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About

Professor Besra heads a world-leading multidisciplinary team investigating key aspects of the microbial physiology of the Mycobacterium tuberculosis cell wall and the potential role of iNKT/CD1d therapeutics. He has been awarded and successfully managed over 35 research grants valued at over £11 million from The Wellcome Trust, the Biotechnology and Biological Sciences Research Council (BBSRC) and the Medical Research Council (MRC) during the period 2001-2011.

He has published over 340 internationally peer-reviewed articles (e.g. in Science, Nature, Immunity, Journal of Experimental Medicine, and Proceedings of the National Academy of Science USA), reviews and book chapters, been cited 15,933 times and has an H-index score of 71 (Google Scholar).

Qualifications

University of Newcastle: Chemistry BSc (HONS)

University of Newcastle: Organic Chemistry PhD

Biography

It was during my PhD studies on TB, under the guidance of Professor David E. Minnikin [Newcastle University], that I developed a thirst for research and realised that if one was to tackle fundamental biological problems, then a multidisciplinary approach would be needed. As a result, on completing my PhD in Chemistry, I undertook a period of post-doctoral training under the direction of Professor Patrick J. Brennan [Colorado State University]. This allowed me to expand my TB research capabilities into the areas of detailed biochemistry and molecular biology.

It was during this "tour abroad" that my career began to flourish: I became established as an independent researcher and continued my academic training at Colorado State University, extending further my interests into TB immunopathogenesis and the novel area of non peptide-based antigens. It was during the period 1993-1998 that my research really took off through the award of several substantial programme grants from the National Institutes of Health, USA. I decided to return to the UK in the summer of 1998 due to family commitments and accepted a position as Reader at Newcastle University. Whilst maintaining my strong collaborations in the USA, this move allowed me to establish a number of additional exciting new collaborative ventures in the UK and Europe. In 2002, I moved to The University of Birmingham to the Bardrick Research Chair of Microbial Physiology and Chemistry within the School of Biosciences.

Postgraduate supervision

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

Research

Research Theme within School of Biosciences: **Molecular and Cell Biology (/research/activity/cellbiology/index.aspx)**

We (GSB) have contributed over the past several years in understanding the characteristics of the cell wall of TB, which has been the site of action of a number of front-line TB agents. We have now opted for a broader strategy: identification of new drug targets and drug development (with Professor Minnikin); vaccine development; identification of mechanisms of intracellular survival, replication and pathogenesis; definition of the fundamental genome of the tubercle bacillus, its phenotype and the functionality of the phenotypic characteristics through derivation of mutants.

It is a widely held view that efforts to relieve the disease burden imposed by tuberculosis must benefit from concerted attempts to understand the basic biochemistry of the organism, particularly in view of the current availability genomic data from the M. Tuberculosis genome. Thus, providing a timely insight into these remarkable bacteria and several novel areas of mycobacterial cell wall physiology

The cell wall of Mycobacterium tuberculosis: A focus for new drug targets and vaccines

There has been no significant decrease in worldwide mortality due to tuberculosis (TB) since before the time of Koch; the advent of sanatoria and chemotherapy, which drastically reduced TB in the more developed countries, has had no profound effect on the global problem. The reasons for the transient increase have been well documented: the HIV/AIDS epidemic, increased immigration and transmission from high-prevalence countries, and the emergence of multi-drug resistant strains of TB.

I am internationally recognised for my work in *Mycobacterium tuberculosis* cell wall physiology. I have contributed to many areas of this field including, microbial pathogenesis, mechanisms of antibiotic resistance and drug development. More specifically, I have been involved in the structural elucidation of a number of glycolipids from mycobacteria, such as the phenolic glycolipid of *M. haemophilum*; the acylated trehaloses of *M. tuberculosis* H37Rv; the lipooligosaccharides from *M. gordonae* and the glycopeptidolipids of *M. xenopi* and *M. senegalense*. I have *extended* our knowledge of the mycolyl-arabinogalactan complex from *M. tuberculosis* and have obtained a more *sophisticated impression* of the primary and secondary relationship of these entities.

More recently, my research interests have also included:

i) the biosynthesis and molecular basis of mycolic acids, glycoproteins, and the complex polysaccharides, arabinogalactan and lipoarabinomannan, which has resulted in the development of new acyltransferase and glycosyltransferase assays, and the identification of key intermediates and characterisation of new products resulting from enzymic synthesis;

ii) the isolation and molecular characterisation of *M. tuberculosis* cell wall mutants, generated through either chemical or genetic means, which has allowed me to evaluate the role of various cell wall structures as virulence determinants;

iii) the mode of action of anti-tuberculosis drugs, such as isoniazid, ethionamide, thiolactomycin and ethambutol, which has resulted in the identification of resistance genes and the structural elucidation of secondary metabolites;

and finally iv) the synthesis of custom-designed antagonists against *M. tuberculosis*. For instance, one of my early key achievements, which was *ground-breaking* in this area of research, was published in ***Science***:the identification of the major excreted protein antigen [antigen 85] as a key mycolyltransferase enzyme involved in the biogenesis of the cell wall of *M. tuberculosis*.

In a second research strand, I have been at the forefront in the discovery of *M. tuberculosis* T-cell antigens and the CD1 antigen presentation pathway. For instance, the initial identification of glucose monomycolate (GMM) as a CD1b-presented glycolipid and its precise structural requirements, antigen processing and presentation to CD1b-restricted T cells were *key* discoveries published in ***Science***, ***EMBO J***. and ***Nature Immunology***.

More recently, I have described in *ground-breaking* articles published in ***Nature*** and ***Journal of Experimental Medicine*** that the T-cell antigen receptor, CD1c protein-mediated recognition is governed by a family of *M. tuberculosis* glycolipids. My research continues to extend significantly the state of the art in both research areas. At the same time I have bridged several research disciplines to set the research agenda in the biosynthesis of the mycobacterial cell wall and the CD1 field, which is evidenced by the quality of my internationally refereed papers, significant funding in the form of several long-term Programme Grants, and ability to attract first-rate international Research Fellows and PhD students.

My research has also been recognised by the award of several prizes (*e.g.* the W.H. Pierce Memorial Prize from the Society for Applied Microbiology; the Carbohydrate Chemistry Award from the Royal Society of Chemistry; Royal Society Wolfson Research Merit Award; the internationally *prestigious* Biochemical Society Award), and numerous plenary lecture invitations (*e.g.* Keystone Research Conferences)

Publications

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Muppidi, J.R., T.I. Arnon, Y. Bronevetsky, N. Veerapen, M. Tanaka, **G.S. Besra**, and J.G. Cyster (2011) Cannabinoid receptor 2 positions and retains marginal zone B cells within the splenic marginal zone. *J. Exp. Med*. 208: 1941-1948.

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Expertise

Research into tuberculosis (TB) to elucidate new biochemical pathways leading to new drug targets, drugs and vaccines

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