

# A NEW TREATMENT STRATEGY FOR CNS INJURIES

A receptor tyrosine kinase-based target for ischemic stroke and other CNS injuries. Target modulation reduces reactive astrocyte activity and glial scarring to promote functional recovery. Validated in a non-human primate (NHP) model of CNS injuries, that is more predictive of disease progression in humans than current models.

- **New, clinically relevant NHP model for testing drugs for CNS disorders**
- **Novel target for attenuating astrocyte activity in adult brain to prevent glial cell scar formation in the days and weeks post ischemic event**
- **Potential for 'First in Class' drugs for ischemic stroke and other brain disorders**

Using a proprietary NHP model with excellent translatability to humans, researchers from Monash University's Australian Regenerative Medicine Institute have shown that the infant brain undergoes less astrocyte activity after stroke, correlating to smaller glial scarring that is more permissible to functional recovery (Fig.1).

The team identified pathways and targets that regulate astrocyte activity after injury in the infant. Using compositions that stimulate the 'infant pathway', strong inhibition of astrocyte preactivity was shown in primate cell models in vitro. This could minimize glial scar formation in the adult brain (especially during the sub-acute period) which, in turn, could drive functional recovery.

Proof-of-mechanism has been shown using the NHP model where target modulation suppressed the reactive astrocyte response after brain injury, resulting in a reduction of the glial scar (Fig. 2), as well as suppressing secondary recruitment and reduction in apoptotic cells at the ischemic core. Primate studies using a selective target ligand indicate significant neuron sparing.

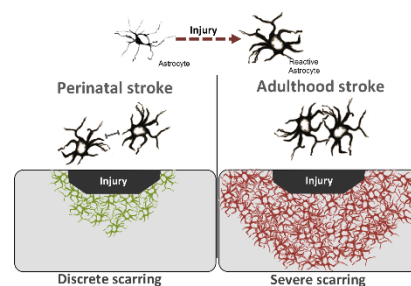
#### Alternative applications

Attenuating astrocyte reactivity can also be applied to improve outcomes after other brain and spinal cord injuries, to suppress the severity and invasiveness of glioblastomas. This strategy can be integrated onto brain-stimulating electrodes to minimise scar formation, increasing the longevity of existing treatments.

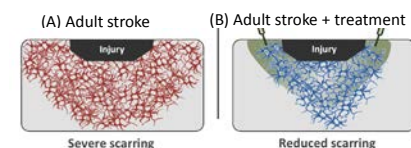
**Intellectual property:** US provisional 62/250380 and Australian application 2015252036 filed on methods to reduce glial scarring and treat CNS damage.

#### THE OPPORTUNITY

Monash seeks a partner to develop new compositions based on the target ligand to attenuate astrocyte activity for ischemic stroke and other brain disorders. The Monash team has extensive experience in the target and stroke biology, and has a biochemical assay for screening. Our proprietary NHP model can be used for testing new drug candidates.



*Figure 1:* Glial scarring infant vs. adult. The infant brain undergoes less prolific scarring compared to adults after stroke, correlating to greater capacity for recovery.



*Figure 2:* (A) Following ischemic stroke in adults, signalling through target results in widespread astroglial response, forming a large, dense glial scar. (B) Treatment with target ligand could reinstate 'infant-like' astrocyte behaviour, reducing adult astroglial response.

#### THE CHALLENGE

15 million people worldwide suffer a stroke each year; nearly 6 million die and 5 million are permanently disabled. Survivors suffer impairments such as motor or sensory loss, speech impediment and memory loss.

Despite the high incidence and socioeconomic burden, only one treatment option is available, thrombolytic tissue plasminogen activator (tPA). Only ~6% of stroke victims qualify for tPA due to the high risk of secondary bleeding and short treatment window (3hr of stroke onset). For those treated, the success rate is only 35%.

**There is a high need for new drugs to treat stroke in more patients, and over an extended time period following a cerebral ischemic event.**

#### THE TECHNOLOGY

The major factor limiting functional recovery in adult stroke patients is formation of scar tissue in the brain during the sub-acute period. This glial scarring (refractory to regeneration) is formed by reactive astrocytes and is exaggerated 2-4 weeks post injury.

#### KEY CONTACT

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