University of Birmingham

Dr Luke Alderwick PhD

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About

In 2010 Dr Luke Alderwick was appointed to the position of Lecturer in Molecular Microbiology and he is one of the youngest members of academic staff in the School of Biosciences. His many research interests revolve around understanding the biochemistry and molecular genetics of cell wall assembly in *Mycobacterium tuberculosis,* which is the causative bacterial agent of TB infections. In close collaboration with Prof Gurdyal Besra and Dr Apoorva Bhatt, Dr Alderwick forms a trio of Principle Investigators heading one of the worlds leading academic research groups studying *M. tuberculosis* physiology, genetics and molecular microbiology

Qualifications

BSc (University of Birmingham)

PhD (University of Birmingham)

Biography

After graduating from the University of Birmingham in 2003 with first class honours degree in BSc Biochemistry, Dr Alderwick continued his academic training *in situ*, progressing from PhD graduate to recently appointed Lecturer in Molecular Microbiology. His PhD studies carried out under the supervision of Prof Gurdyal Besra and centred on uncovering the molecular genetics and biochemistry of cell wall assembly in *Mycobacterium tuberculosis*.

The research carried out during his PhD training culminated in 5 scientific publications and he was subsequently awarded the Dr S. W, Challinor Prize for the best PhD thesis of the 2007. Many of his results generated during his PhD formed the basis of a Wellcome Trust program grant, which was successfully awarded and enabled Dr Alderwick to remain in the lab and continue his post-doctoral research investigating the molecular processes behind complex cell wall polysaccharide biosynthesis in mycobacteria. In 2010, Dr Alderwick was appointed to the position of Lecturer in Molecular Microbiology in the School of Bioscience. In 2012, Dr Alderwick was made Director of the Birmingham Drug Discovery facility.

Teaching

The successful career progression of Dr Alderwick, from undergraduate to scientific researcher and lecturer, is partly due to the excellent training and teaching he received at the School of Biosciences. As a result, he has a unique insight and appreciation of the modern day student studying at Birmingham. Dr Alderwick teaches course material in the following modules

Year 1

- Microbiology and Infectious Disease
- Physical Biochemistry
- Human Biochemisry
- Biochemistry

Year 2

- Membranes, Energy and Metabolism

Year 3

- Molecular Basis of Bacterial Infection

Postgraduate supervision

For a list of possible PhD projects offered by Dr Alderwick **www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Alderwick (http://www.findaphd.com/search/customlink.asp?inst=birm-Biol&supersurname=Alderwick)**

Research

Research Theme

Molecular Microbiology

Cell wall biosynthesis and assembly in *Mycobacterium tuberculosis*

Tuberculosis (TB) affects a third of the worlds population and causes 1.7 million deaths annually. *Mycobacterium tuberculosis*, the causative agent of TB, has a unique cell envelope which differs substantially from the cell wall of both Gram-negative and Gram-positive bacteria. This accounts for its unusual low permeability and hence, contributes to resistance against common antibiotics. The main structural element consists of a cross-linked network of peptidoglycan (PG) in which some of the muramic acid residues are substituted with a complex polysaccharide, arabinogalactan (AG), attached to which are long chain mycolic acids (Figure 1 below).

Aspects of mycobacterial cell wall biosynthesis remain fragmented, particularly those associated with mechanisms of PG biosynthesis and how the cell wall is 'stitched' together. A broad aim of my research involves understanding the mechanisms of mycobacterial PG biosynthesis and how this crucial cell wall structure is recycled during dormancy. Furthermore, I am also interested in how large polysaccharide structures are translocated and covalently attached to the mycobacterial cell wall. Biochemical and structural analysis of these crucial enzymes will shed new light on how mycobacteria assembles its murein sacculus. It will also provide invaluable information regarding subtle alterations that are present in mycobacterial PG, which could reveal potential mechanisms for inhibition and the eventual pursuit of new therapies targeted towards dormant TB infection.

The advent of multi-dug and extensively-drug resistant TB means there has never been a greater need to identify new novel drug targets.

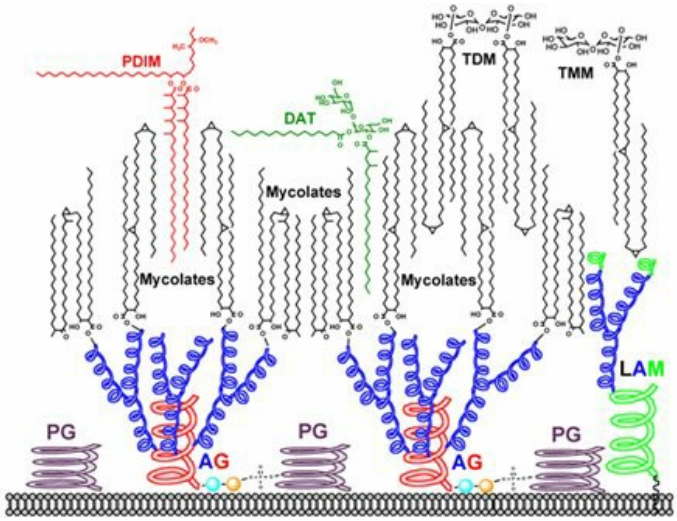

Figure 1

The *M. tuberculosis* cell wall is composed of peptidoglycan (PG), arabinogalactan (AG), mycolic acids and lipoglycans such as phosphoinositolmannosides (PIM), lipomannan (LM) and lipoarabinomannan (LAM). Other cell wall associated lipids include trehalose dimycolate (TDM), trehalose monomycolate (TMM), sulpholipids (SL), phthiocerol dimycocerosate (PDIM) and di-acyl trehalose (DAT).

The University of Birmingham Drug Discovery and Screening Facility

Dr Alderwick is the Director of the University of Birmingham Drug Discovery and Facility. This £700k investment provides a cutting-edge research facility which is located in the School of Biosciences at the Institute of Microbiology and Infection (IMI). The state-of-the-art lab enables our world-leading research groups to undertake cutting-edge drug discovery research in areas such as infectious diseases and cancer. Academia has contributed immensely in advancing the frontiers of science related to fundamental medical research. However, it has generally been ”Big Pharma” that has translated this research into the discovery and development of new drugs. The primary reason for this disparity has been the cost of the various facets of modern drug discovery, particularly the necessary equipment to quickly and efficiently carry out screening experiments in a high throughput capacity.

Other activities

Dr Alderwick is a keen cyclist and has various other sporting interests, which include football, rugby and golf. When he’s not busy working he enjoys listening to contemporary music, but spends most of his free time at home with friends and family.

Publications

Batt SM, Jabeen T, Bhowruth V, Quill L, Lund PA, Eggeling L, Alderwick LJ, Fütterer K, Besra GS. Structural basis of inhibition of Mycobacterium tuberculosis DprE1 by benzothiazinone inhibitors. *PNAS*. 2012 Jul 10;109(28):11354-9. doi:10.1073/pnas.1205735109. Epub 2012 Jun 25. PMCID: PMC3396498
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Alderwick LJ, Dover LG, Veerapen N, Gurcha SS, Kremer L, Roper DL, Pathak AK, Reynolds RC, Besra GS. Expression, purification and characterisation of soluble GlfT and the identification of a novel galactofuranosyltransferase Rv3782 involved in priming GlfT-mediated galactan polymerisation in Mycobacterium tuberculosis. Protein Expr Purif. 2008 Apr;58(2):332-41. Epub 2007 Dec 8. PubMed PMID: 18248822.

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