

Director of the Research Center

Professor Sir Marc Feldmann
 MBBS BSc FRCPPath, FRCP FMedSci FAA FRS

**Institution**

Kennedy Institute of Rheumatology Division
 Imperial College London
 The Charing Cross Hospital Campus
 Arthritis Research Campaign Building
 65 Aspenlea Road
 London W6 8LH, UK
 Phone +44 (0)20-8383-4400
 Fax: +44 (0)20-8563-0399
 Email: m.feldmann@imperial.ac.uk

Members of the Center**Senior Staff**

Jeremy Saklatvala, PhD, Professor
 Hideaki Nagase, PhD, Professor
 Sir Ravinder Maini, Emeritus Professor
 Fionula Brennan, PhD, Professor
 Patrick Venables, MD, Professor
 Peter C. Taylor, PhD, Professor
 Jagdeep Nanchahal, FRCS, PhD, Professor
 Francesco Dazzi, MD, Professor
 Andrew Clark, PhD, Senior Lecturer
 Ewa Paleolog, PhD, Senior Lecturer
 Claudia Monaco, PhD, Clinical Lecturer
 Yoshifumi Itoh, PhD, Senior Lecturer
 George Bou Gharos, Reader
 Robin Wait, PhD, Senior Lecturer
 Tonia Vincent, PhD, Consultant
 Rheumatologist/Clinical Scientist
 Richard Williams, PhD, Senior Scientific Officer
 Nicole Horwood, PhD, Lecturer
 Kim Midwood, PhD, Lecturer
 Christopher Murphy, PhD, Lecturer
 Irina Udalova, PhD, Lecturer
 Jonathan Dean, PhD, Lecturer
 Abhi Jain, PhD, Snr Clinical Lecturer
 Fiona Watt, PhD, Consultant Rheumatologist/Clinical
 Scientist

j.saklatvala@imperial.ac.uk
h.nagase@imperial.ac.uk
r.maini@imperial.ac.uk
f.brennan@imperial.ac.uk
p.venables@imperial.ac.uk
peter.c.taylor@imperial.ac.uk
j.nanchahal@imperial.ac.uk
f.dazzi@imperial.ac.uk
andy.clark@imperial.ac.uk
e.paleolog@imperial.ac.uk
c.monaco@imperial.ac.uk
y.itoh@imperial.ac.uk
g.gharios@imperial.ac.uk
r.wait@imperial.ac.uk
t.vincent@imperial.ac.uk

richard.o.williams@imperial.ac.uk
n.horwood@imperial.ac.uk
k.midwood@imperial.ac.uk
c.murphy@imperial.ac.uk
i.udalova@imperial.ac.uk
jonathan.dean@imperial.ac.uk
Abhilash.Jain@imperial.nhs.uk
f.watt@imperial.ac.uk

<i>Post-Docs (excluding Senior Staff)</i>	45
<i>PhD students</i>	35
<i>Support personnel (Technicians)</i>	27

Current Fields of Research

The Kennedy Institute of Rheumatology is one of the world's largest centres of research in arthritis, so the ensuring description is of necessity, brief and incomplete, not all groups can be discussed. The KIR is a 'translational' research institute, with a full complement of research activities from uncovering new signalling and regulatory pathways to clinical trials.

In terms of pathogenesis of rheumatoid arthritis (RA), the regulation of TNF production is key and a number of strands have emerged. Thus the role phosphatases in the mechanism of gene regulation by corticosteroids is being analysed, the binding proteins to the AU rich regions of 3' untranslated regions of inflammatory proteins, the role of IRF in cytokine production, role of toll like receptors, the role of atypical T cells in synovial TNF production, role of NK cells, role of antigen presenting cells and their accessory molecules e.g., CD200, OX40 and so on.

From these studies potential therapeutic targets are uncovered which are tested in animal models of arthritis, chiefly collagen-induced arthritis, both in DBA/1 mice and C57BL/6. Clinical trials in RA and in ankylosing spondylitis are performed, and research is focused on new imaging and other outcome measures.

In terms of osteoarthritis research, there are a number of programs to study mechanisms of cartilage degradation and how to prevent it, and also work in pathogenesis of osteoarthritis (OA) in animal models. This is performed using the model of cutting the medial tibio-meniscal ligament. A variety of transgenic and knockout mice are being analysed. The role of matrix metalloproteinase enzymes and their inhibitors in the degradation of collagen and cartilage is being explored, as is the role of ADAM family enzymes. Complications of arthritis are being studied, atherosclerosis in particular. Here the focus is unravelling the cellular and molecular interactions to establish in more detail the mechanism of progression and thrombosis.

Selected Publications

1. Krausgruber, T, Blazek, K, Smallie, T, Alzabin, S, Lockstone, H, Sahgal, N, Hussell, T, **Feldmann, M, Udalova, IA**. IRF5 promotes inflammatory macrophage polarization and T_H1 - T_H17 responses. Nat Immunol epub ahead of print Jan 16 2011
doi:10.1038/ni.1990.
IF 26.000
2. Notley, CA, Inglis, JJ, Alzabin, S, McCann, FE, McNamee, KE, **Williams, RO**. Blockade of tumor necrosis factor in collagen-induced arthritis reveals a novel immunoregulatory pathway for Th1 and Th17 cells. J Exp Med Oct 27 2008
205(11):2491-7.
IF 14.505
3. Abraham, SM, Lawrence, T, Kleiman, A, Warden, P, Medghalchi, M, Tuckermann, J, **Saklatvala, J, Clark, AR**. Antiinflammatory effects of dexamethasone are partly dependent on induction of dual specificity phosphatase 1. J Exp Med Aug 7 2006
203(8):1883-9.
IF 14.505
4. Lymeri, S, **Horwood, N**, Marley, S, Gordon, MY, Cope, AP, **Dazzi, F**. Strontium can increase some osteoblasts without increasing hematopoietic stem cells. Blood Feb 1 2008 111(3):1173-81.
IF 10.555

5. Krausgruber, T, Saliba, D, Ryzhakov, G, Lanfrancotti, A, Blazek, K, **Udalova, IA**. IRF5 is required for late-phase TNF secretion by human dendritic cells. *Blood* Jun 3 2010 115(22):4421-30.
IF 10.555
6. **Monaco, C**, Gregan, SM, Navin, TJ, **Foxwell, BMJ**, Davies, AH, **Feldmann, M**. Toll-like receptor-2 mediates inflammation and matrix degradation in human atherosclerosis. *Circulation* Dec 15 2009 120(24):2462-9.
IF 14.816
7. Inglis, JJ, McNamee, KE, Chia, SL, Essex, D, **Feldmann, M**, **Williams, RO**, Hunt, SP, **Vincent, T**. Regulation of pain sensitivity in experimental osteoarthritis by the endogenous peripheral opioid system. *Arthritis Rheum* Oct 2008 58(10):3110-9.
IF 7.332
8. Lundberg, K, Kinloch, A, Fisher, BA, Wegner, N, Wait, R, Charles, P, Mikuls, TR, **Venables, PJ**. Antibodies to citrullinated α -enolase peptide 1 are specific for rheumatoid arthritis and cross-react with bacterial enolase. *Arthritis Rheum* Oct 2008 58(10):3009-19.
IF 7.332
9. **Taylor, PC**, Steuer, A, Gruber, J, Cosgrove, DO, Blomley, MJ, Marsters, PA, Wagner, CL, McClinton, C, **Maini, RN**. Comparison of ultrasonographic assessment of synovitis and joint vascularity with radiographic evaluation in a randomized, placebo-controlled study of infliximab therapy in early rheumatoid arthritis. *Arthritis Rheum* Apr 2004 50(4):1107-16.
IF 7.332
10. Glass, GE, Chan, JK, Freidin, A, **Feldmann, M**, **Horwood, NJ**, **Nanchahal, J**. TNF- α promotes fracture repair by augmenting the recruitment and differentiation of muscle-derived stromal cells. *Proc Natl Acad Sci U S A* Jan 25 2011 108(4):1585-90.
IF 9.432

Current Funding

Arthritis Research Campaign
British Heart Foundation
Celgene/Signal Pharma
CRUK
Dyax Corporation
European Commission
Graham Dixon Charitable Trust
GlaxoSmithKline
Healing Foundation
Hammersmith Hospitals Trust Research Committee
Imperial College Healthcare NHS Trust
Imperial Innovations
Kennedy Institute of Rheumatology Trust
Leukaemia Research Fund
Medical Research Council
National Institute of Health/Cornell
Novo Nordisk
Nuon Therapeutics Inc.
Royal College of Surgeons (England)
Rosetta Inpharmatix LLC
Somalogic
University of Glasgow
Wellcome Trust

Training of Fellows in Research

We have well established programs for training in both clinical and laboratory research, of all major techniques of cell culture, molecular biology and serology.

WebPages

<http://www1.imperial.ac.uk/medicine/>
<http://www1.imperial.ac.uk/medicine/about/divisions/kennedy/>