Abstract:

Background: Alzheimer's disease is the most common form of dementia and has a significant patient and societal burden. With numbers of affected individuals forecast to continue rising it is becoming increasingly important to develop disease-modifying treatment. In order to do this it is vital to elucidate the disease mechanism. There is growing appreciation of the vascular contributions to Alzheimer's development with particular focus on the correlation between cerebral hypoperfusion and Alzheimer's onset. Pericytes are involved in blood regulation through cerebral capillaries and therefore of significant interest.

Aim: Through this project I will be assessing the contractile response of human brain derived pericytes to EDN1 and Ang-II.

Method: Firstly the pericytes will be assessed for the presence of contractile proteins and receptors to EDN1 and Ang-II through immunofluorescence and western blots. The contractile response of pericytes to EDN-1 and Ang-II will be established by measuring changes in α-SMA expression through western blots.

Hypothesis: EDN-1 and Ang-II mediate pericyte contraction contributing to cerebral hypoperfusion.

Conclusion: EDN1 induces increased α-SMA levels in human brain pericytes and this effect is potentiated by the presence of $A\beta_{40}$ and $A\beta_{42}$. EDN1 also increases proliferation of pericytes but this is suppressed by $A\beta_{42}$. Contrary to the hypothesis, Ang-II appeared to have little affect on expression of α-SMA or cell proliferation in pericytes. The result reveals a potential mechanism by which cerebral hypoperfusion occurs in AD. In the future it may be possible to target this pathway in an attempt to counteract the reduction in CBF observed in AD therefore slowing AD pathology.