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Professor David Sansom BSc, PhD

Honorary Professor of Immune Cell Biology

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About

David Sansom is a Professor of Immune Cell Biology in the College of Medical and Dental Sciences.

David has published numerous papers in internationally recognised scientific journals mostly in the field of T cell immune regulation and its relevance to autoimmune diseases such as rheumatoid arthritis. He has received substantial grant funding from a wide range of biomedical research funders including BBSRC, The Wellcome Trust, Arthritis Research UK and the Medical Research Council.

David gives talks at both national and international meetings on the subject of T cell immune regulation as well as to lay audiences and fundraisers. His laboratory has presented at local Science museums as well as provided researchers in residence to schools. The Sansom lab hosts 6th form students for laboratory experience

Qualifications

- PhD Immunology 1988
- BSc (Hons) Applied Biology 1985

Biography

David obtained a First Class Hons degree in Biological Sciences from Bristol Polytechnic in 1985. His PhD work was carried out at the UK Transplant Service in Bristol where he became interested in the genetics of the Major Histocompatibility Complex (MHC). David's PhD involved using molecular biology to probe new MHC associations with rheumatoid arthritis in collaboration with Prof. Peter Maddison at the Royal National Hospital for Rheumatic Diseases.

Following his PhD, David worked as a Research Fellow at the Imperial Cancer Research Fund laboratories (now CRUK) in London with John Trowsdale. Here he began working on the molecular requirements for T cell stimulation and ultimately the role of "co-stimulatory" molecules such as those in the B7-CD28 pathway.

In 1991 he moved to the University of Bath to start his own laboratory. With generous support from ARC (now Arthritis Research UK) David was awarded a postdoctoral Research Fellowship and subsequently Senior Research Fellowships with which he established himself in the area of T cell costimulation and immune tolerance.

In 2000 David moved to University of Birmingham where his is now Professor of Immune Cell Biology. This reflects his increasing interests in the molecular and cellular basis of immune control.

David's interest and experience in human T cell immunology allows him to work closely with clinicians interested in both rheumatoid arthritis and type-1 diabetes in Birmingham.

David has been a member several national funding committees including the BBSRC's Biochemistry and Cell Biology panel and Asthma UK. David is currently a member of the Fellowships Committee at Arthritis Research UK.

Teaching

Teaching Programmes

- **MBChB (/undergraduate/courses/med/medicine.aspx)** (Immunology)
- **MRes (/postgraduate/courses/combined/med/health-research.aspx)**

Postgraduate supervision

David is interested in supervising doctoral research students in the following areas:

- T cell immunity and tolerance.
- The molecular basis of T cell costimulation and inhibition
- The effect of vitamin D and other environmental factors on immune regulation.

If you are interesting in studying any of these subject areas please contact David on the email address above.

Research

RESEARCH THEMES

Immune Regulation. T cell responses in Autoimmune disease.

RESEARCH ACTIVITY

CTLA-4 biology

The major effort of our lab in the last few years has been to try and understand the molecular mechanism by which CTLA-4 can control T cell responses.

We have used ligand based approaches to study CTLA-4 and identified that expression of CTLA-4 is sufficient to confer regulatory behaviour to T cells in a cell–extrinsic manner. This has led to a re-evaluation of the mechanisms of CTLA-4 action. We have recently identified a novel mechanism “trans-endocytosis” whereby CTLA-4 acts as a molecular pump that removes costimulatory ligands from APCs. This mechanism of action may be sufficient to explain the cell extrinsic suppressive function of CTLA-4.

Vitamin D and immune regulation.

T cell responses are influenced by the environment in which T cell stimulation occurs. This is relevant since the genetics of autoimmune disease suggests that T cells are important in the aetiology but that there are significant environmental effects on disease. We have begun to look at the effect of vitamin D,an environmentally regulated vitamin, on human T cell responses. We have recently shown that vitamin D can profoundly influence the cytokine profiles of T cells in response to stimulation inhibiting several inflammatory cytokines and promoting expression of regulatory associated markers including CTLA-4

The role of co-stimulatory pathways in regulating T cell responses.

An important focus of the Sansom lab is understanding the function of the CD28 /CTLA-4 pathway and how this regulates T cell responses. This has proven a complex problem given that the system employs two different ligands which both bind to a pair of receptors of opposite function. Over many years, our work has involved the study of the two natural ligands CD80 and CD86 and their role in T cell stimulation. We initially identified PI3kinase as a signalling target for CD28 pathway as well as the transcriptional targets AP-1 and NfKB. More recent work has focused on the role of these ligands in Treg biology including Treg proliferation and function. Current projects are aimed at determining the distinct role of each ligand in influencing immune responses.

Other activities

- Editorial board of “Immunology”
- Member of Arthritis Research UK Fellowships implementation committee

Publications

Walker, L.S., and D.M. Sansom. 2011. The emerging role of CTLA4 as a cell-extrinsic regulator of T cell responses. Nature Reviews Immunology 11:852-863.

Qureshi, O.S., Y. Zheng, K. Nakamura, K. Attridge, C.N. Manzotti, E.M. Schmidt, J. Baker, L.E. Jeffery, S. Kaur, Z. Briggs, T.Z. Hou, C. Futter, G. Anderson, L.S.K. Walker, and D.M. Sansom. 2011. Trans-endocytosis of CD80 and CD86: A molecular basis for the cell extrinsic function of CTLA-4: . Science 332:600-603

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Schmidt, E.M., C.J. Wang, G.A. Ryan, L.E. Clough, O.S. Qureshi, M. Goodall, A.K. Abbas, A.H. Sharpe, D.M. Sansom, and L.S. Walker. 2009. Ctla-4 controls regulatory T cell peripheral homeostasis and is required for suppression of pancreatic islet autoimmunity. J Immunol 182:274-282.

Zheng, Y., C.N. Manzotti, F. Burke, L.M. Dussably, O. Qureshi, L.S.K. Walker , and D.M. Sansom. 2008. Acquisition of suppressive function by activated human CD4+ CD25- T cells is associated with the expression of CTLA-4 not FoxP3. J.Immunol. 181:1683-1691.

Sansom, D.M., and L.S. Walker. 2006. The role of CD28 and cytotoxic T-lymphocyte antigen-4 (CTLA-4) in regulatory T-cell biology. Immunol Rev 212:131-148.

Manzotti, C.N., M.K.P. Liu, F. Burke, L. Dussably, Y. Zheng, and D.M. Sansom. 2006. Integration of CD28 and CTLA-4 function results in differential responses of T cells to CD80 and CD86. Eur. J Immunol. 36:1413-1422.

Mead, K.I., Y. Zheng, C.N. Manzotti, L.C. Perry, M.K. Liu, F. Burke, D.J. Powner, M.J. Wakelam, and D.M. Sansom. 2005. Exocytosis of CTLA-4 Is Dependent on Phospholipase D and ADP Ribosylation Factor-1 and Stimulated during Activation of Regulatory T Cells. J Immunol 174:4803-4811.

Gough, S.C.L., L.S.K. Walker, and D.M. Sansom. 2005. CTLA4 gene polymorphism and autoimmunity. Immunological Reviews 204:102-115.