Progress Report

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Title of Project: Pre-clinical assessment of arginine-rich peptides as a treatment to reduce brain damage following traumatic brain injury (TBI).

Summary: (approximately 1,000 words)
Our research group has worked for many years on neuroprotective treatments primarily focusing on ischaemic stroke. We have recently demonstrated for the first time that certain arginine-rich peptides are able to protect *in vitro* cultured brain cells from damaging processes similar to those that occur in the brain following traumatic brain injury (TBI). Furthermore, we have also shown that these peptides are able to reduce brain damage *in vivo* in rats after stroke. This is an important finding, as the brain damaging processes that occur in TBI closely resemble those in ischaemic stroke. This suggested to us that the peptides that reduce brain damage after stroke might be equally efficacious in reducing brain damage after TBI. Hence, the aim of this project is to determine if selected arginine-rich peptides are able to reduce brain damage and improve outcomes following TBI in a rat model.

If successful, this project will allow for an appropriate peptide to be selected for assessment in additional pre-clinical studies, with the ultimate goal being to develop a new treatment to minimise brain injury and improve patient outcomes after TBI. This is important, as presently there is no neuroprotective treatment available that aims to directly preserve brain tissue after TBI.

In order to assess the neuroprotective efficacy of the peptides, the first aim of the project was to establish a TBI model in the rat. A number of different rat models of TBI have been developed for studying pathophysiological consequences of head injury and for assessing the effectiveness of potential neuroprotective treatments. For this project we selected the controlled weight-drop TBI model in the Sprague Dawley rat as developed by Foda and Marmarou (1994), and often referred to as the “Marmarou model”. This model has now been successfully established in our laboratory. In addition, we have also established behavioural tests (Barnes maze, rota-rod and adhesive tape paw removal) for the assessment of functional outcomes in rats following TBI.

As part of the assessment of the TBI model we are currently performing a single dose (IV: 300nmol/kg) peptide study using one of our arginine-rich peptides (poly-arginine 18 or R18), as well as two positive control peptides (APP96-110 and COG1410). Following this, we will perform a peptide dose response study (IV; 30, 100, 300, 1000nmol/kg) using R18 and one of the positive control peptides. Interestingly, our *in vitro* studies using cultured brain cells (cortical neurons) and a glutamate excitotoxic injury, have revealed that R18 as previously demonstrated was highly neuroprotective, while the APP96-110 and COG1410 peptides displayed no to little neuroprotection.

Hypothesis vs Findings

Hypothesis: poly-arginine peptide R18 will reduce brain injury and improve functional outcomes after TBI in the rat.

Findings: This project is in progress and the final findings are still to be determined.

Unanswered Questions

As project is in progress we do not know if poly-arginine peptide R18 has the capacity to reduce brain injury and improve functional outcomes after TBI.

What these research outcomes mean

Once the project has been completed, we will know if R18 has beneficial effects following TBI. If R18 is effective following TBI, it will pave the way for additional pre-clinical and clinical neuroprotection studies and future development of the peptide as a therapeutic for TBI.