Neuroprotective peptides

Researchers at the University of Western Australia’s Centre for Neuromuscular and Neurological Disorders have revealed intrinsic neuroprotective properties of arginine-rich peptides, presenting the possibility of a new class of neuroprotective molecules for the treatment of a range of neurological disorders, including stroke.

Problem
Stroke is one of the leading causes of death and disability worldwide. One in six people will have a stroke in their lifetime. The risk of stroke increases with age as well as other co-morbidities such as diabetes, obesity, high cholesterol and/or blood pressure.

Globally, it is estimated that stroke affects about 16 million people annually (Di Carlo, 2009), typically causing death in 20% and disability in 50% of survivors.

Solution
We have demonstrated that arginine-rich peptides have potent, dose-dependent neuroprotective properties in in vitro injury models that mimic the effects of stroke, as well as in vivo after i.v. administration in:

(i) both permanent and transient middle cerebral artery occlusion (MCAO) induced stroke in the rat (Meloni et al., 2015; Milani et al., 2016)
(ii) the validated endothelin-1 middle cerebral artery constriction rat stroke model from CNS|CRO (behavioural effects)
(iii) the traumatic brain injury model
(iv) the perinatal hypoxia brain injury model
(v) hemorrhagic model

Importantly, these peptides dose-dependently provide neuroprotection following intravenous (IV) administration several hours after stroke onset (mimicking the clinical situation), that was more potent than the current candidate in phase III clinical trials, TAT-NR2B9c (NA-1, NoNo Inc.).

Cell penetrating
Importantly, it is well documented that arginine-rich cell-penetrating peptides (e.g. TAT, penetratin) are capable of traversing the plasma membranes of eukaryotic cells and successful intracellular delivery of many biologically active macromolecules has been accomplished using these peptides. i.e. this neuroprotective peptide is also a delivery agent.

Stage of development
Preclinical validation of this neuroprotective compound has been demonstrated in in vitro models and in five different CNS in vivo models to date. A CRO validated these preclinical results using the ET-1 model. Moreover, our lead compound does not exacerbate bleeding in a hemorrhagic model and hence can be delivered irrespective of stroke type, therefore in the field (by ambulance paramedics or a rural hospital), providing greater potential for preserving brain tissue and improving outcomes.

This peptide’s mechanism of action and intravenous toxicity has been initially assessed.

Further preclinical experimentation includes use of animals with a brain type more like humans (Non-Human Primates); and pre-IND toxicity and safety studies.

Intellectual Property
The IP position contains well-enabled and commercially relevant claims. The patent application: PCT/AU2014/050326 entitled “Neuroprotective peptides” (includes poly-arginine and arginine-rich peptides) entered national phase into US, EU, China and Japan jurisdictions on 30 April 2016.

The team
A/Prof Bruno Meloni has >20 yrs experience as a research scientist in the field of stroke/cerebral ischaemia.

Clinical Prof Neville Knuckey is a neurosurgeon, whose main area of expertise is the development and use of stroke, global cerebral ischaemia, perinatal hypoxia and traumatic brain injury models.

Clinical Prof David Blacker is an acute stroke clinician/neurologist who has previous experience initiating neuroprotection clinical stroke trials in Western Australia (e.g. minocycline).

UWA is seeking a commercial partner to in-licence and develop this technology as a neuroprotective therapy for stroke, traumatic brain injury and potentially other neurological disorders.

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