James MacRae, J Comput Sci Syst Biol, 5:1
doi: http://dx.doi.org/10.4172/0974-7230.S1.06

OMICS Group Conferences
Accelerating Scientific Discovery

International Conference and Exhibition on
Metabolomics & Systems Biology

20-22 February 2012 San Francisco Airport Marriott Waterfront, USA

Metabolomic approaches to delineating fatty acid biosynthesis in the apicomplexan parasite *Toxoplasma gondii*

James Ian MacRae

University of Melbourne, Australia

Apicomplexan parasites are responsible for high impact human diseases such as malaria, toxoplasmosis and cryptosporidiosis. These obligate intracellular pathogens are dependent on both *de novo* lipid biosynthesis as well as the uptake of host lipids for biogenesis of parasite membranes and the membranes of vacuoles within which they reside. Genome annotations and biochemical studies indicate that apicomplexan parasites can synthesize fatty acids via a number of different biosynthetic pathways that are differentially compartmentalized. However, the relative contribution of each of these biosynthetic pathways to total fatty acid composition of intracellular parasite stages remains poorly defined. Here we use a combine metabolomics with genetic and biochemical approaches to delineate the contribution of fatty acid biosynthetic pathways in *Toxoplasma gondii*. Metabolic labeling studies with ^{13}C-glucose and ^{13}C-acetate showed that intracellular tachyzoites synthesized a range of long and very long chain fatty acids (C14:0-26:1). Genetic disruption of type II fatty acid synthase (FASII) resulted in greatly reduced synthesis of saturated fatty acids up to eighteen carbons long, leading to reduced intracellular growth that was partially restored by addition long chain fatty acids. In contrast, synthesis of very long chain fatty acids was primarily dependent on a fatty acid elongation system comprising three elongases, two reductases and a dehydratase that were localized to the endoplasmic reticulum. The function of these enzymes was confirmed by metabolomics and heterologous expression in yeast. This elongase pathway appears to have a unique role in generating very long unsaturated fatty acids (C26:1) that cannot be salvaged from the host.

Biography

James MacRae completed his PhD in 2005 at the University of Dundee, Scotland, studying the surface glycoconjugates and glycobiology of Trypanosoma cruzi. He then attained a Royal Society Fellowship in the laboratory of Professor Malcolm McConville at the University of Melbourne, where he has been leading development of metabolomic approaches in the investigation of, and identification of potential drug targets in, protozoan parasites, including Plasmodium falciparum, Toxoplasma gondii, Leishmania spp and fungi. He is also collaborating closely with Metabolomics Australia (a government-funded nationwide initiative) in order to develop systems biology techniques.