JAMES RENNIE BEQUEST

REPORT ON EXPEDITION/PROJECT/CONFERENCE

Expedition/Project/Conference Title: Keystone Symposia: Regulatory T cells.....

Travel Dates: 29th January 2007 – 16th February 2007 .....

Location: Fairmont Hotel, Vancouver, Canada .....

Group Member(s): Henry McSorley .....

Aims: Presentation of my results (poster), forming links with other laboratories .....

OUTCOME (not less than 300 words):-
The Keystone Symposium conferences are regarded to be the best in the field of Immunology, and this Regulatory T cell conference lived up to these expectations. The speakers present were the leaders in their field, with the first speaker being Shimon Sakaguchi, the discoverer of regulatory T cells and still one of the leading figures in the field. He gave an excellent presentation on the history of Treg research, also presenting some excellent unpublished research on some new molecules involved in Treg differentiation, and how these affect the function of the cell. The rest of the first day was dedicated to molecular events within Tregs, with some fascinating insights Anjana Rao into what FoxP3 (a transcription factor in Tregs, and the best marker for Tregs) does within the cell, and how this leads to either effector cells, anergic cells or Tregs. Other data presented by Shohei Hori investigated how FoxP3 affects gene transcription in Treg differentiation and function.

Disappointingly for me, Richard Flavell was not available to attend the meeting, however one of his PostDocs, Ming Li, took his place in the second session and gave an excellent presentation on the role of TGF-β in Treg differentiation. This was very useful to me as my project hinges around TGF-β and its role in inducing Treg differentiation during parasitic infections, and also as he was presenting a lot of data using the TGF-βR DN mouse strain we have recently received and will be using shortly. A discussion with him after his presentation allowed me to explain some of my results involving blocking TGF-β using antibodies, and so was extremely useful. Amongst the presentations that day was one by Tobias Bopp, showing Tregs and Teffectors transferring intracellular material, a previously unknown method of interaction, which could have big implications for Treg function. Debbie Fowle presented some data on the kinetics of Treg suppression, showing that Tregs suppress Teffectors before the first cell division – within the first 10 hours. Harold Boehmer gave a very entertaining talk on delivering antigens to immature dendritic cells specifically, using DEC-205, which resulted in antigen-specific Treg expansion.

A common feature of many of the presentations was the TcR repertoire of Tregs and Teffectors, and the results presented all seemed to agree that they have quite strictly non-overlapping repertoires, obviously indicating Tregs and Teffectors recognise different antigens. This may have an impact on my own research as if the Tregs are recognising a different antigen than the Teffectors, they not be come from a separate lineage, rather than differentiating from the Teffectors during the response as we have supposed. However, none

of the data presented on Treg TcR repertoires was in the context of an infection, and so other factors may come into play here.

The following day, Ethan Shevach,gave the first talk, where he caused controversy by proposing that TGF-β induced Tregs may have FoxP3, but be non-functional. This is against the accepted dogma that FoxP3+ cells are all suppressive, however in his hands these FoxP3+ TGF-β induced cells did not seem to be able to suppress as they should, and these results were backed up by other presentations during the conference. Lauren Collison gave an interesting talk about IL-34, a relatively new cytokine which has suppressive effects and is upregulated in Tregs, therefore may be an important previously unknown method of suppression. The second session of the day presented infection data and Treg involvement, with talks on Hepatitis, Chlamydia and Theiler's virus. The last session of the day was themed around "unconventional Treg subsets, including data presented by Adrian Hayday on γδTregs.

That evening I presented my poster and was able to speak to several people about my research, which was very useful. I also managed to contact Yasmine Belkaid, Kingston Mills and Fiona Powrie, and was able to enquire about possible positions in their labs after my PhD, all of which sounded very positive.

The first session of the 3rd day was again concerning infection and Tregs, with presentations by both Kingston Mills and Yasmine Belkaid, both of whose research I have been following closely. Kingston Mills work uses a liver fluke which (as in my model of *B. malayi*) induces a Treg response in the peritoneal cavity. However his data shows a Tr1 response which I do not see in my model, and it was interesting to compare our results. Yasmine Belkaid's work on Leishmania shows an induction of natural Tregs at the effector site, and is what much of my own work is based around. Her more recent work concerns a gut model using a bacterial infection which again encouraged natural Treg accumulation at the effector site.

The last session of the day began with Fiona Powrie speaking on the role of CD103 on Tregs. As my data also shows a very significant CD103 induction on my induced Tregs, this was very interesting to me. Much of her data concerned CD103 positive or negative dendritic cells, and showed that the CD103+ DCs induced regulation, whereas the CD103- DCs induced inflammation. This has implications for my work, and I will be looking in the future for CD103 on the DCs in my system also. Alf Hamann also presented data on CD103, showing that CD103+ Tregs have an effector/memory phenotype, and seem to suppress at the site of inflammation, whereas CD103- Tregs suppress at the lymph node.

The final day of the conference was concerned mostly with autoimmunity, transplantation and tumour immunity, and the role for Tregs here. Although this is not the area in which I am most interested, there were some excellent talks, includingthe first talk of the day by Jeffrey Bluestone, who presented some very interesting results using diabetes-prone NOD mice, indicating that a subset of DCs expressing CD101 are involved in Treg induction, and could possibly be manipulated in human disease.

Overall this was a very enjoyable and useful conference, and as well as giving me ideas for future directions in my project, I also made many useful contacts which will help me with my future career.