EuroSciCon

August 08-09, 2019
Paris, France

EuroSciCon Joint Event On
Biotechnology , Biochemistry and Aquaculture

Biochem Mol biol J 2019, Volume: 5

ENGINEERING THE BONA FIDE NATURAL DIELS-ALDERASE, ABYU

Kavita Tiwari, Laurence Maschio, Sbu Mbatha, Chris Willis and Paul Race
University of Bristol, UK

The Diels-Alder reaction, a [4+2] cycloaddition to yield cyclohexenes, is one of the most powerful chemical reactions known in synthetic chemistry. It is used extensively in the preparation of a multitude of many important compounds, including antibiotics, anti-cancer drugs and agrochemicals. In biocatalytic processes, natural catalysts, such as enzymes, perform chemical transformations on organic compounds. Applications of bio catalysts are driven by the need for more sustainable manufacture of chemicals and catalytic, (enantio) selective methods for the synthesis of pharmaceutical intermediates. Development of novel biocatalysts for the reactions would potentially enable new, efficient and 'green' synthetic routes to a wide variety of valuable bioactive compounds. Revolutionary developments in protein engineering and directed evolution for the optimisation of enzyme function and performance has totally changed the biocatalysis landscape today. Discovering and inventing new biocatalytic processes, based on (meta) genomic sequencing, evolving enzyme promiscuity, chemo mimetic bio catalysis, artificial metalloenzymes, and the introduction of non-canonical amino acids into proteins, are pushing back the limits of bio catalysis function. Recently, we discovered a key enzyme, AbyU, involved in the biosynthesis of the broad-spectrum antibiotic abyssomicin C. Abyssomicin C is a broad-spectrum antibacterial natural product that was first isolated from a dep-sea bacterium *Verrucosispora maris*. AbyU, a spirotetronate cyclase, was subsequently shown to be a bona fide natural Diels-Alderase. Efforts to evolve promiscuity of AbyU that could open up a raft of potential applications for synthetic chemist are presently on. Here I outline progress across two strands of activity: a mutagenesis programme focused on expansion of the substrate selectivity of AbyU, in an effort to further diversify the range of accessible spirotetronates beyond those reported from natural sources; fundamental studies of the engineered variants of AbyU, exploring the kinetic mechanism by which the catalysis is achieved.

kt17533@bristol.ac.uk