

Dr Andrew Hislop

Senior Research Fellow

School of Cancer Sciences

Contact details

Telephone [+44 \(0\)121 414 7983 \(tel:+44 121 414 7983\)](tel:+44%20121%20414%207983)

Fax +44 (0)121 414 4486

Email [a.d.hislop@bham.ac.uk \(mailto:a.d.hislop@bham.ac.uk\)](mailto:a.d.hislop@bham.ac.uk)

School of Cancer Sciences
College of Medical and Dental Sciences
University of Birmingham
Edgbaston
Birmingham
B15 2TT
UK



About

Andrew Hislop is a viral immunologist with an interest in how T lymphocytes control oncogenic human viruses and how these viruses evade recognition and clearance by such immune effectors. His studies focus on Kaposi sarcoma-associated herpesvirus, Epstein-Barr virus and Merkel cell virus.

Qualifications

PhD in Surgery, University of Queensland 1999

B App Sc (Hons) in Life Science, Queensland University of Technology 1990

B App Sc in Medical Laboratory Science, Queensland University of Technology 1989

Biography

Andrew obtained a B App Sci in Medical Laboratory Science in 1989 and a B App Sci (Hons) in life Sciences in 1990, both from the Queensland University of Technology. He then spent three years at the Australian National University working as a research assistant, studying the cellular entry and pathogenesis of alphavirus infections. After this he undertook a PhD at the Queensland Institute for Medical Research and University of Queensland, studying T lymphocyte control of the B cell tropic oncogenic retrovirus Bovine Leukaemia virus.

In 1998 he then came to the University of Birmingham to join the laboratory of Professor Alan Rickinson as a research fellow, studying the T cell response to Epstein-Barr virus. In 2007 he was awarded a New Investigator Award from the Medical Research Council to establish his own group, studying T cell immunity to Kaposi sarcoma-associated herpesvirus; a project undertaken in collaboration with the Medical Research Council laboratories in The Gambia. Currently studies continue on Epstein-Barr virus and Kaposi sarcoma-associated herpesvirus, with more recent studies being established examining the T cell control of the recently identified oncogenic virus Merkel cell virus.

Teaching

- [Medicine and Surgery MBChB \(/undergraduate/courses/med/medicine.aspx\)](#) Cancer:Causes to Cures
- [Medical Science BMedSc \(/undergraduate/courses/med/biomedical-science.aspx\)](#) Clinical Sciences (Intercalated)
- [Immunology and Immunotherapy MSc \(/postgraduate/courses/taught/med/immunology-and-immunotherapy.aspx\)](#)
- Biomedical Research - Molecular and Cellular Medicine MRes

Postgraduate supervision

Dr Hislop supervises PhD students and MSc students in the field of immunity to oncogenic virus infections.

Research

As part of their biology of infection, some viruses can induce entry of the cell into cycle. If the viral genome is maintained in the cell episomally or through integration into the host genome, this can lead to the proliferation of these infected cells and ultimately to the development of cancer.

A vital control mechanism in this process is the immune response, particularly the T lymphocyte component of the antiviral response. Our group studies which viral antigens T lymphocytes respond to, how these T cells recognise virally infected cells and how the viruses evade T cell recognition and clearance. The viruses we study are Epstein-Barr virus, Kaposi sarcoma-associated herpesvirus, and Merkel cell polyomavirus. Our research is split into the following areas:

CD8+ T cell antigen choice in Epstein-Barr virus infection

Epstein-Barr virus encodes many gene products which could potentially act as T lymphocyte targets. However our preliminary studies suggest that only a fraction of these products are targeted by T lymphocytes, with responses focussing on particular viral antigens. We are conducting comprehensive surveys for immune targets in the entire Epstein-Barr virus proteome to understand the pattern of immune targeting and further understand antigen selection by the immune system.

Immune evasion by Kaposi sarcoma-associated herpesvirus

Viruses such as Kaposi sarcoma-associated herpesvirus which cause persistent infections have evolved to co-exist in immunocompetent hosts. To achieve this, they have developed immune evasion mechanisms to decrease the efficiency of targeting by the immune response. Some proteins, most notably the latent proteins, show features

which may reduce efficient targeting by CD8+ T lymphocytes. We are testing then the efficiency with which KSHV- specific CD8+ T lymphocytes recognise these antigens, if these mechanisms can be overcome and whether other immune effectors such as CD4+ T lymphocytes are sensitive to these evasion mechanisms.

Making KSHV-transformed cells more sensitive to T lymphocyte mediated killing

We have found that cells derived from one of the malignancies associated with Kaposi sarcoma-associated herpesvirus are insensitive to KSHV-specific CD4+ T lymphocyte mediated killing, despite the T lymphocytes being able to kill other target cell types. As the virus is known to express proteins with anti-apoptotic function, we are assessing whether gene products expressed by the virus are protecting these cells from killing by CD4+ T lymphocytes. Furthermore, we are using chemical inhibitors to interfere with cell signalling pathways involved in preventing apoptosis to restore sensitivity of these malignant cells to T lymphocyte mediated killing.

Developing primary B lymphocyte infection models for KSHV

Kaposi sarcoma-associated herpesvirus establishes latency in B lymphocytes, however few in vitro methods exist to infect B lymphocytes to study immune targeting of these cells, the biology of infection and manipulation of the cell by the virus. We have developed a mechanism by which to infect primary B cells and propagate these infected cells allowing us to examine in detail how these infected cells can be targeted by T lymphocytes. Furthermore, this model will be used to understand viral transformation of these cells.

Identifying T lymphocyte targets of Merkel cell polyomavirus and using these to understand immune control of Merkel cell carcinoma

Merkel cell polyomavirus is a recently discovered virus which appears to be part of the skin flora, but has been associated with the development of Merkel cell carcinoma. These carcinoma cells express fragments of the Merkel cell polyomavirus antigens. We are currently isolating T lymphocytes specific to these Merkel cell polyomavirus antigens to determine whether these will recognise Merkel cell carcinoma cells and whether these can be used therapeutically to control disease caused by this virus.

Other activities

Peer reviewer for a range of journals

Publications

1. Sabbah S, Jagne YJ, Zuo J, de Silva T, Ahasan MM, Brander C, Rowland-Jones S, Flanagan KL, **Hislop AD**. 2012. T-cell immunity to Kaposi's sarcoma-associated herpesvirus: recognition of primary effusion lymphoma with LANA-specific CD4+ T cells. **Blood**. 119:2083-92.
2. Misstear K, Chanas SA, Rezaee SA, Colman R, Quinn LL, Long HM, Goodyear O, Lord JM, **Hislop AD**, Blackburn DJ. 2012. Suppression of Antigen-Specific T Cell Responses by the Kaposi's Sarcoma-Associated Herpesvirus Viral OX2 Protein and Its Cellular Orthologue, CD200. **J Virol**. 86:6246-57.
3. Jayasooriya S, **Hislop A**, Peng Y, Croom-Carter D, Jankey Y, Bell A, Dong T, Rowland-Jones S, Rickinson A, Walther M, Whittle H. 2012. Revisiting the effect of acute *P. falciparum* malaria on Epstein-Barr virus: host balance in the setting of reduced malaria endemicity. **PLoS One** 7:331142.
4. Zuo J, Thomas WA, Haigh TA, Fitzsimmons L, Long HM, **Hislop AD**, Taylor GS, Rowe M. 2011. Epstein-Barr Virus Evades CD4 T Cell Responses in Lytic Cycle through BZLF1-mediated Downregulation of CD74 and the Cooperation of vBcl-2. **PLoS Pathog**. e1002455.
5. Palendira U, Low C, Chan A, **Hislop AD**, Ho E, Phan TG, Deenick E, Cook MC, Riminton DS, Choo S, Loh R, Alvaro F, Booth C, Gaspar HB, Moretta A, Khanna R, Rickinson AB, Tangye SG. 2011. Molecular pathogenesis of EBV susceptibility in XLP as revealed by analysis of female carriers with heterozygous expression of SAP. **PLoS Biol**. e1001187.
6. Zuo J, Quinn LL, Tamblin J, Thomas WA, Feederle R, Delecluse HJ, **Hislop AD**, Rowe M. 2011. The Epstein-Barr virus-encoded BILF1 protein modulates immune recognition of endogenously processed antigen by targeting major histocompatibility complex class I molecules trafficking on both the exocytic and endocytic pathways. **Journal of Virology** 85:1604-14.
7. **Hislop AD**, Palendira U, Leese AM, Arkwright PD, Rohrlisch PS, Tangye SG, Gaspar HB, Lankester AC, Moretta A, Rickinson AB. 2010. Impaired Epstein-Barr virus-specific CD8+ T cell function in X-linked lymphoproliferative disease is restricted to SLAM family positive B cell targets. **Blood** 116:3249-3257.
8. Croft NP, Shannon-Lowe C, Bell AI, Horst D, Kremmer E, Rensing ME, Wiertz EJ, Middeldorp JM, Rowe M, Rickinson AB, **Hislop AD**. 2009. Stage-specific inhibition of MHC class I presentation by the Epstein-Barr virus BNLF2a protein during virus lytic cycle. **PLoS Pathogens**. 5: e1000490.

