EuroSciCon

EuroSciCon Congress on

Enzymology and Molecular Biology

August 13-14, 2018
Paris, France

Insights Enzyme Res 2018, Volume 2
DOI: 10.21767/2573-4466-C1-003

# SUBSTRATE LOCKING PROMOTES DIMER-DIMER DOCKING OF AN ENZYME ANTIBIOTIC TARGET

**Matthew A Perugini[1,2], Sarah C Atkinson[1,2,3], Con Dogovski[2], Kathleen Wood[4], Michael D W Griffin[2], Michael A Gorman[5], Lilian Hor[1], Cyril F Reboul[3], Ashley M Buckle[3], Joachim Wuttke[6], Michael W Parker[2,5] and Renwick C J Dobson[7]**

[1]La Trobe University, Melbourne, Australia
[2]Bio21 Institute, University of Melbourne, Victoria, Australia
[3]Monash University, Clayton, Australia
[4]Australian Nuclear Science & Technology Organisation, New South Wales, Australia
[5]St. Vincent's Institute of Medical Research, Victoria, Australia
[6]JCNS-Heinz Maier-Leibnitz Zentrum (MLZ), Forschungszentrum Juelich GmbH, Garching, Germany
[7]University of Canterbury, Christchurch, New Zealand

**Protein dynamics manifested through structural flexibility play a central role in the function of biological molecules. Here we explore the substrate-mediated change in protein flexibility of an enzyme antibiotic target, *Clostridium botulinum* dihydrodipicolinate synthase (DHDPS). We demonstrate that the substrate, pyruvate, stabilizes the more active dimer-of-dimers or tetrameric form of the enzyme. Surprisingly, there is little difference between the crystal structures of apo and substrate-bound DHDPS, suggesting protein dynamics may be important. Neutron and small angle X-ray scattering experiments were used to probe substrate-induced dynamics on the sub-second timescale, but no significant changes were observed. We have therefore developed a simple technique, coined Protein Dynamics-Mass Spectrometry (ProD-MS), which enables measurement of time-dependent alkylation of cysteine residues. ProD-MS together with X-ray crystallography and analytical ultracentrifugation analyses indicates that pyruvate locks the conformation of the dimer that promotes docking to the more active tetrameric form, offering new insight into ligand-mediated stabilization of multimeric enzymes.**

M.Perugini@latrobe.edu.au