JAMES RENNIE BEQUEST

REPORT ON EXPEDITION/PROJECT/CONFERENCE

Expedition/Project/Conference Title: Molecular Approaches to Malaria 2004 (MAM2004).....

Travel Dates: 1st-5th February 2004.....

Location: Lorne, Victoria, Australia.....

Group Member(s): Lisa Sharling, ICAPB.....

Aims:
(1) To present my work at the 2004 Molecular Approaches to Malaria meeting, a highly focused international conference, and to discuss my work with experts in the field.
(2) To keep up to the minute with advances in a fast moving and competitive field in order to plan carefully the final year of my PhD.
(3) To meet potential employers for post-doc positions.

OUTCOME (not less than 300 words):-

The Molecular approaches to Malaria 2004 (MAM2004) conference was the sequel to a meeting of the same name held in Lorne, Australia in 2000. The focus of the first MAM meeting in 2000 was to assess the progress made towards sequencing the genome of *Plasmodium falciparum*, the causative agent of the most severe form of malaria in humans, and to identify future challenges. An international consortium of scientists initiated the enormous task of sequencing *P. falciparum's* genome in 1996 and the 23 million base pairs of DNA from a *P. falciparum* clone were completely sequenced in 2002. The mission of MAM2004 therefore, was to discuss the progress made towards translating the wealth of information held by the parasite's genome sequence into discoveries that improve our understanding of the parasite's biology and pathogenicity in order to develop novel malaria intervention strategies. MAM2004 was a small meeting of just 380 delegates, but as the aim of the meeting was extremely focused every talk and session was often directly relevant to my PhD, and if not still extremely interesting. As sessions were not run in parallel oral presentations were extremely competitive and of the highest standard.

Aim (1)

Since oral presentations were limited and highly competitive I presented a poster at MAM2004. The poster sessions were well attended and in some respects became the focus of the meeting.

Generally discussion at the poster sessions was lively and I was pleasantly surprised by the interest shown in my poster.

My poster fitted nicely into the proteomics session. During my PhD my primary aim as been to develop a proteomics approach to identify the surface antigens on *P. falciparum* infected erythrocytes that bind to placental receptors in cases of pregnancy associated malaria (PAM). Such an approach has become possible since the completion of a *P. falciparum* genome sequence. However, since the molecules I am trying to identify are vaccine candidates for PAM many labs internationally are working towards the same goal. While attending MAM2004 I was anxious to discover who else in the field had started to move towards a proteomics based approach and to assess their progress, especially as a crucial step in my approach was proving problematic and I was not making great headway. A 'discussion' about this aspect of my work gave me great encouragement to continue with the troublesome, but crucial step in my PhD. Judging by the disbelief shown by one expert in the field with regard to my positive results when applying the technique to the mouse model of malaria *P. chabaudi* it was clear that I was not the only one who a) was attempting to apply this approach and b) was also struggling. Actually this interaction was not so much a critical scientific discussion, but more reminiscent of a pantomine sketch.

Scientist X: *You can't surface label infected cells with biotin.*
Me: *Actually it's worked well with P. chabaudi.*
Scientist X: *Oh no you can't.*
Me: *Oh yes I can, look!*
Scientist X: *Oh no you can't.*
e.t.c

On my return to Edinburgh I persisted with optimising the technique and finally it has been successfully applied *P. falciparum* infected erythrocytes.

Aim (2)

A number of the talks and posters presented at MAM2004 had a direct impact on how I approached the final year of my PhD. K. Chotivanich presented a poster showing erythrocytes infected with *P. vivax*, a less virulent species of human malaria, also bind to placental receptors. Placental binding had originally thought to be restricted to *P. falciparum*. The findings of K. Chotivanich I found especially interesting as the genes encoding the PfEMP1 protein, the prime candidate for placental binding and, therefore, inclusion in a vaccine for *P. falciparum* PAM are not present in the genome

of *P. vivax*. One reason for developing a proteomics approach was it's potential to identify any protein encoded by the parasites genome. K. Chotivanich's work along with a number of other studies presented at MAM2004 further support the need to consider approaches that are not limited to detecting only PfEMP1. K. Chotivanch was interested in the methods I had been optimising to characterise *P. falciparum* erythrocyte surface antigens and she is now applying my protocol to *P. vivax* infected erythrocytes.

Two talks were particularly relevant to my project. The first of these was presented by T. Staalsoe and described experiments focused at determining which PfEMP1 is expressed by placental binding parasites. PfEMP1 is encoded by a multi-gene family called *var*. *Var* genes are large and are present in approximately 60 *var* copies per parasite genome, both these traits make these genes particularly tricky to study using current molecular techniques. T. Staalsoe, however, described a carefully controlled transcriptional study that identified a *var* gene that is upregulated following selection of the parasite for placental receptor binding. The *var* transcript described by T. Staalsoe is the third *var* to be associated with PAM and it will be interesting to see whether protein expression data or proteomics data will confirm the candidacy of any of the growing number of PAM associated *var* genes. One on the last talks presented at MAM2004 was by John Hyde, who described a sophisticated quantitative proteomics approach specifically for labelling *Plasmodium* proteins. Before we all boarded the coach back to the airport shortly after John's talk I managed to arranged to visit him in Manchester to discuss the possibility of collaborating and applying his technique to PAM relevant *P. falciparum* clones and a number of potential *P. chabaudi* proteins I had identified. A collaboration was initiated following a successful meeting in Manchester.

Aim (3)

During MAM2004 I talked with a number of people that were carrying out really exciting research. However, a post-doc position did not result from attending MAM2004. I have now accepted a post-doc position with Boris Striepen. I shall work in his lab on two parasites, which are closely related to Plasmodium and whose biology are equally as fascinating as Plasmodium's. Boris Striepen carried out his post-doctoral training with David Roos, one of the most interesting scientists and personalities at MAM2004. It was partly Boris Stripen's experience of working with David Roos that attracted me to his advertised post.