KEYNOTE:

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Dr. David Jakeman received his BSc and PhD degrees at the University of Sheffield in the United Kingdom studying bioorganic chemistry with Michael Blackburn and Michael Williamson. He then moved to Washington State University in the USA and worked on enzyme mechanisms with Dr. Jeremy Evans. Subsequently he moved to the University of British Columbia where he developed an appreciation for carbohydrate enzymology with Dr. Stephen Withers, and moved to the College of Pharmacy at Dalhousie University in August 2001. His research interests include carbohydrate active enzymes, synthesis of bioactive molecules and natural products

Rhamnose biosynthesis as an antibacterial target

L-Rhamnose biosynthesis is a ubiquitous pathway in many pathogenic Gram-positive, Gram-negative and mycobacteria. Genetic studies have demonstrated that the pathway contributes significantly to virulence and pathogenicity of many organisms, including Mycobacterium tuberculosis and the ESKAPE organisms that have developed multi-drug resistance. Rhamnose is a 6-deoxy-L-sugar absent from mammalian cells, and, thus, the biosynthesis of rhamnose offers multiple potential drug targets. The five biochemical steps for L-rhamnose biosynthesis are well documented, with glucose 6-phosphate ultimately being converted to thymdine diphospho rhamnose (TDP-beta-L-Rha). We will discuss rationales for the discovery of inhibitors of the enzymes in rhamnose biosynthesis, and describe the synthetic, chemoenzymatic, computational, enzymological and structural characterization of inhibitors and their targets, and the challenges and successes.