

ARMI SPECIAL SEMINAR

2022



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Promoting cardiac Function through Adeno-associated virus-directed manipulation of Neuregulin/ErbB4 Signalling

Dr. Melissa Reichelt

Abstract

I will provide an overview of my research program, which aims to understand the factors that promote healthy cardiac growth and adaptation throughout the lifespan. This will be followed by a more detailed examination of my work investigating the role of Neuregulin/ErbB4 signalling in cardiac growth and adaptation. Heart failure (HF) is a leading cause of death worldwide. With a lack of effective treatments, there is rising interest in stimulation of myocardial proliferation/growth, with the goal of recapitulating healthy cardiac tissue. ErbB4, an epidermal growth factor receptor, and its ligand neuregulin-1 (NRG-1), represent a dynamic signalling cascade important in myocardial development, including cardiomyocyte proliferation and survival. We utilised a Cre-Lox recombination model with adeno-associated virus (AAV)-mediated iCre delivery, to delete *ErbB4* from cardiomyocytes in adult and neonatal mice. While deletion of ErbB4 in the cardiomyocytes of adult mice caused only mild contractile dysfunction, deletion in neonatal mice resulted in a rapid progression to dilated heart failure with reduced ejection fraction. We next evaluated the effect of AAV-directed expression of NRG-1 β in neonates infected at P1, identifying a significant increase in cardiac mass without modification of classical markers of pathological hypertrophy (collagen increases, foetal gene re-expression). AAV directed NRG-1 β expression also rescued cardiac survival in ErbB4 cKD mice associated with upregulation of ErbB3 expression. Together, I have identified a critical role for the ErbB4/NRG axis in the immediate postnatal period, which is rescued with AAV-directed NRG. I will also discuss the future directions of this work.

Bio

I am a continuing teaching and research academic in The University of Queensland's School of Biomedical Sciences. I completed my PhD in cardiovascular physiology at Griffith University before working as a postdoctoral fellow at The Victor Chang Cardiac Research Institute (VCCRI, Sydney), the University of California, San Diego (USA) and the University of Melbourne. I was a NHMRC Peter Doherty Postdoctoral Fellow from 2020 to 2013, and I'm currently funded by Australian Research Council Discovery Project and Diabetes Australia grants. My work has been published in leading cardiovascular journals including *Circulation*, *Circulation Research*, *Basic Research in Cardiology*, *Cardiovascular Research*, *Hypertension* and broader or specialist journals including *Autophagy*, *The Proceedings of the National Academy of Sciences*, *Antioxidant and Redox Signalling*, *Journal of Infectious Disease* and *Scientific Reports*.

EVENT DETAILS

DATE:

December 07, 2022

TIME:

11.00 – 12.00p.m.

VENUE:

G19, 15 Innovation Walk

Zoom:

<https://monash.zoom.us/j/84779021685?pwd=dUICWmxQSi9VSkxwK0xiM0lUR3hsZz09>

Password: 415589

HOST:

Peter Currie



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