Report for the Christine and T Jack Martin Research Travel Grant 2007

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I was very fortunate to be awarded the 2007 Christine and T Jack Martin Research Travel Grant at the 17th ANZBMS annual meeting in Queenstown. This award has allowed me to travel to Europe for the first time. My main destination was the Botnar Research Centre in Oxford, UK, however I also briefly visited Stuart Ralston's group in Edinburgh, and attended the ECTS meeting in Barcelona, and the Bone Research Society and British Orthopaedic Research Society joint meeting in Manchester. Overall it was a wonderful trip that allowed me to meet a lot of other researchers, and learn new experimental techniques.

Botnar Research Centre

My main destination in Europe was Dr Philippa Hulley's lab in the Botnar Research Centre, University of Oxford. Botnar is a purpose-built research facility for musculoskeletal research and is part of the Nuffield Department of Orthopaedic Surgery. It houses a number of research groups who investigate different aspects of bone and joint biology. Philippa's group studies signal transduction in osteoblasts, chondrocytes and tenocytes, with research focussing on pathological processes in osteoarthritis, rotator cuff injury, multiple myeloma, and mechanisms of bone growth in distraction osteogenesis. The interests of other research groups in the Botnar include osteoclast biology, osteoarthritis genetics, bisphosphonate mechanisms of action, tissue engineering and orthopaedic biomedical engineering.

We have recently established a collaboration with Philippa, Dr Zhidao Xia, and Professor Graham Russell aiming to develop bone cell cultures in three dimensional collagen scaffolds that provide a structure similar to the *in vivo* environment and are suitable for testing anabolic factors, and for investigating genes potentially involved in Paget's disease. Researchers in the Department of Materials at the University of Oxford produce scaffolds from type I collagen suitable for growth of bone cells. We believe these scaffolds have the potential to provide a better system than two dimensional cultures for examining the effects of various factors on osteoblastic cell signalling, differentiation, and matrix production. I worked with Philippa, Dao, and a postdoctoral researcher in the lab, Rachel Locklin, to set up cultures on scaffolds with primary cultures of mesechymal stromal cells which they grow from bone marrow taken from orthopaedic surgery of patients at the nearby Nuffield Orthopaedic Centre. A major part of my PhD project has been examining differential gene expression in osteoblasts from Paget's disease bone lesions, and one of the significantly upregulated genes was the intermediate filament keratin 18. I have recently been investigating the effects of overexpressing keratin 18 using an adenoviral vector. Given the potential effects changes in a cytoskeletal protein could have on cell shape and adherence, we thought it would be interesting to examine the effects of overexpressing this protein in three dimensional cultures. I was able to efficiently transduce the mesenchymal stromal cells, and these were then grown on collagen scaffolds. These experiments exposed me to a number of new techniques which we do not routinely perform in our lab, including confocal microscopy and cryosectioning. I also prepared some samples for electron microscopy and had an opportunity to assist with examining some of my samples using scanning electron microscopy. We are now in a position to be able to

repeat much of this work in Auckland. In addition, we performed co-culture experiments using transwell plates which I also hope to repeat in Auckland. I also visited the Department of Materials on a couple of occasions, and met Asma Yahyouche, the student who is making the scaffolds for us, and her supervisor Jan Czernuszka, and saw their equipment and facilities, and the methods they use to make scaffolds.

I presented my PhD research to a group at Botnar, including Dr Matthew Kemp, an expatriate New Zealander from the MRC Functional Genetics Unit at Oxford who has extensive experience working with intermediate filaments, and this produced useful discussions. I was also fortunate to be present for the Nuffield Department of Orthopaedic Surgery research day. It was fascinating to hear the range of research going on at Botnar, particularly the genetics and bioengineering research, which is quite different from what we do in Auckland, and utilises very different methodology to most of the research I am familiar with.

I very much enjoyed my time at Botnar. It was great to get some experience in a different lab, and working in a smaller institute was nice. While Philippa's research group is much smaller than our group in Auckland, the centre is quite small and friendly, so it was easy to meet people from other groups within the department. It was great to meet the researchers from Professor Nick Athanasou's group, one of whom was also doing research on Paget's disease. I enjoyed staying in Oxford, with the extensive history, and had dinner at Christ Church one night. I also knew Dr Andrew Stockley, senior tutor at Brasenose College from when he was principal of my undergraduate hall of residence, and had dinner with him and the principal of the college Professor Roger Cashmore, a successful physicist, and very interesting and entertaining man one evening.

ECTS Meeting, Barcelona

I attended the 35th European Symposium on Calcified Tissues, the premier European bone meeting, in Barcelona, Spain, which attracted almost 2900 delegates. I presented a poster at this meeting, which yielded some interesting discussions. The scientific program was very interesting, with many excellent talks and posters. I found this meeting much more manageable, and less overwhelming, than the ASBMR meeting which I attended in 2007, as there were generally only two sessions at once, meaning you could attend a wide range of sessions. There were a number of presentations about Paget's disease, one demonstrating that patients with SQSTM1 mutations develop disease earlier, and more extensively than those without, and tend to have higher rates of complications such as bone deformity and fractures. There was also an interesting presentation about mice with a 'knock-in' of the SQSTM1 P392L mutation, which develop lytic lesions in their limbs, and whose cells show increased osteoclastogenesis *in vitro*. There were also interesting sessions on osteoimmunology, osteoclast-osteoblast relationships, bone metastases and notch signalling. I also enjoyed the hot topics session, particularly the presentation about the role of microRNAs in bone formation.

One of my PhD supervisors, Jill Cornish, and my advisors Ian Reid and Tim Cundy were also at the meeting which gave me a great opportunity to touch base with them. I was also fortunate to meet Professor Roland Baron who has a research group at

Harvard University in Boston who do a lot of interesting research on signal transduction in bone cells.

BRS/BORS Meeting, Manchester

At the completion of my stay at the Botnar Research Centre I attended the Bone Research Society and British Orthopaedic Research Society joint meeting in Manchester with most of the members of Philippa Hulley's research group, and a number of other researchers from the Nuffield Department of Orthopaedic Surgery. This was a much smaller and more intimate meeting than the ECTS, and there were a number of interesting sessions, including a new investigators session entitled, 'Shaping your future in skeletal biology', which, although targeted specifically at a British audience, still presented a lot of useful information about developing an academic career. There were interesting presentations on a variety of topics including osteoclastogenesis in Paget's disease, changes in sclerostin expression in osteocytes in response to loading, effects of hypoxia on osteoclasts, the effects of inhibiting Dkk1 on osteolytic bone disease in multiple myeloma, and a variety of aspects of tissue engineering. There was also ample time for poster viewing and discussion.

While this was certainly an interesting and worthwhile meeting, it certainly made me appreciate the high standard of both invited speakers and local work that is presented at the ANZBMS annual meetings. I was also reminded of what a privilege it was to receive this grant, especially considering the prestigious research travel grant, the Barbara Mawer Visiting Fellowship, awarded by the BRS is only worth up to £3000.

University of Edinburgh

I made a brief visit to the Rheumatic Diseases Unit at the University of Edinburgh, and presented my research to the group there. Unfortunately Stuart Ralston wasn't available on the days I was in Edinburgh, but I met most of the other members of the research group, and Michael Hooper from Sydney who was also visiting at the time. It was great to be able to have a look at their lab facilities and see the sorts of techniques they are using. In particular, Dr Javier Rojas and Dr Omar Albagha showed me interesting results from some of the research they are doing on mouse models of Paget's disease and related diseases.

Summary

Overall this trip was an amazing experience for me, giving me an excellent opportunity to meet scientists from all over the world, and exposing me to a number of new research techniques. Being in Europe also gave me a chance to visit some of my cousins who are currently living in London, Moscow, and northern Italy, and visit Laura Tinti who visited our lab earlier in the year from the University of Siena in Tuscany. I would like to extend a huge thank you to Jack Martin and the ANZBMS for awarding me this grant, Amgen for providing the funding, and Philippa Hulley and all the other people I worked with in Oxford for being such good hosts.