Design and implementation of de novo biosynthetic cascades

Sabine L Flitsch, School of Chemistry & MIB, The University of Manchester (www.flitschlab.com)

The combination of sequential biocatalytic reactions in non-natural synthetic cascades is a rapidly developing field and leads to the generation of complex valuable chemicals from simple precursors. As the toolbox of available biocatalysts continues to expand, so do the options for biocatalytic retrosynthesis of a target molecule, leading to new routes employing enzymatic transformations. The implementation of such cascade reactions requires careful consideration, particularly with respect to whether the pathway is constructed *in vitro* or *in vivo*. This lecture will showcase three successful *de novo cascades* and discuss the relative merits of *in vitro*, *in vivo* or hybrid approaches to building biocatalytic cascades and analytical challenges. Biocatalysts were obtained either directly from genomic libraries, or by re-design of enzyme activity to suit requires substrate specificity and selectivity.

Recent references: ACS Catalysis 2017, 7, 710; ACS Catalysis 2017, 7, 2920; JACS 2017, 139, 1408; ACIE 2017, 56, 1; ACIE 2017, 56, 14498; Nature Comm 2017, 8, 973; ACIE 2016, 55, 1511; Nature Chemistry 2014, 6, 65; JACS 2012, 134, 4521.