JAMES RENNIE BEQUEST

REPORT ON EXPEDITION/PROJECT/CONFERENCE

Expedition/Project/Conference Title: Keystone Immunoregulatory Networks

Travel Dates: 1st – 6th April, 2011

Location: Breckenridge, Colorado

Group Member(s): Stephen Redpath

Aims:

- To meet the principal scientists in the field of Immune regulation and search out potential postdoctoral opportunities
- Present current research in poster format
- Attend high profile plenary talks, oral presentations and poster presentations
- Networking and discussing new ideas with fellow immunologists

---

OUTCOME (not less than 300 words):-

Keystone Immunoregulatory Networks conference report:

The Keystone Immunoregulatory Networks conference aimed to address a number of key issues in the field of immune regulation, namely; development and maintenance of regulatory cells, molecular mechanisms governing regulatory networks, and mechanisms of regulatory function. Immune regulation is central to the prevention of autoimmune diseases, but it may also inhibit anti-tumour immunity and curb protective immunity to pathogens. As such, the study of immune regulation is of principal importance for the development of novel therapies for the treatment of cancer, autoimmune disease and allergy, and for treatment of pathogenic diseases. Keystone conferences are the most prestigious scientific meetings, and I was extremely grateful for the opportunity to present my work there, and also to discuss ideas with the top scientists within the immunoregulatory field.

The meeting was opened on Friday evening by a plenary talk from Dianne Mathis, of Harvard Medical School, who described her novel research into distinct regulatory T cell (Treg) populations within adipose tissue, and how manipulation of these adipose Treg can be used for the treatment of type 2 diabetes. This exciting data emphasised the importance of the long term goals of my own research, in that development of a Treg therapy for the treatment of disease is indeed possible.

Saturday's plenary sessions focused on the molecular mechanisms controlling regulatory cell function, and I was excited to hear talks on this subject from Steven Ziegler and Alexander Rudensky. Both talks dealt with issues regarding the induction of the Treg master transcription factor Foxp3, and production of the suppressive cytokine IL-10 from $Foxp3^+$ Treg. The data presented was of direct relevance to my project, a tenet of which is the role of the inducible co-stimulator (ICOS) in $Foxp3^+$ Treg IL-10 production, and it led to a number of new hypotheses for the final stages of my laboratory work. In addition, Daniel Campbell gave an overview of the different 'flavours' of Treg that develop under various immunological conditions; this gave us the idea to distinctly characterise the Treg generated in response to helminth infection.

Sunday began with a number of talks centred on Treg development and Immunomodulation. Of note, Michael Croft of the La Jolla Institute of Allergy and Immunology gave an interesting presentation on the role of TNFR family members in Treg development, in which he provided evidence that TNFR receptor

agonists can be used to manipulate Treg responses such that the symptoms of asthma are ameliorated. Later in the morning David Artis of the University of Pennsylvania talked about his current work on mucosal regulation by intestinal epithelial cells, and he described the importance of intestinal epithelial cells for the development of Th2 responses to gastrointestinal helminths. This was both interesting and insightful for my own research, which deals with the development of Th2 responses in the small intestine following *H.polygyrus* infection. On Sunday afternoon I attended a workshop of short talks on Cellular Immunoregulatory Networks. There were a number of interesting talks, but in particular I was excited to hear a description of a novel T cell coreceptor of the Ig superfamily named VISTA which acts as a negative regulator of Treg.

On Monday the plenary sessions focused on cytokine modulation of regulatory networks and there were talks from some of the biggest names in the regulatory field. For example, Dario Vignali presented work on the newly discovered regulatory cytokine IL-35, and Chris Hunter described his latest research into the role of IL-27 in the regulation of immune responses. I was especially looking forward to hear Chris's talk, having read much of his work relating to IL-27, because IL-27 has been shown to induce both ICOS and IL-21, which act together to promote production of IL-10.

The final day's talks were directed on new modulators of regulatory networks and immunotherapy, and also on the plasticity of regulatory populations. Arlene Sharpe talked about the role of PD-1 in T cell activation and tolerance, and Suzanne Toplian subsequently showed that this research translated directly to the clinic, in that blockade of the PD-1 axis can be used as an effective cancer therapy. Later in the day, having read a number of his insightful reviews into mechanisms of costimulation, I was happy to hear a presentation from Jeff Bluestone of the University of California. Jeff presented his recent data suggesting that ablation of microRNA can impair Treg function and lead to the development of autoimmune disease, thus highlighting an additional target for novel Treg therapies.

Poster sessions ran at the end of each day, and I was glad to have the opportunity to present my own poster on Monday evening. There was a substantial amount of interest in my poster and I had a number of exciting discussions about my work, with the result that I came away with several new ideas for avenues of research. This was a unique opportunity for discussion with the leaders in the field of immune regulation and I was extremely grateful for this experience.

One of my principal aims for the conference was to network with the top immune regulation scientists in order to discover potential postdoctoral opportunities. I was able to make contact with the labs of Chris Hunter, Dario Vignali, Daniel Campbell and Jeff Bluestone, who gave me some useful advice about applying for postdoc jobs and I hope that this will be of value in the near future.

This conference stood out above all previous conferences I have attended. Every talk was of interest to my own research, all the key immune regulation scientists were in attendance, the quality of the presentations was extremely high and the discussions they generated were stimulating and insightful. I would like to express my sincere gratitude to the James Rennie foundation for provision of a travel grant, without which I would not have been able to attend this conference, which was of principal importance in my development as a scientist.