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Arthritis Research UK Career Development Fellow

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About

Helen McGettrick is an experimental biologist who specialises in developing multi-cellular in vitro models to examine the processes by which tissue resident cells influence leukocyte adhesion and migration during inflammation. **Find out more (/schools/immunity-infection/research/ii-shorts/mcgettrick-helen.aspx)**

Helen's research focuses on leukocyte recruitment and stromal cell biology in health and disease, in which she has several publications. She is currently using this expertise in the fields of rheumatology, diabetes, stem cell biology and cancer biology. She has received grants from Arthritis Research UK, in the form of a Career Development Fellowship, Wellcome Trust, British Heart Foundation, Enterprise Birmingham Fund, and Pfizer.

Video clip - **Frustrated migration of human peripheral blood lymphocytes on cytokine-stimulated endothelium: (/Audio/college-mds/ll-staff-profiles/Helen-McGettrick-PBL-on-TNFIFN-EC-on-plate-n=3.avi)** *During inflammation, lymphocytes migrate over the surface (white, bright cells), through and underneath (dark cells) activated endothelial cells to enter the tissue. If the lymphocytes do not receive an appropriate signal, their migration becomes frustrated, as they transit into and out of the endothelial monolayer searching for it.*

Qualifications

- PhD in Medical Science - University of Birmingham, 2006
- MSc in Immunology – Distinction, University of Birmingham, 2002
- BSc (Hons) in Biochemistry - First Class, University of Lancaster, 2001

Biography

Helen graduated from the University of Lancaster in 2001 with a BSc (Hons) in Biochemistry, during this course she spent a year studying aboard at Oregon State University, USA. She obtained a MSc. in Immunology from the University of Birmingham in 2002, undertaking a research project looking at neutrophil apoptosis (cell death) with Janet Lord and Dagmar Scheel-Toellner in the School of Immunity and Infection. She subsequently joined Gerard Nash's Cardiovascular Rheology Group in the School of Clinical and Experimental Medicine, where she completed her PhD in Medical Sciences in 2006.

Helen has continued to work in Birmingham investigating the processes controlling leukocyte recruitment and fate both in health and disease, focusing on the role of the tissue microenvironment. She was appointed as a University Fellow in Inflammation Biology within the System Science for Health multidisciplinary translational research consortium at Birmingham in 2011.

In 2012, Helen was awarded an Arthritis Research Career Development Fellowship to explore the role of synovial fibroblasts in regulating leukocyte accumulation during the development of persistent arthritis.

Helen is currently organising the 27th UK Cell Adhesion Society Meeting to be held in September 2015 at the University of Birmingham.

Teaching

- **Immunology and Immunotherapy MSc (/postgraduate/courses/taught/med/immunology-and-immunotherapy.aspx)**
- **Medical Science BMedSc (/undergraduate/courses/med/biomedical-science.aspx)** - Year 3 Immunity and Inflammation
- **Medical Science BMedSc (/undergraduate/courses/med/biomedical-science.aspx)** - Year 3 Vascular Biology and Pathology
- **Medical Science BMedSc (/undergraduate/courses/med/biomedical-science.aspx)** - Biomaterials - Year 1

Previously

- MRes Maths & Computing in Biology & Medicine
- **Medicine and Surgery MBChB (/undergraduate/courses/med/medicine.aspx)** – Year 2; Integrated problems

Previous undergraduate research projects

- Fibroblasts regulate inflammation: What changes in early rheumatoid arthritis to make it persist? (2015)
- Characterising the ability of mesenchymal stem cell-derived adipocytes and osteoblasts to influence leukocyte recruitment to vascular endothelial cells (2015)
- Investigating how platelets influence the recruitment of mesenchymal stem cells from the blood (2015)
- Examining the immunomodulatory properties of MSC (2014)

- Characterising the ability of mesenchymal stem cells to influence the migration of leukocytes through vascular endothelial cells (2013)
- How do lymphatic endothelial cells influence lymphocyte migration during inflammation? (2013)
- Establishing the role of CD248 in influencing PDGF signalling during angiogenesis (2012-2013)
- Characterising the process of leukocyte migration through lymphatic endothelium: which leukocytes can exit tissue? (2012)
- Characterising new steps in T-cell migration into tissue during inflammation (2011)
- Characterisation of a new regulatory step in T-cell penetration of tissue during inflammation (2010)

Previous summer research projects

- Improving engineered tissue constructs for compatibility with human leukocytes (2014)
- Characterising how MSC influence leukocyte migration through endothelium using novel in vitro constructs (2013).
- Developing an in vitro construct to model the entry and exit of lymphocytes in inflamed tissue (2013).

Postgraduate supervision

Helen currently supervises PhD students on the following projects:

- MSC as endogenous regulators of inflammation: Changes in chronic inflammation. Lewis Clarke (Oct 2014).
- Manipulating the immunomodulatory effects of mesenchymal stem cells. Hafsa Munir (Oct 2012-present).

Find a PhD - **http://www.findaphd.com/search/ProjectDetails.aspx?PJID=53722&LID=139 (http://www.findaphd.com/search/ProjectDetails.aspx?PJID=53722&LID=139)**

Previous Masters projects

- Examining the immunomodulatory capacity of mesenchymal stem cells: Is there a role for metabolites? (Oct 2014-Mar 2015)
- Examining the impact of migration on T cell function (May-Aug 2014).
- Characterising the effects of chronic inflammation on the phenotype of MSC (May-Aug 2014).
- Mesenchymal stem cells as modulators of neutrophil recruitment (Jan-Apr 2014).
- A new regulatory step in T-cell migration into tissue during inflammation; separating the wanted from the unwanted (May-Aug 2011).

Research

Helen's research concentrates on the concept that the state of the local tissue (stromal) microenvironment defines the responsiveness of endothelial cells, and also the subsequent fate of recruited leukocytes. This has involved the development and validation of novel in vitro, multi-cellular, multi-layered static and flow-based culture systems. Her goal is to develop a more complete understanding of the molecular circuitry regulating tissue migration and egress during acute and chronic inflammation reactions, with a view to developing anti-inflammatory, pro-resolution therapeutic strategies. A novel approach that we are investigating is to manipulate the local stroma to instruct recruited cells to leave chronically inflamed tissue, in effect to "switch on" resolution, or alternatively to stop leukocytes entering the inflamed site by "turning off" recruitment.

RESEARCH THEMES

Chronic Inflammation – Rheumatoid Arthritis

- Fibroblast-endothelial cell crosstalk regulating lymphocyte recruitment in resolving and persistent arthritis
- Adiponectin-PEPITEM axis and regulation of T-cell migration in Rheumatoid Arthritis

Mesenchymal Stem Cells

- Immunomodulatory effects of mesenchymal stem cells on leukocyte recruitment and vascular inflammation
- Modulation of mesenchymal stem cell responses by their local microenvironment

Regulation of Migration

- Vascular-lymphatic endothelial cell crosstalk and leukocyte exit from tissue
- Multi-cellular 3-D in vitro models examining the migration, fate and function of leukocytes entering inflamed tissue

RESEARCH GRANTS

Principle Investigator

2015-2017 - ***Pfizer***
Defining the therapeutic potential of a novel peptide regulator of T-cell recruitment in rheumatoid arthritis

2014-2016 - ***Enterprise Birmingham Fund***
Demonstrating the utility of a biomarker to detect Rheumatoid Arthritis at a very early pre-symptomatic stage.

2012-2017 – ***Arthritis Research UK Career Development Fellowship***
Exploring the role of synovial fibroblasts in regulating leukocyte accumulation during the development of persistent arthritis.

2009 – ***Wellcome Trust VIP Fellowship***
Regulation of lymphocyte migration and retention by the stromal microenvironment.

Co-investigator

2015-2018 – ***British Heart Foundation***
Mechanisms, optimisation, and in vivo application of the vascular protective effects of mesenchymal stem cells.

2010-2012 – ***Wellcome Trust***
Role of fibroblasts in induction of tissue-specific recruitment of memory T-cell subsets.

RESEARCH ACTIVITY

Chronic Inflammation – Rheumatoid Arthritis

In collaboration with the Rheumatology Research Group, we have access to blood samples and synovial tissue from patients attending the Birmingham Early Arthritis Clinics (BEACON) with newly presenting joint pain or joint swelling.

In RA, synovial fibroblasts acquire a pathogenic phenotype allowing them to bypass many of the regulatory checkpoints that coordinate the successful resolution of an inflammatory episode. Indeed we have shown that rheumatoid synovial fibroblasts activate endothelium to inappropriately recruit leukocytes (McGettrick, et al., 2009 EJI). Extending this further, we have recently reported for the first time that synovial fibroblasts undergo 2 distinct phenotypic changes as RA evolves: first is the early loss of the immunosuppressive capability of normal fibroblasts, second is the slower acquisition of an intrinsically stimulatory phenotype.

Mesenchymal Stem Cells

Mesenchymal stem cells (MSC) act as endogenous regulators of inflammation. We found that MSC communicated with neighbouring vascular endothelial cells to limit leukocyte recruitment induced by inflammatory cytokines. Preliminary evidence suggests that MSC differentiation causes loss of immunoprotective capability, and may indeed actively promote leukocyte recruitment. This raises another unexplored scenario; that change of MSC phenotype in chronic inflammation contributes to uncontrolled leukocyte infiltration.

Regulation of Migration
The key step in leaving tissue is for leukocytes (namely T-cells) to migrate through endothelial cells lining the lymphatic vessels. Leukocytes obtain messages as they migrate into tissue though vascular endothelium, which change their subsequent behaviour and ability to migrate through lymphatic endothelium. In addition, vascular endothelial cells communicate with neighbouring cells, including lymphatic cells, to regulate migration. However, the mechanisms regulating the migration of leukocytes through and out of inflamed tissue are poorly understood.

Other activities

Editoral Board

- Scientific Reports (2015 - present)
- Annals of Autoimmunity and Research

Committee Membership

- British Society of Immunology, Leukocyte Migration Affinity Group - Meeting Organiser (**www.immunology.org/Leukocyte-Migration (http://www.immunology.org/Leukocyte-Migration)**)
- UK Adhesion Society (**www.ukadhesion.org (http://www.ukadhesion.org)**)

Conference Organisation

- 27th UK Cell Adhesion Society Meeting - Birmingham, 2015
- 2nd BSI Leukocyte Migration Affinity Group - Birmingham, 2015
- 26th UK Adhesion Society - Birmingham, 2013
- 24th UK Adhesion Society - Birmingham, 2011
- British Microvascular Society - Workshop - Birmingham, 2009

Membership and Affiliation

- Fellow of the Higher Education Academy
- British Society of Immunology
- Society of Leukocyte Biology

Publications

Recent Peer Reviewed Publications

M. Chimen*, **H.M. McGettrick***, B. Apta, J.S. Kuravi, C.M. Yates, A. Kennedy, A. Odedra, M. Alassiri, M. Harrsion, A. Martin, F. Barone, S. Nayar, J.R. Hitchcock, A.F. Cunningham, K. Raza, A. Filer, D.A. Copland, A.D. Dick, J. Robinson, N. Kalia, L.S.K. Walker, C.D. Buckley, G.B. Nash, P. Narendran and G.E. Rainger. (2015). Homeostatic regulation of T cell trafficking by a B cell derived peptide is impaired in autoimmune and chronic inflammatory disease. *Nature Medicine* **Epub** doi**:10.1038/nm.3842***(* joint authorship)*

D. Luo, **H.M. McGettrick**, PC, Stone PC, GE, Rainger GE and GB Nash (2015) **The roles of Integrins in function of Human Neutrophils after their migration through endothelium into interstitial matrix (http://www.ncbi.nlm.nih.gov/pubmed/?term=10%3Ae0118593)** . *PloS One* 10(2):e0118593

H. Munir, G.E. Rainger, G.B. Nash, and **H.M. McGettrick**. (2014) Analysing the effects of stromal cells on the recruitment of leukocytes from flow**.** *Journal of Visualised Experiments*.**95**:e52480, doi:10.3791/52480 (**http://www.jove.com/video/52480 (http://email.jove.com/wf/click?upn=-2Bx7dpxF9xg52ckyzY5GokUvNRZlKvidYgTQWxhduOO-2F0-2BrEUTdiMxz6pmqMByZUd_GR4GTmve99O2HQVsU8WizA0-2Fl7ndvpefoRVyOOglz8yE4dF6TKdmePZjMGUgATdVxWqrW-2Fr3yGCqZLZ3iOgeZE2DgVUd2C7qRPxCJcPdLVu1Z8D-2Fbg22owBVygLMJb-2BilNhB-2FrkESp8ZReFTyEXFHxq3zgcNFbeRr2Y83fpGr0-2F8-2B2cHR5L5z0pSH1CII-2BMQPFcT0q8tsqUp3mPwUcLIg7mLdwTmtCC-2BvOH0d4-2FOHYc9VuxHVXw7DRryp46SpQKqBRm4Vk3cWkKDQrd0mrfI6g-3D-3D)**)

A. Zalli, N. Riddell, **H.M.McGettrick,** and P. Moss, G.R. Wallace (2014). Targeting 2-adrenergic receptors regulates T-cell function directly and indirectly.*Brain Behaviour and Immunity*, S0889-1591(14)00563-7. doi: 10.1016/j.bbi.2014.12.001

A. Naylor*, **H.M. McGettrick***, W. Maynard, P. May, F. Barone, A. Croft, S. Egginton and C.D. Buckley (2014).A differential role for CD248 (Endosialin) in different forms of physiological angiogenesis in skeletal muscle. *PLoS One* **9**:e107146 *(* joint authorship)*

J.S. Kuravi*, **H.M. McGettrick***, S.C. Satchell, M.A. Saleem, L. Harper, J.M. Williams, G.E. Rainger and C.O. Savage (2014). Podocytes regulate neutrophil recruitment by glomerular endothelial cells via IL-6 mediated cross-talk. *Journal of Immunology* **193**:234-243*(* joint authorship)*

Recent Reviews

J. Wragg, S. Durant, **H.M. McGettrick**, K. Sample, S. Egginton and R. Bicknell (2014). Shear stress regulated gene expression and angiogenesis – origins and development. *Microcirculation* **21**:290-300

H.M. McGettrick, L.M. Butler, C.D. Buckley and G.E. Rainger and G.B. Nash. (2012). Stromal tissue as a regulator of leukocyte recruitment in inflammation. *Journal of Leukocyte Biology,* **91**:385-400

Full listing of publications (http://www.ncbi.nlm.nih.gov/pubmed/?term=mcgettrick+hm+%5Bau%5D)