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 AWARDEE REPORT FORM

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| NAME | Thomas Hawkins |
| UNIVERSITY | University College London |
| NAME OF AWARD | Symington Bequest Fund |
| PURPOSE OF AWARD *conference attended (full name) with city and dates* |
| 12th International Conference on Cerebral Vascular Biology, 28th November 2017 to 1st December 2017, Melbourne, Australia |
| REPORT: What were your anticipated benefits? |
| I was attending the conference to communicate an abstract regarding a novel lymphatic cell in the meninges of zebrafish based on a recent collaborative publication: Intracellular uptake of macromolecules by brain lymphatic endothelial cells during zebrafish embryonic development eLife 2017;6: e25932 DOI:10.7554/eLife.25932.I was seeking feedback from the brain vascular community regarding this cell type (by communication of the poster). I also anticipated benefit through attending the conference to learn the state of the art regarding glymphatic clearance of the brain. The term “glymphatic” is a recent neologism created to describe a newly discovered mechanism by which the brain is drained in a lymphatic-like manner involving glial cell processes. It is still certainly a controversial idea but one gaining traction; the potential implications for brain pathology, particularly neurodegeneration, are great. This is related to our recent findings because we have found cells expressing lymphatic markers, that uptake macromolecules, in the meninges of the zebrafish, exactly how this might relate to the glymphatic mechanism is not yet clear. |
| COMMENTS: Describe your experience at the conference / lab visit / course / seminar. |
| The conference was excellent. Both in terms of the poster presentation sessions and the oral presentations. It was well worth travelling such a long way to attend.My poster was well received at the relevant sessions with comments from several key people in the field, including Professor Robert Thorne of U. Wisconsin-Madison (USA), Professor Jeff Iliff of Oregon Health and Science University (USA) and Dr Jean-Francois Ghersi-Egea of Claude Bernard Lyon University (France), among others. There were many suggestions for experiments that we should attempt and positive feedback in general about our findings. Prof. Jeff Iliff, as one of the discoverers of the glymphatic hypothesis was particularly engaged with us and we are planning to carry out some collaborative experiments together.The quality of the oral scientific presentations was very high. Some (subjectively judged) highlights are described below.**Highlight 1.** During the “blood-brain barrier as a player in neurodegenerative disorders” session, chaired by Professor Gregory Bix, there was a fantastic talk by Professor Francesca Ciccetti of Université Laval, Canada. In her talk, Prof. Ciccetti examined the brains of patients suffering with Huntington’s disease who had received grafts of fetal tissue. The brains were examined post mortem and she had discovered nuclear aggregates characteristic of Huntington’s disease within the grafted tissues. Since Huntington’s has a monogenic cause and it was known that the grafts were from healthy, non-mutant brains, it was very surprising that there appeared to be a transformation or invasion of the healthy grafted tissue so that it displayed Huntington’s-type pathology. It had apparently been problematic to publish as she described the paper as having had 9 reviewers! They had then investigated mechanisms and, having excluded axonal/dendritic invasion, they investigated the possibility of a neurovascular mechanism and through investigating this possibility they found that Huntington’s brains and rodent model brains have neurovascular defects. Their final hypothesis for the mechanism of transfer between unhealthy and healthy tissue is that aggregates are transferred between cells in exosomes. They offered some evidence by infusing healthy mice with exosomes derived from Huntington’s mice, demonstrating the transfer of a disease state.**Highlights 2 & 3**. In the session entitled “Going with the flow: latest insights into CSF and ISF flow” chaired by Professor Joan Abbot (KCL), there were two excellent talks.The first was delivered by Dr Regina Faubel from Pittsburgh, USA. She described some incredibly delicate experiments investigating cilia flow in the wall of the 3rd ventricle using explants. She first described how there appeared to be ‘channels’ of fluid flow formed at the interfaces between cilia beating in different directions; they call this the cilia logistic network. Then she went on to describe a mechanism by which the flow of the cilia changes over a 24hr period, with dramatic changes during the circadian night. It is definitely preliminary work but it is completely fascinating to consider how these mechanisms may interact with the glymphatic hypothesis.The second impressive talk in this session was delivered by Prof. Jeff Iliff. He described how the ageing brain appears to have deficits in the glymphatic clearance of amyloid via perivascular routes. An important component of this perivascular clearance seems to be aquaporin channels that are normally present on the vascular-facing surface of the glial processes forming the glia limitans. Knockout of aquaporin 4 (AQP4) negatively affects amyloid clearance. This offers a tantalising new route to pursue regarding investigation of the pathological accumulation of amyloid in the brains of Alzheimer’s patients.Before the conference I also had the opportunity to visit the laboratories of Professor Pete Currie and Professor Jan Kaslin in Monash University in Melbourne. |
| REPORT: In relation to skills, what were the most important things you gained? *(does not apply to equipment grant)* |
| To pick up skills was not really the central mission of attending the conference. As mentioned above, I did obtain excellent feedback on our recent work while also getting a comprehensive grounding in the topics currently being investigated in the brain vascular biology worldwide community.I made several useful contacts during the poster/networking sessions and these have already resulted in plans for collaborative experiments in the future. |
| REPORT: How do you think you will put this learning experience into practice in the future? |
| As mentioned, from attending the conference I now have more context for our work on brain lymphatic cells and I have already planned experiments based on feedback received at the meeting. |
| SIGNATURE | Tom Hawkins | DATE | 19/12/2017 |

*If submitted electronically, a type-written name is acceptable in place of a hand-written signature*

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