University of Birmingham

Professor Ian Henderson PhD

Professor of Microbial Biology

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About

Ian Henderson is Professor of Microbial Biology in the College of Medical and Dental Sciences.

Ian has published over 70 articles in the fields of bacteriology, biochemistry and infection immunology. He has received major grants from the Medical Research Council and the Biotechnolofy and Biological Sciences Research Council.

Ian is enthusiastic about public engagement in the Sciences and has given frequent talks to various groups at both the local and national level. He helped set up the Medicine Matters exhibit at the ThinkTank, Birmingham's contemporary science museum. Ian frequently contributes to both the local and national media.

Qualifications

- Ph.D. Molecular Microbiology, Trinity College Dublin, 1991-1996
- B.Sc. (Hons) 2.i. Microbiology (Chemistry minor), University College Dublin, 1986-1990

Biography

Prof. Henderson began his academic studies reading an Honours degree in Microbiology at University College Dublin. After University he worked as a research assistant position studying HIV at the Wellcome Laboratories. He then returned to study for a Ph.D. in molecular bacteriology at Trinity College Dublin. The success of his Ph.D. led to a productive postdoctoral position at the Centre for Vaccine Development, University of Maryland, USA working with Prof. James Nataro. After his postdoctoral studies, he took up a faculty position in Queens University Belfast before rapidly transitioning to the University of Birmingham. At Birmingham he established a group investigating protein secretion and developed an expansive network of University-wide collaborations. Prof. Henderson has been involved with the Society for General Microbiology for over 10 years and became chair of the Prokaryotic Division in 2009. He has been an editor for several Microbiology journals and has served on a variety of grant-awarding bodies.

Teaching

Teaching Programmes

BMedSci (/undergraduate/courses/med/medicine.aspx) Years 1, 2 and 3

Postgraduate supervision

Ian is interested in supervising doctoral research students in the following areas:

- The biochemical understanding of bacterial protein secretion mechanisms
- The genetic and biochemical basis of outer membrane integrity
- Immune responses to bacterial surface proteins
- Pathogenesis of Salmonella, *E. coli* and Pseudomonas infections.

If you are interesting in studying any of these subject areas please contact Ian using the contact details above, or for any general doctoral research enquiries, please email: **dr@contacts.bham.ac.uk (mailto:dr@contacts.bham.ac.uk)** .

For a full list of available Doctoral Research opportunities, please visit our **Doctoral Research programme listings (http://www.bham.findaphd.com/?es=y&apl=y&aplt=&show)** .

Research

RESEARCH THEMES

Protein secretion, Cell envelope biology, Bacterial pathogenesis, Immune response to Bacterial infections, Antimicrobials

RESEARCH ACTIVITY

My research interests focus on the bacterial cell surface. This focus is based on the philosophy that the bacterial cell surface offers a rich source of molecules which can be utilized and adapted to treat or prevent infections.

Autotransporters

Protein secretion machines are the instruments of microbial warfare! Using these machines bacteria produce adhesins, toxins, enzymes and mediators of motility. These proteins are either secreted to or beyond the bacterial cell surface. These secreted proteins may interact directly with host cells resulting in disease. The simplest and most widely utilised secretion systems fall under the rubric of Type 5 secretion systems (T5SS). This category comprises those proteins secreted by the classical Autotransporter system, the two-partner system and the trimeric Autotransporter system. The importance of proteins secreted via the T5SS is illustrated by the fact that in some cases they form part of current human vaccines; thus filamentous haemagglutinin and pertactin are essential components of the acellular whooping cough vaccine. Furthermore, Autotransporters are often essential virulence factors and in the case of Shigella, the agent of bacillary dysentery, abolition of the gene encoding the Autotransporter IcsA results in an attenuated strain which forms the basis for a live attenuated Shigella vaccine. Thus, further understanding of these proteins may lead to greater healthcare benefits. For the last 17 years Prof. Henderson's work has focussed on group the Autotransporter proteins. This work has ranged from investigating the mechanisms of gene regulation, the molecular mechanisms of biogenesis, interaction of proteins with host cells and exploiting the system for commercial protein production.

Outer membrane protein biogenesis

The outer membranes of Gram-negative bacteria are lipid bilayers. They consist of a phospholipid inner leaflet and a lipopolysaccharide outer leaflet with two major classes of protein: □-barrel proteins (OMPs) and peripheral lipoproteins. These four major components provide an interface between the bacterium and its environment; they work in concert to protect the organism from noxious substances while permitting the selective uptake of nutrients. To survive bacteria must produce OMPs that directly or indirectly allow the organism to sense the environment, to move, to stick to inanimate surfaces, host cells or each other, to exchange genetic material, to evade host defences and in the case of pathogens, to cause disease. Furthermore, OMPs are exposed, elicit immune responses and are targets of antibody and therefore a source of antigens for vaccines. In Gram-negative bacteria Antibiotic resistance is often dependent on the OMP diffusion porins (e.g. OmpF/C) and transenvelope spanning efflux complexes (e.g. ArcAB-TolC). Therefore, understanding the nature of outer membrane is crucial to the development of strategies to prevent and treat infections. For the last 5 years Prof. Henderson's group has investigated the molecular basis for outer membrane protein biogenesis.

Pathogenesis of Infection

Secreted proteins are the main nodes of interaction between pathogens and the host. Prof. Henderson's group utilises a variety of approaches to study the different mechanisms by which secreted proteins influence infection. Key outcomes to these investigations include (i) elucidating why HIV patients are more susceptible to non-typhoidal Salmonella infections (Dr. Cal MacLennan's group led this study); (ii) understanding how the immune system senses and responds to particular surface antigens (Dr. Adam Cunningham's group have led these studies); and (iii) demonstrating that not all surface proteins can elicit a protective immune response.

Bacterial Genomics

Prof. Henderson's group have been involved in sequencing bacterial genomes for over 10 years. Utilising Sanger, Illumina and 454 technologies Prof. Henderson's group have completed the genomes of the type strains for several diarrheal pathogens. These organisms place a huge societal and economic burden on populations in developing countries and afflict the youngest disproportionately. They are among the largest killers of children under age 5. The genome sequences provide the basis for developing strategies to tackle these sinister organisms.

Other activities

- 2010-2014, Governing body of St. Edwards Primary School
- 2007-2011, Society for General Microbiology, Prokaryotic Division Chair and Chair-Elect
- 2005-2008, Society of General Microbiology, Convener of the Cell and Cell Surfaces Committee
- 2005-2008, Microbiology, Associate Editor
- 2004-present, FEMS Microbiology Letters, Reviews Editor
- 2004-2005, Microbiology, Guest Editor
- 2003-2004, FEMS Microbiology Letters, Member of the Editorial Board
- 2003-2004, Science Foundation Ireland, Member of the Research Grants Microbiology Panel
- 2001-2004, Society of General Microbiology, Member of the Cell and Cell Surfaces Committee

Publications

Beatson SA, MG de Luna, AC Freitas, PA dos Santos, JTB de Melo, DL Squire, AF Cunningham, JR Fitzgerald and **IR Henderson.** 2011. Genome sequence of the emerging pathogen *Aeromonas caviae*.**J. Bacteriol.** 193:1286-1287.

Siggins MK, AF Cunningham, JL Marshall, TR Hughes, **IR Henderson**, CA MacLennan. 2011. Absent bactericidal activity of mouse serum against invasive African non-typhoidal Salmonella results from impaired complement function but not lack of antibody. **J. Immunol.** 186:2365-71.

Knowles TJ, D Browning, M Jeeves, R Maderbocus, D Squires, DL Leyton, **IR Henderson** and M Overduin. 2011. Structure and function of BamE, a member of the b-barrel assembly machinery. **EMBO Reports.** 12:123-8 (highlighted in EMBO Reports with associated comment article).

Tsai JC, M Yen, R Castillo, DL Leyton, **IR Henderson** and MH Saier, Jr. 2010. The bacterial Intimins and Invasins: a large and novel family of secreted proteins. **PLoS ONE.** 5: e14403.

Lehr U, M Schütz, P Oberhettinger, F Ruiz-Perez, J Donald, T Palmer, D Linke, **IR Henderson,** IB Autenrieth. 2010. C-terminal amino acid residues of the trimeric autotransporter adhesin YadA of *Yersinia enterocolitica* are decisive for its recognition and assembly by BamA. **Mol. Microbiol. 78**:932-46.

Ruiz-Perez F, **IR Henderson** and JP Nataro. 2010. Involvement of FkpA, a peptidyl-prolyl *cis*/*trans* isomerase in the biogenesis of EspP autotransporter protein. **Gut Microbe.** 1:339-344.

Crossman LC, RR Chaudhuri, SA Beatson, TJ Wells, M Desvaux, AF Cunningham, NK Petty, V Mahon, C Brinkley, JL Hobman, SJ Savarino, SM Turner, MJ Pallen, CW Penn, J Parkhill, AK Turner, TJ Johnson, NR Thomson, SGJ Smith and **IR Henderson**. 2010. A commensal gone bad: complete genome sequence of the prototypical enterotoxigenic *Escherichia coli* strainH10407. **J. Bacteriol.** 192:5822-31

Leyton DL, MG de Luna, YR Sevastsyanovich, K Tveen Jensen, DF Browning, A Scott-Tucker and **IR Henderson.** 2010. The unusual extended signal peptide region is not required for secretion and function of an *Escherichia coli* autotransporter. **FEMS Microbiol. Letts.** 311:133-9.

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