Profile Anne O'Garra

Place of birth: Gibraltar
Scientific training (places): (1977-1980) B.Sc. -1 st Class Honours Microbiology/Biochemistry. Chelsea College, University of London, England. (1980-1983) Ph.D. thesis: Adhesion of coagulase negative Staphylococci to human epithelial cells. -Division of Microbiology National Institute for Medical Research, Mill Hill, England. (December 1983) -Postdoctoral Fellow: Cytokines in B Cell Growth differentiation.. (January 1987) -(funded by Glaxo Research) Division of Immunology, National Institute Medical Research, Mill Hill, England.
Former supervisors: Supervisor: Dr. J. B. Ward, Dr G.G.B. Klaus Current areas of research: Immunoregulation and Tuberculosis
Present affiliation: National Institute for Medical Research, Mill Hill, London UK
Email: aogarra@nimr.mrc.ac.uk
Website: http://www.nimr.mrc.ac.uk/
Laboratory: how many students and post-docs: 12
Laboratory: available techniques: Immunology and Molecular Biology

A Word with the Speaker: Anne O´Garra

-Question: What were your greatest motivations to enter your current area of research?
-Speaker: Interest in basic understanding of immune regulation and the problems with tuberculosis.

- Question: In your opinion, which were the breakthroughs in this area of research in the last years?
-Speaker: Th1/Th2/Th17/Tregs/TLR function on DC and macrophages.

- Question: What do you consider to be a particularly relevant or challenging question to be answered in this area of research?
-Speaker: There are many.

- Question: What do you regard to be a particularly challenging question to be answered in Immunology?
-Speaker: How to get the right immune response to clear a pathogen with minimum damage to the host.

- Question: In your opinion, what is an important scientific contribution that you and your group have made? And why?
-Speaker: Mechanism of action and expression of IL-10.

- Question: Do you think your results have the potential to be translated into some clinical application? Tell us how and if you think this could be achieved in the near future.
-Speaker: Enhancing immune responses on neutralization of IL-10.

-Two of your most important papers:

Fiorentino, D. F., Zlotnik, A., Mosmann, T. R., Howard, M., and O'Garra, A. (1991a). IL-10 inhibits cytokine production by activated macrophages. J Immunol 147:38153822.

Macatonia, S. E., Hosken, N. A., Litton, M., Vieira, P., Hsieh, C. S., Culpepper, J. A., Wysocka, M., Trinchieri, G., Murphy, K. M., and O'Garra, A. (1995). Dendritic cells produce IL-12 and direct the development of Th1 cells from naive CD4+ T cells. J Immunol 154:5071-5079.

Brief CV -Anne O'Garra

Anne O'Garra obtained her Ph.D. at the National Institute for Medical Research (NIMR), Mill Hill, London, UK. At the DNAX Research Institute, California, USA, she

made seminal contributions to our understanding of the intricate network of cell-cell and cytokine interactions responsible for inducing and inhibiting cellular immune responses. Importantly she first elucidated that interleukin 10 (IL-10) has broad immunosuppressive functions, inhibiting antigen presentation by dendritic cells and macrophages and their production of inflammatory cytokines. She elucidated fundamental mechanisms regulating the activation of T-cell subsets with distinct effector functions, discovering that: IL-12 induced T-helper 1 (Th1) cells secreting IFN , essential for eradication of intracellular pathogens; the key antigen presenting cell, the dendritic cell, produced IL-12, under tight control of IL-10. These findings have major implications for regulation of the immune response to pathogens. O'Garra returned to the UK as Head of the new Division of Immunoregulation at the NIMR, Mill Hill, London, to interface the divisions of immunology and infectious diseases, where she is continuing her work on immunoregulation with specific emphasis on mechanisms of immunepathogenesis in tuberculosis. In 2005 she was elected as a Fellow of the Academy of Medical Sciences, UK.

Publications – Last 3 years – Anne O'Garra

1. Vieira, P.L., Christensen, J.R., Minaee, S., O'Neill, E.J., Barrat, F.J., Boonstra, A., Barthlott, T., Stockinger, B., Wraith, D.C., and O'Garra. A. (2004). Interleukin-10-secreting regulatory T cells do not express Foxp3 but have comparable regulatory function to naturally occurring $CD4^{+}CD25^{+}$ regulatory T cells. J. Immunol. 172: 5986-5993.

2. Okada, T., Miller., M.J., Parker, I., Krummel., M.F., Neighbors, M., Hartley, S.B., O'Garra, A., Cahalan, M.D., and Cyster, J.G.(2005). Antigen-engaged B cells undergo chemotaxis toward the T zone and form motile conjugates with helper T cells. Plos Biol. 150.Epub 2005 May 3.

3. Asselin-Paturel, C., Brizard, G., Chemin, K., Boonstra, A., O'Garra, A., Vicari, A., and Trinchieri, G. (2005). Type I interferon dependence of plasmacytoid dendritic cell activation and migration. J Exp Med 201(7): 1157-67.

4. Barthlott, T., Moncrieffe, H., Veldhoen, M., Atkins, C.J., Christensen, J., O'Garra, A., and Stockinger, B. (2005). CD25+ CD4+ T cells compete with naive CD4+ T cells for IL-2 and exploit it for the induction of IL-10 production. Int.Immunol. 17(3): 279-88.

5. Saraiva, M., Christensen, J., Tsytsykova., A., Goldfeld, A.E., Ley. S., Kioussis, D., and O´ Garra. A.(2005). Identification of a Macrophage-Specific Chromatin Signature in the IL-10 Locus. J. Immunol. 175: 1041-1046.

6. Xystrakis, E., Kusumakar, S., Boswell, S., Peek, E., Lavender, P., Urry, Z.,. Richards, D.R., Adikibi, T., Pridgeon, C., Dallman, M., Loke, T-H., Robinson, D.S., Barrat,

Reversing the defective induction of IL-10 secreting T regulatory cells in glucocorticoid resistant asthma patients. J.Clin Invest. 116: 146-155.

7. Haque, A., Easton, A ., Smith, D., O'Garra, A., Van Rooijen, N., Lertmemongkolchai, G., Titball, RW., Bancroft, GJ. (2006). Role of T Cells in Innate and Adaptive Immunity against Murine Burkholderia pseudomallei Infection. J Infect Dis. 193: 370-379.

8. Shoemaker, J., Saraiva, M., O'Garra, A. (2006). GATA-3 directly remodels the IL10 locus independently of IL-4 in CD4+ T cells. J. Immunol. Vol. 176 (6): 34703479.

9. Papoutsopoulou, S. Symons, A., Tharmalingham, T., Belich, M. P. , Kaiser, F., Kioussis, D., O'Garra, A., Tybulewicz, V., and Ley, S. C.. 2006. ABIN (A20-binding inhibitor of NF-B)-2 is required for optimal activation of the TPL-2 / ERK MAP kinase pathway. Nature Immunol.

10. Sponaas, A-M., Cadman, E.T., Voisine, C., Harrison, V., Boonstra, A., O'Garra, A., and Langhorne, J. 2005. Malaria infection changes the ability of splenic dendritic cell populations to stimulate antigen-specific T cells. 2006. J.Exp.Med, 203, No. 6, 1427.

11. Rowland CA, Lertmemongkolchai G, Bancroft A, Haque A, Lever MS, Griffin KF, Jackson MC, Nelson M, O'Garra A, Grencis R, Bancroft GJ, Lukaszewski , RA. . 2006. Critical role of type 1 cytokines in controlling initial infection with Burkholderia mallei. Infect Immun. 74(9):5333-40.

12. Boonstra, A., Rajsbaum R., Holman, M., Marques, R., Asselin-Paturel, C., Pereira, J.P., Bates, E.M., Akira, S., Vieira, P., Liu, Y-J., Trinchieri, G., and O'Garra,A. 2006. Macrophages and myeloid DC, but not plasmacytoid DC, produce IL-10 in response to MyD88-and TRIF-dependent TLR signals, and TLR-independent signals. J.Immunol. 177, 7551 – 7558.

13. Neighbors, M., Hartley, SB., Xu, X., Castro, AG., Bouley, DM and O'Garra, A. 2006 Breakpoints in immunoregulation required for Th1 cells to induce diabetes. Eur J Immunol. Sep;36(9):2315-23.