JAMES RENNIE BEQUEST

REPORT ON EXPEDITION/PROJECT/CONFERENCE

Expedition/Project/Conference Title: Gene Expression during Pancreas Development

Travel Dates: 9th June 2008 -15th August 2008

Location: University of California at San Francisco

Group Member(s): Fiona Docherty

Aims: To investigate the changes in gene expression that occur during the development of the pancreas that give rise to insulin-secreting β cells.

OUTCOME (not less than 300 words):-

James Rennie Bequest

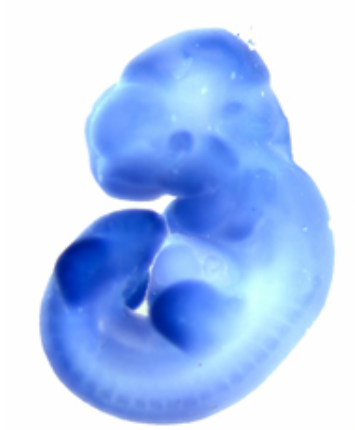
As a third year Biochemistry student at Edinburgh University I found myself with the annual pre-summer holidays panic. The question of what to do with my fast approaching four months of freedom was hot on my mind. Should I get a job and start paying back my loan? Would it be irresponsible to go on an extended holiday somewhere exotic? Or, should I try and find some kind of work experience, do something to further my career etc? These are questions no doubt faced by most University students every year.

I was understandably delighted when I was offered an internship in a top class medical research lab in San Francisco, this was my chance to gain both lab experience and life experience of the highest quality. With the financial aid provided by the James Rennie Bequest I was able to accept the placement at UCSF and the best summer of my life was set to begin.

On the 9th of June 2008 I began work in the Diabetes Centre at the University of California at San Francisco in Professor M. German's lab. I was placed under the supervision of Dr Anastasia Mavropoulos and was allowed to participate in two of the many projects she had on the go at the time. The work was primarily concerned with gene expression during pancreas development, working under the idea that in order to fully understand Diabetes it is necessary to first understand how the all important insulin-secreting β cells of the Pancreas arise.

The first project I was working on involved mapping the expression of certain genes of interest known to be expressed during pancreas development. I looked at their expression in sections of mouse embryos of different developmental stages via the techniques of immunostaining which utilises labelled antibodies specific to the protein of interest to mark its location and in-situ hybridisation that uses labelled

RNA molecules specific to the gene of interest. In this way it was possible to trace the lineage of insulin producing cells throughout embryonic development. I learned some really interesting and specialised techniques, from embryo cryo-sectioning to in-situ hybridisation, that I never would have come across otherwise.



The second project was to investigate the role of microRNAs in post transcriptionally regulating expression of the gene encoding Nkx6.1. Nkx6.1 is a transcription factor involved in the final differentiation of β cells from their Ngn3 expressing progenitors. Consequently the Nkx6.1 protein is only found in β cells however, unexpectedly the mRNA that encodes Nkx6.1 has also been found in other cells lines of the pancreas. We hypothesised that perhaps micro RNA, short lengths of RNA that when complimentary to a coding sequence of mRNA inhibit its translation into a functional protein, were involved in restricting the expression of Nkx6.1 during development. We set about testing this theory by transfecting mouse pancreatic cell lines with a plasmid containing a luciferase reporter gene upstream of the 3'UTR of Nkx6.1. When introduced to the cells the plasmid DNA would be transcribed and translated to produce a functional luciferase protein whose presence is detectable via luciferase assay. In order to test the effect of microRNAs on the luciferase activity we co-transfected the cells with the plasmid DNA and specific RNAs. If the microRNAs bound to the Nxk6.1 sequence on the plasmid then they would prevent the luciferase protein being transcribed and translated and so the luciferase activity would be lowered. Again these were new techniques and ideas that I had to master.

I spent ten weeks at UCSF working with Anastasia, I can safely say that I worked harder in those ten weeks than I ever had before. The hours were demanding and the work required constant concentration however, I loved every minute of it. The work that I did formed the basis for research that Anastasia was to continue, consequently the data I produced is not mine to show you. A number of the experiments I carried out yielded interesting results and may well be published in the next year or so, until then however you'll have to take my word for it!

My internship at UCSF has been invaluable in boosting my confidence in my abilities and has given me the ambition required to pursue a career in medical research. The experience I gained will no doubt prove invaluable in my future lab projects. In fact, I am already off to an encouraging start career wise having recently been accepted for a PhD placement at Cambridge University; I am certain that without my experience at UCSF last summer I would not have made it through the competitive selection process. I'd like to take this opportunity to thank the James Rennie Bequest for their generous support that made this all possible, thank you!

Diabetes Center
University of California, San Francisco