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About

Dr Heather Long is a Kay Kendall Leukaemia Fund Research Fellow in the School of Cancer Sciences, University of Birmingham.

Heather has published a number of research papers on the immune response to Epstein-Barr virus (EBV). Her long-term interest is in developing immune-based therapies for the treatment of EBV-associated and non virus-associated lymphomas. In particular, her group is focussed on understanding the specificity and function of immune cells with the greatest potential to target lymphoma.

Qualifications

- PhD in Cancer Studies, University of Birmingham, 2005
- BSc (Hons) Biomedical Science, University of Hull, 2001

Biography

Heather Long was awarded a BSc (Hons) in Biomedical Science from the University of Hull in 2001. During an integrated training year at the haematology and blood transfusion laboratory at St James' University Hospital, Leeds, she qualified with the Institute of Biomedical Science as a Biomedical Scientist.

In 2001, Heather joined the School of Cancer Sciences at the University of Birmingham, where she obtained her PhD in 2005.

After post-doctoral research projects in the laboratory of Prof Alan Rickinson, in 2012, Heather was awarded a Kay Kendall Leukaemia Fund Travel Fellowship to continue her own independent research. This will include a working visit to the Ludwig Institute in Brussels.

Teaching

- MBChB 'Cancer: Causes to Cures' Small group tutor
- Supervisor of PhD, MRes and BSc project students

Postgraduate supervision

Heather is supervising students in the following areas:

- T lymphocyte responses to Epstein-Barr virus (EBV) and their role in the control of EBV-associated associated lymphoma
- Identification of T lymphocyte target antigens in lymphoma

Research

The rationale for T cell therapy for cancer is that tumour cells express a different repertoire of proteins, compared to healthy tissue, which may be targeted by the immune response. Heather's long-term research interest lies in developing immune T cell-based therapies for the treatment of lymphoma, the 5th most common cancer world-wide. This interest stems from her earlier work studying the CD4+ T cell response to the Epstein-Barr virus (EBV), a wide-spread human virus that, in a small minority of people, is associated with a number of different B cell lymphomas.

CD4+ T cells are key orchestrators of the cellular immune system, where they perform several critical helper roles in the processes that lead to development and maintenance of long-term immunity. In addition, it is now clear that many CD4+ T cells can also directly recognise MHC class II positive target cells expressing their target antigen. For infections or malignancies occurring within MHC class II positive cells, such as B cells, this opens up exciting possibilities for therapeutic exploitation of CD4+ T cells; if suitable target antigens can be identified.

The B cell-tropic Epstein-Barr virus (EBV) has provided an instructive model in which to study the human immune response to an oncogenic virus. In recent years, we have characterised the CD4+ T cell response to EBV, from primary to persistent infection and have demonstrated that some EBV-specific CD4+ T cells can directly recognise and kill virus-infected cells. These important observations may well explain the increased clinical efficacy of virus-specific T cell preparations (CTLs) containing higher percentages of CD4+ T cells to treat EBV-associated post-transplant lymphoproliferative disease (PTLD). Ongoing projects are investigating the identity/functional characteristics of the CD4+ T cells present in adoptively transferred therapeutic CTLs and are following their kinetics *in vivo*. In this way, we hope to identify the virus-specific CD4+ T cells with the greatest potential to target virus-infected cells.

However, many B cell lymphomas are not associated with viral infection, and T cell therapy relies on immune targeting of cellular antigens. We have recently shown that

EBV transformation leads to up-regulation of not only viral antigens, but also cellular antigens that can be recognised by the CD4+ immune system. Importantly, these cellular targets are also expressed in at least some other non-virus-associated lymphomas, and may provide novel therapeutic targets for lymphoma. Therefore, in a separate project, we are exploring the identity of these novel target antigens and assessing their potential as therapeutic target antigens for immune therapy of wider non-virus associated lymphoma.

Other activities

Memberships:

- British Society for Immunology
- Society for General Microbiology

Reviewer experience:

- Invited reviewer for Immunology and Journal of General Virology

Committees:

- Cancer Immunotherapy and Immunology Centre Advisory Board

Publications

- 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.7(12):e1002455 (http://www.ncbi.nlm.nih.gov/pubmed/22216005)** .
- Long HM, Chagoury OL, Leese AM, Ryan GB, James E, Morton LT, Abbott RJM, Sabbah S, Kwok W and Rickinson AB. (2013). MHC II Tetramers visualising human CD4+ T cell responses to Epstein-Barr virus infection: atypical kinetics of the EBNA1 response. **J Exp Med. May 6;210(5):933-49 (http://www.ncbi.nlm.nih.gov/pubmed/23569328)** .
- **Long, HM.**, Leese, AM., Chagoury, OL., Connerty, SR., Quarcoopome, J., Quinn, LL., Shannon-Lowe, C., Rickinson, AB. (2011) Cytotoxic CD4+ T cell responses to Epstein-Barr virus contrast with CD8 responses in breadth of lytic cycle antigen choice and in lytic cycle recognition. **J Immunol.**187:92-101.
- **Long, HM.**, Taylor, GS., Rickinson, AB. (2011) **Immune defence against EBV and EBV-associated disease. Curr Opin Immunol. 23(2):258-64. (http://www.ncbi.nlm.nih.gov/pubmed/21269819)** 23(2):258-64.
- Fox, CP., Haigh, TA., Taylor, GS., Lee, SP., **Long, HM.**, Shannon-Lowe, C., O'Connor, S., Bollard, CM., Iqbal, J., Chan, WC., Rickinson, AB., Bell, AI., Rowe, M. (2010) A novel latent membrane 2 transcript expressed in Epstein-Barr virus-positive NK and T cell lymphoproliferative disease encodes a target for cellular immunotherapy. **Blood**. 116(19):3695-704.
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- **Long, HM.**, Zuo, J., Leese, AM., Gudgeon, NH., Jia, H., Taylor, GS., Rickinson, AB. (2009) **CD4+ T-cell clones recognizing human lymphoma-associated antigens: generation by in vitro stimulation with autologous Epstein-Barr virus-transformed B cells. (http://www.ncbi.nlm.nih.gov/pubmed/19443664?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum&ordinalpos=2) Blood**114:807-15.
- Kelly, GL., **Long, HM.**, Stylianou, J., Thomas, WA., Leese, A., Bell, AI., Bornkamm, GW., Mautner, J., Rickinson, AB., Rowe, M. (2009) **An Epstein-Barr virus anti-apoptotic protein constitutively expressed in transformed cells and implicated in burkitt lymphomagenesis: the Wp/BHRF1 link. (http://www.ncbi.nlm.nih.gov/pubmed/19283066?itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum&ordinalpos=3) PLoS Pathog**. 5(3):e1000341.
- Taylor, GS*., **Long, HM*.,** Haigh, TA., Larsen, M., Brooks, J., Rickinson, AB. (2006) A role for intercellular antigen transfer in the recognition of EBV-transformed B cell lines by EBV nuclear antigen-specific CD4+ T cells. **J Immunol.**177:3746-56.*Joint 1st author

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