University of Birmingham

Dr Graham Wallace BSc, PhD

Senior Lecturer in Immunity and Infection

School of Immunity and Infection

Contact details

Telephone +44 (0)121 371 3255 (tel:+44 121 371 3255)

Email g.r.wallace@bham.ac.uk (mailto:g.r.wallace@bham.ac.uk)

Centre for Translational Inflammation Research
University of Birmingham Research Laboratories
Queen Elizabeth Hospital
University of Birmingham
Edgbaston
Birmingham, B15 2TT

About

Graham Wallace is a Senior Lecturer in the School of Immunity and Infection.

Graham has published over 75 research papers in scientific journals as well as reviews in the fields of ocular immunology, Behcet's Disease and immunogenetics. He has received grants from Guide Dogs for the Blind Association, Fight for Sight, and the Wellcome Trust.

He is an enthusiastic communicator on the theme immune responses in the eye and the effects of gene polymorphgisms on ocular diseases. Graham is on the Medical Panel of the Behcet's Syndrome Society and speaks at meetings of patient groups on a regular basis

Qualifications

- PhD Immunology 1988
- BSc Immunology 1985

Biography

Graham Wallace qualified with a BSc Immunology from the University of London in 1985. He went on to study for a PhD in Immunology at University College London which was awarded in 1988. Following a postdoctoral position at the London School of Hygiene and Tropical Medicine , London Graham started a postdoctoral position at St Thomas' Hospital London in ocular immunology. One of the diseases that was of interest to the group was Behcet's Disease. That initiated his interest in the condition, and it has been part of his laboratory's work ever since. Behcet's is an immunological enigma and therefore provides many interesting avenues for research. A particular interest is the genetic basis of the disease as the geographical spread suggests an aetiology that matches the name the Silk Road disease. This work on the immunogenetic basis of ocular disease is at the forefront of current studies and is being prepared as a major review which we believe will alter the current paradigms. Samples from his DNA bank collected from patients at Birmingham, London and the Middle East are currently being used in further studies by colleagues in Leeds, Dublin, Rotterdam and Lisbon, and Portland, Oregon.

In the broader field of inflammatory eye disease (uveitis) the effects of the local environment on inmmune response is a major part of Graham's work. In a particular, the role of endogenous cortisol and vitamin D3 production on responses in ocular cells is investigated. The use of pathological specimens to study these elements has been a significant theme in Graham research.

Teaching

Teaching Programmes

- **Medicine and Surgery MBChB** (/undergraduate/courses/med/medicine.aspx)
- **Medical Science BMedSc** (/undergraduate/courses/med/medical-sci.aspx)
- **Health Research MRes** (/postgraduate/courses/combined/med/health-research.aspx)

Postgraduate supervision

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

- The effect of vitamin D production in ocular barrier cells
- The effects of hypoxia on inflammatory responses
- The role of the immune response in the effectiveness of antibiotic treatment for antibiotic-susceptible and resistant bacteria

If you are interesting in studying any of these subject areas please contact Graham on the contact deatils above, or for any general doctoral research enquiries, please email: **dr@contacts.bham.ac.uk** (mailto:dr@contacts.bham.ac.uk) or call +44 (0)121 414 5005.

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

Ocular Immunology, Behcet's Disease, Immunogenetics

RESEARCH ACTIVITY

Behcet's Disease (BD)

In Behcet's Disease, in collaboration with colleagues in Birmingham (PI Murray), London (Prof MR Stanford, King's College and Prof Farida Fortune, Queen Mary's College) and the Middle East (Dr Marwen Ghabra, Damascus, Dr Wafa Madanat, Amman, Dr Eldad Ben-Chetrit and Dr Katherine Greiner, Jerusalem) Graham has identified several single nucleotide polymorphisms (SNP) including those associated with increased production of tumour necrosis factor, and Factor V Leiden, both linked to severe vascular disease (retinal occlusion), and MHC class I-related protein MICA*009, which I have postulated is involved in control and licensing of NK cells (see below). Recently, Graham has analysed SNP in PTPN22 and CTLA-4, two genes regarded as genetic masterswitches for autoimmunity, and found that CTLA-4 SNP were not associated with BD, while PTPN22 620W was inversely associated. These results support the view that BD is an autoinflammatory condition and not autoimmune. In collaboration with Professor Luke O'Neill we have shown a SNP in TIRAP, a signalling molecule in the Toll-like receptor pathway to be associated with BD, but only in our European cohort. This work on the immunogenetic basis of ocular disease is at the forefront of current studies and has resulted in my involvement along with Dr Oliver Brand (Oxford) in a genome-wide association study for BD, in collaboration with Dr Elaine Remmers, NIH and Dr Ahmet Gul, Istanbul, which has recently been published in Nature Genetics.

Ocular Immunology

Research has focussed on the effect of the ocular microenvironment on macrophage activation by Toll-like receptor ligands, to address the conditions in which immune privilege may be maintained or broken. In related studies, in collaboration with Miss Si Rauz (School of Immunity and Infection) and Dr Elizabeth Walker, (CEDAM) the effect of TLR signalling on antimicrobial defensins and chemokine production by corneal epithelial cells is being addressed. The effects of TLR stimulation are being analysed in the presence of both cortisol and vitamin D3 production to investigate interaction between these endogenous (protective) and exogenous (inflammatory pathways. The results have shown for the first time that corneal epithelial cells can make active vitamin D3, while fibroblasts make active cortisol, but that neither affects TLR stimulation.

On the cellular side with Dr Jos Bosch (Sports and Exercise Sciences) Graham has been investigating the effects of stress on immune cell populations. The results show a rapid influx of cytotoxic cells into the blood in response to catecholamine release. In collaboration with Professor Adrian Hayday (King's College, London) Graham has investigated the functional relevance of the HLA-MICA coexpression indetified by his genetic studies in BD. The results show that while a differential response of inhibition of killing in patients compared to controls. This may be an important element in BD, and a similar molecule which has been shown to be protective in Middle Eastern patients, does not show a similar response

Other activities

- Executive Board Member of The International Society for Behcet's Disease
- Secretary of the International Society of Inflammation Societies
- Elected to the rare Diseases UK Hall of Fame i

Publications

Liu L. Walker EA. Kissane S. Khan I. Murray PI. Rauz S. Wallace GR. Gene Expression and miR Profiles of Human Corneal Fibroblasts in Response to Dexamethasone. Invest Ophthalmol Vis Sci (in press)

Durrani O. Banahan K. Sheedy FJ. McBride L. Ben-Chetrit E. Greiner K. Vaughan RW. Kondeatis E. Hamburger J. Fortune F. Stanford MR. Murray PI. O'Neill LA. Wallace GR. TIRAP SerR180Leu polymorphism is associated with Behcet's Disease. Rheumatology (in press)

Denniston AK, Kottoor SH, Khan I, Oswal K, Williams GP, Abbott J, Wallace GR, Salmon M, Rauz S, Murray PI, Curnow SJ. (2011) Endogenous cortisol and TGF-beta in human aqueous humor contribute to ocular immune privilege by regulating dendritic cell function. J Immunol. 186:305-11.

Wallace GR, Niemczyk E. (2011) Genetics in ocular inflammation--basic principles. Ocul Immunol Inflamm. 19:10-8

Remmers EF, Cosan F, Kirino Y, Ombrello MJ, Abaci N, Satorius C, Le JM, Yang B, Korman BD, Cakiris A, Aglar O, Emrence Z, Azakli H, Ustek D, Tugal-Tutkun I, Akman-Demir G, Chen W, Amos CI, Dizon MB, Kose AA, Azizlerli G, Erer B, Brand OJ, Kaklamani VG, Kaklamanis P, Ben-Chetrit E, Stanford M, Fortune F, Ghabra M, Ollier WE, Cho YH, Bang D, O'Shea J, Wallace GR, Gadina M, Kastner DL, Gül A. (2010) genome-wide association study identifies variants in MHC class I, Il-10 and IL-23R/IL-12RB2 regions associated with Behcet's Disease. Nat Genet 42:698-702

Young SP, Nessim M. Banerjee S. Falciani F, Trevino V, Scott RAH. Murray PI. Wallace GR. (2009) Metabolomic analysis of human vitreous humor differentiates ocular inflammatory disease. Mol Vis 15;1210-1217.

Young SP. Wallace GR. (2010) Metabolomic analysis of human disease and its application to the eye. J Ocular Biol. Dis Informatics. 2; 235-242

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