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## Current Fields of Research

**Inflammatory arthritis:** Leeds is internationally recognised for its work in early inflammatory arthritis. It has the largest Biologics clinic in Europe and a combination of imaging and basic science has allowed unique experiments in the understanding of the pathogenesis of early inflammatory arthritis. A number of seminal publications have described algorithms for the treatment of the early phase of disease including oligoarthritis, undifferentiated arthritis, early polyarthritis, and early rheumatoid arthritis. A major research undertaking has been the investigation of the pathophysiology of remission in RA patients receiving therapy. Induction regimes have been implemented which have ultimately allowed patients to cease medication. A region-wide study assessing the ability to prevent loss of jobs has just been successfully completed. The achievement of getting more patients into remission on biologics and understanding when patients can cease therapy has enabled a new approach to treatment.

**Osteoarthritis:** The Section has pioneered high resolution MRI in early generalised OA and has provided evidence that OA begins not in the cartilage or bone but ligaments. This work has also determined the importance of synovitis and the prevalence of multiple joint problems in the community.

**Allied Health Professionals:** The Section has established itself as a centre of excellence in AHP clinical research. Focussing initially on podiatry and nursing, the AHP portfolio now also includes physiotherapy and occupational therapy, with the AHPs working collaboratively with colleagues from medicine, engineering and other faculties. The AHP research team in the ASMD is already recognised nationally as a centre of excellence in clinical research and is increasingly recognised internationally.

**Imaging:** Studies undertaken within the Section utilising MRI have confirmed the primacy of synovitis in RA and that suppression of synovitis prevents joint damage. Studies have also confirmed the utility of MRI in following disease classification, progression and response to treatment. The success of the *arc* funded MRI programme to date has also led to Leeds jointly heading the OMERACT working group for MRI scoring in RA and the EULAR working group for scoring in spondyloarthritis. Leeds has led the way in understanding the link between bone, synovium and the enthesis in the pathogenesis of disease. In ultrasound imaging, Leeds has demonstrated that classification of disease based on clinical examination alone may not be accurate and has demonstrated that sub-clinical disease is common in patients in "clinical remission".

**Innate Immune Mechanisms:** McDermott identified the genetic defect (mutations in *CIAS1/NALP3* gene) in Muckle-Wells syndrome (MWS) and familial cold urticaria (FCU) in 2002; this work has added new insights to this field, such as the continuum between the MWS and FCU phenotype. Investigation of the IgG/ Fc $\gamma$  Receptors (Fc $\gamma$ Rs) in the context of RA pathogenesis has been a major research focus in Leeds. Morgan has identified a genetic association between the *FCGR* genetic locus and RA, particularly nodular RA. Ponchel has established that RA patients have significantly less Treg in the peripheral blood, and has described the importance of the Jagged/Notch pathway in the onset of early disease. The most important breakthrough of the group was the association of IL-7 with RA pathogenesis and its implication in several physiological processes.

**Mesenchymal Stem Cell/Tissue Engineering:** The group has been working on Mesenchymal Stem cells, as they are the source of IL-7 secretion in several tissues, including joints, and has been successful in isolating and differentiating Mesenchymal progenitor stem cells (MSCs) from the bone marrow of healthy individuals and from patient joints.

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**Selected Publications**

- Emery P, Breedveld F, Hall S, Durez P, Chang DJ, Robertson D, Singh A, Pedersen RD, Koenig A, Freundlich B. Clinical Remission, Normalized Function, and Radiographic Nonprogression in Subjects With Active Early Rheumatoid Arthritis: Results of the Randomized, Double-blind Combination of Methotrexate And Etanercept in Active Early Rheumatoid Arthritis (COMET) Trial. *The Lancet-D-08-02275R1*, pgs1-111.  
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- Thomson W, Barton A, Ke X, Eyre S, Hinks A, Bowes J, Donn R, Symmons R, Hider S, Bruce IN, Wellcome Trust Case Control Consortium, Wilson AG, Morgan A, Emery P, YEAR consortium Carter A, Steer S, Hocking L, Reid DM, Wordsworth P, Harrison P, Farrar C, Strachan D, Worthington J. Investigation of putative rheumatoid arthritis susceptibility loci identified in the WTCCC study confirms association with a novel locus at 6q23. *Nat Genet* 2007;39: 1431-1433.  
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JIF: 7.667
- Emery P, Fleischmann R, Filipowicz-Sosnowska A, Schechtman J, Szczepanski L, Kavanaugh A, Racewicz AJ, van Vollenhoven RF, Li NF, Agarwal S, Hessey EW, Shaw TM, DANCER Study Group. The efficacy and safety of rituximab in patients with active rheumatoid arthritis despite methotrexate treatment: Results of a phase IIB randomized, double-blind, placebo-controlled, dose-ranging trial. *Arthritis Rheum* 2006; 54 (5); 1390-1400.  
JIF: 7.667

- Edwards JCW, Szczeparski L, Szechinski J, Filipowicz-Sosnowska A, Emery P, Close DR, Stevens RM, Shaw T. Efficacy of B-cell targeted therapy with rituximab in patients with rheumatoid arthritis. *N Engl J Med* 2004;350:2572-81. JIF: 52.589.
- Kremer JM, Westhovens R, Leon M, Giorgio ED, Alten R, Steinfeld S, Russell A, Dougados M, Emery P, Nuamah IF, Williams RG, Becker JC, Hagerty DT, Moreland LW. Treatment of rheumatoid arthritis by selective inhibition of T-cell activation with fusion protein CTLA4Ig. *N Engl J Med* 2003;349:1907-15. JIF: 52.589.

### **Current Funding**

The Section has secured over £13.5 million (€17 million) in competitive grant income in order to support over the past five years. This includes over £1.5 million (€2 million) from the Arthritis Research Campaign for two programme grants for work in early rheumatoid arthritis and two MRC grants worth just under £1million (€1.25 million) for work in multi-disciplinary foot research and imaging classification of arthritis.

Of note, we have recently been awarded funding to establish the NIHR Leeds Musculoskeletal Biomedical Research Unit (LMBRU). The funding is based on strong collaborative links and the foundations of excellence in musculoskeletal research activities between the LTHT and the University of Leeds. This grant formalises collaborative links between two world-class research units: the Section of Musculoskeletal Disease (MSKD) and the Institute of Medical and Biological Engineering (iMBE), both of whom have the delivery of patient focussed research driven by scientific evidence as the core of their activities. Activities within LMBRU will be centred on research programmes which bring together existing strengths within Leeds to create an integrated unit which will become the UK's leading musculoskeletal research facility and contribute to the international knowledge economy through transforming basic biomedical research into responsive patient care.

The Leeds Musculoskeletal Biomedical Research Unit (LMBRU) is based around five research themes, bringing together existing strengths within Leeds to create an integrated unit. Integral to the activities of all groups will be building research capacity in imaging science. Through this investment, the LMBRU will exploit the significant potential that exists through the transfer of basic biomedical science into quality patient care. The Unit has been devised to exploit existing strength and capitalise on the synergies that exist between the groups. Research programmes are be conducted through the following groups:

- (i) Musculoskeletal Clinical Research Group
- (ii) Bioengineering and Surgical Intervention Group
- (iii) Regenerative Medicine Group
- (iv) Experimental Rheumatology Group
- (v) Musculoskeletal Imaging and Tissue Characterisation Group

### Training of Fellows in Research

The University of Leeds is one of the top ten research institutions within the UK and has a well established reputation for developing research leaders. The University also recognises the issues that support and flexibility are key in the career progression of clinical academics and have developed several short courses to address these needs (<http://www.leeds.ac.uk/sddu/top/a-z.html>). The University also has a formal mentoring scheme, which the candidate will be encouraged to capitalise on (<http://www.leeds.ac.uk/sddu/research/mentoring.html>).

The Section has well developed and structured procedures for the development of clinical researchers. In addition to the formal requirements for ongoing monitoring and assessment of the Fellow's activities, peer review will be undertaken twice a semester through our strong research training group. Currently, we have 30 SpRs and research fellows, nine Professors and a research active academic staff of over 50 which provides an excellent opportunity for interaction and feedback.

### WebPages

Section Webpage:

<http://www.leeds.ac.uk/medicine/musculoskeletal/>

Leeds Institute of Molecular Medicine:

<http://limm.leeds.ac.uk/about.htm>

Research Groups:

[http://limm.leeds.ac.uk/research\\_sections/musculoskeletal\\_disease/research\\_groups.htm](http://limm.leeds.ac.uk/research_sections/musculoskeletal_disease/research_groups.htm)

Academic Unit of Musculoskeletal Nursing (ACUMEN):

<http://www.leeds.ac.uk/acumen/>

Foot and Ankle Studies in Rheumatology:

<http://www.leeds.ac.uk/medicine/FASTER/>

Rehabilitation:

<http://www.leeds.ac.uk/medicine/rehabmed/nhs%20rehab%20med%20services.htm>

Psychometric Laboratory:

[http://home.btconnect.com/Psylab\\_at\\_Leeds/Courses.htm](http://home.btconnect.com/Psylab_at_Leeds/Courses.htm)

Institute of Medical and Biological Engineering:

<http://www.imbe.org.uk/>

LMBRU: Under construction