



Heng Group

The Heng Group focuses on understanding the molecular and cellular mechanisms that control nerve cell production and maturation within the mammalian brain.

By understanding nerve cell development during embryogenesis, we will gain further insight into the pathogenesis of brain disorders (such as epilepsy and mental retardation) which can arise as a consequence of abnormal neural development. These studies could, in turn, lead to the development of novel drug treatments or gene therapies for these disorders. In addition, knowledge of the signalling pathways that control nerve cell production will inform on future therapies which exploit the limited endogenous capacity for self-repair within the adult brain.

The Group uses cutting edge molecular techniques to study the birth and development of cerebral cortical neurons within fetal mouse brain *in vivo* as well as *in vitro*. These studies are combined with Bioinformatics approaches to identify then characterise genes responsible for aspects of the maturation of newborn nerve cells.

Dr Julian Heng

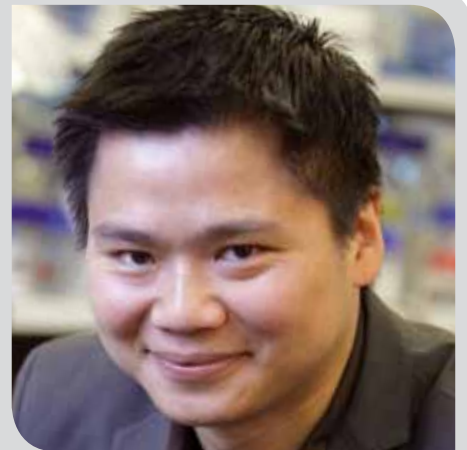
Dr Heng studies how nerve cells of the brain are produced, and how they assemble into the final remarkable structure that is the cerebral cortex.

He has a long-standing interest in the role of DNA-binding transcription factors which control the expression of genes necessary for nerve cell maturation within mammalian brain.

His goals are:

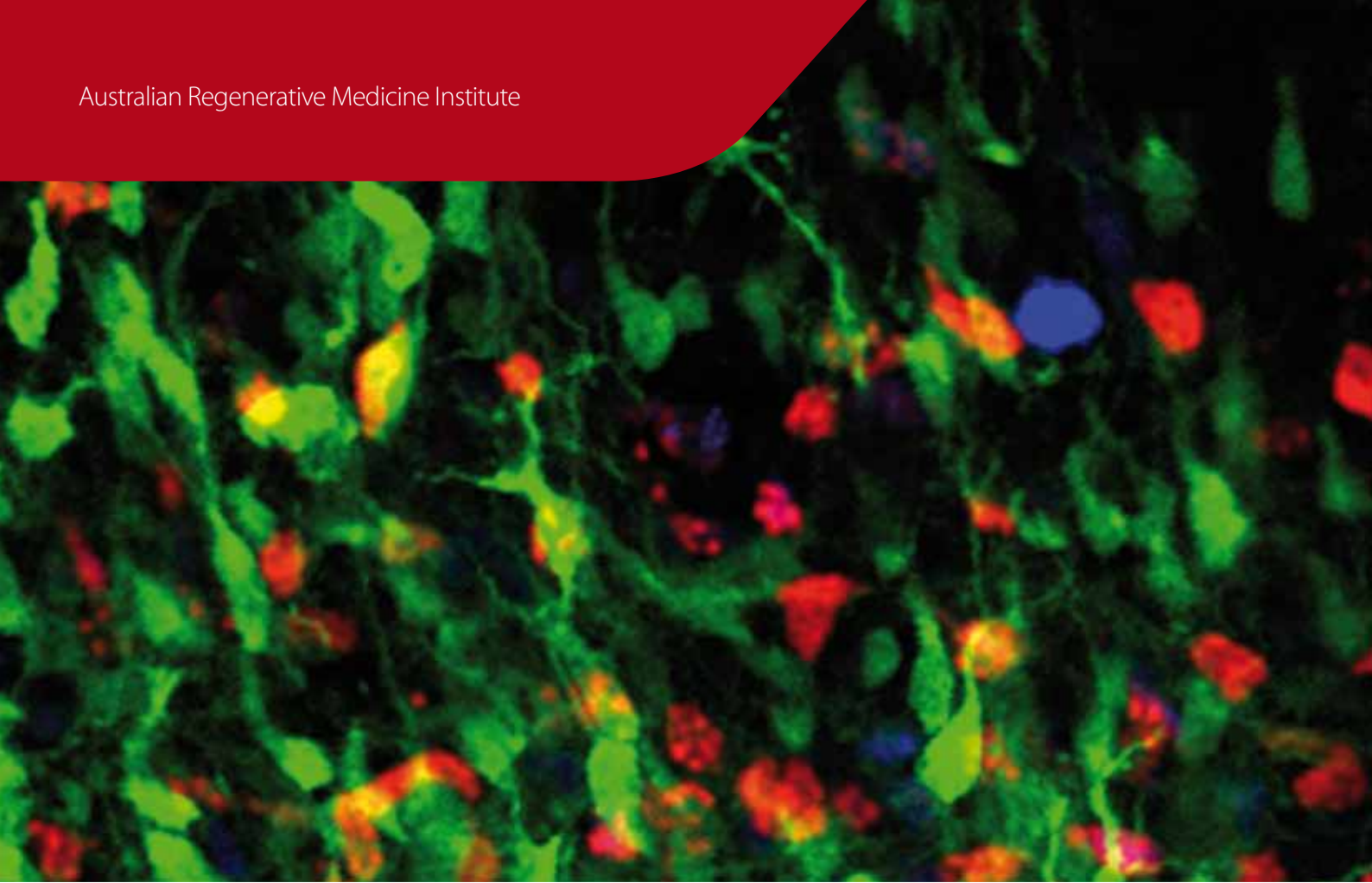
- to understand how neural diversity is generated within the mammalian central nervous system
- to investigate novel approaches to enhance the limited regenerative capacity within brain.

Dr Heng was awarded a prestigious CJ Martin Fellowship (NH&MRC, Australia) to conduct his postdoctoral research at the National Institute for Medical



Research (UK). He extended his overseas tenure through an MRC Career Development Fellowship (UK) before returning to Melbourne to complete his training at the Howard Florey Institute as a Research Fellow.

Dr Heng joins ARMI as a Group Leader through a Monash Fellowship, and runs projects that are currently funded by the National Health and Medical Research Council (NH&MRC) of Australia. He also maintains collaborations with research groups in Japan and Europe.



Research Themes

Control of nerve cell production by transcription factors

The development of the cerebral cortex involves many steps, including nerve cell production, cell migration and final maturation of correctly-positioned neurons within fetal brain. We have discovered that Neurogenin2, a master regulator for neuron production in the cerebral cortex, initiates a proneural transcription factor cascade which is necessary for the generation of excitatory projection neurons of the developing cerebral cortex¹.

This project will explore the functional interaction(s) between transcription factors which are downstream of Neurogenin2, and how they impart the necessary information for proper cortical neuron differentiation. In addition, we are interested in identifying the downstream target genes for proneural transcription factors such as Neurogenin2 and to understand how these are important for controlling aspects of nerve cell maturation, including their proper migration and final connectivity.

References

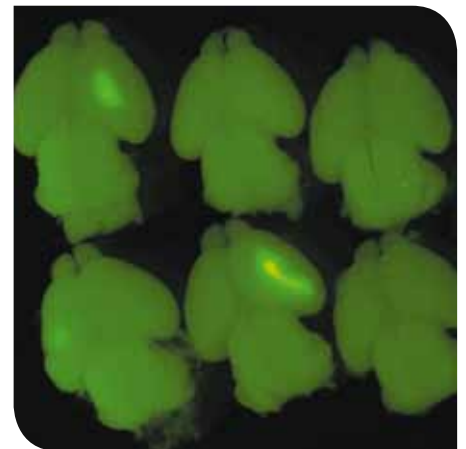
- 1 Heng et al, Nature 2008 Sep 4; 455 (7209): 114–8
- 2 Heng et al, Trends in Neurosciences. 2010 Jan;33(1):38–47

The molecular basis of nerve cell migration during their maturation

During fetal brain development, neurons must undergo active cell migration to reach their proper position within developing brain. Failure to carry out this critical function within immature neurons can lead to aberrant brain development, mental retardation and epilepsy.

Recent reports have underscored the importance of a highly regulated gene expression program for the correct production of migration-promoting factors to control this important developmental process in newborn neurons².

Through our knowledge of the requirement for Neurogenin2 in the specification of the motile-properties of neurons¹, we are seeking to identify further genetic factors that predetermine the migratory capacity of these neurons as part of their cell-intrinsic programming. It is anticipated that we may be able to use this knowledge to direct the migration of newborn nerve cells to sites of injury within damaged brain.



Do complex brain disorders arise from abnormal brain development?

Neurological disorders such as autism and schizophrenia are prevalent in our community, and yet we know little of how genes (as well as the environment) may be important for the pathogenesis of these conditions. By focusing on clinically-relevant gene(s) that are known to be important for diseases such as autism, we aim to better understand their impact on the early steps of brain development. This project will characterise a novel mouse model of autism, with investigations on how the candidate gene controls nerve cell maturation, connectivity and brain behaviour.

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