically pure chiral amines by deracemisation or desymmetrisation of substrates. Recently new variants of MAO-N have been developed via a combination of directed evolution and rational design in order to broad the enzyme's substrate specificity.[2] The new mutants have been used for the deracemisation of primary and secondary amines such as (R)-4-chlorobenzhydrylamine (building block for the synthesis of Levocetirizine), (S)-1-phenyl-1,2,3,4-tetrahydroisoquinoline (for the synthesis of Solifenacin) and the two alkaloids (R)-Harmicine and (R)-Eleagnine.

The integration of several biocatalytic transformations into multi-enzyme cascade systems has also been a focus of recent work in our laboratories. In this context MAO-N has been used in combination with other biocatalysts and chemocatalysts in order to complete a cascade of enzymatic reactions.,[3,4] Other engineered biocatalysts that can be used in the context of cascade reactions include ω-transaminases[5], phenylalanine ammonia lyases[6], amine dehydrogenases[7] and imine reductases.[8]

References

1 N.J. Turner and E. O'Reilly, *Nature Chem. Biol.*, **2013**, *9*, 285-288. 2 D. Ghislieri, A.P. Green, M. Pontini, S.C. Willies, I. Rowles, A. Frank, G. Grogan and N.J. Turner, *J. Am. Chem. Soc.*, **2013**, *135*, 10863-10869. 3 N.J. Turner, E. O'Reilly, C. Iglesias, D. Ghislieri, J. Hopwood, J.L. Galman and R.C. Lloyd, *Angew. Chem. Int. Ed.*, **2014**, *53*, 2447-2450. 4 V. Koehler *et al.*, *Nature Chem.*, **2013**, *5*, 93-99. 5 A. Green, N.J. Turner and E. O'Reilly, *Angew. Chem. Int. Ed.*, **2014**, *53*, 10714-10717. 6 F. Parmeggiani, S.L. Lovelock, N.J. Weise, S.T. Ahmed and N.J. Turner, *Angew. Chem. Int. Ed.*, **2015**, *54*, 4608–4611. 7 F.G. Mutti, T. Knaus, N.S. Scrutton, M. Breuer and N.J. Turner, *Science*, **2015**, *349*, in press. 8 R.S. Heath, M. Pontini, S. Hussain and N.J. Turner, *ChemCatChem*, **2015**, in press.

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