

## The PEMRIG Interviews

Lab Visit Dr Ian Harrison, University College, London. June 24<sup>th</sup> 2021.

<https://www.youtube.com/watch?v=zuwk-1IYTOU>

In this youtube video Ian introduces viewers to the newly discovered glymphatic system in the brain and he discusses its relevance to Parkinson's. The visit lasts over an hour and we learn about the methods they use including the use of mice. The use of animals is essential. Ian's research is funded by Parkinson's UK and he tells us that his ambition to work on neurological conditions stems from the fact that when he was growing up his grandad was diagnosed with Alzheimer's. He elected to work on Parkinson's for his PhD and he has continued this interest in his subsequent career.

Ian firstly explains that the glymphatic system in the brain does much the same job as the lymphatic system in the rest of the body, ie it removes waste products. He shows how the glymphatic system can be tracked in the brain using probes which can be detected in a very powerful scanning MRI device. He discusses how the glymphatic system is responsible for removing the toxic protein alpha-synuclein ( $\alpha$ Syn) so preventing it entering other nerve cells causing their death. In animals with a model of Parkinson's the glymphatic system is down regulated so it can't remove  $\alpha$ Syn efficiently. The  $\alpha$ Syn then enters other neurones leading to their death. A water-channel protein, aquaporin 4 (AQP4), is responsible for CSF movement from arterial capillaries into the CNS and then its uptake into venous capillaries. Ian points out that in Parkinson's where this water channel is highly expressed  $\alpha$ Syn levels are low and vice versa. Ian hypothesises that in Parkinson's the AQP4 channel is not working well so the glymphatic system is underactive resulting in poor removal of  $\alpha$ Syn and infection of adjacent neurones leading to their death.

Ian also describes how they can inject fibrils of  $\alpha$ Syn into the brains of mice so its spread around the CNS can be correlated with how an animal's motor-co-ordination properties change. At the same time the team can monitor the efficiency of the glymphatic system. Other workers have shown that the glymphatic system in mice works better when animals are asleep, during exercise or are given low doses of alcohol. The group are also investigating if drug-induced activation of the AQP4 channel results in enhanced glymphatic system activity and  $\alpha$ Syn clearance.

Dr Doug Lopez, a post-doc in Ian's group takes us round the histology lab showing how incredibly thin sections of frozen mouse brain are cut in a Cryostat and then stained for specific proteins. Ian introduces Lauren Wallis, a biochemistry graduate who is spending the summer studying if the distribution of AQP4 channels in mouse brain correlates with the accumulation of  $\alpha$ Syn.

This was a most relaxed and informative visit with Ian answering many questions. Well worth watching! Thanks to Ian Harrison and his group for a most interesting session describing such new work.