UNSW SYDNEY

Neuroscience & Non-Communicable Diseases
WEBINAR – All welcome

Friday 30 April 2021, 3pm

'BET Inhibition Blocks Inflammation-Induced Cardiac Dysfunction and SARS-CoV-2 Infection'.

Speaker: Associate Professor James Hudson, Group Leader of the Cardiac Bioengineering Lab at QIMR Berghofer

BIO: Associate Professor James Hudson is a Group Leader of the Cardiac Bioengineering Lab at QIMR Berghofer. James completed a Bachelor of Chemical and Biological Engineering (2006) followed by a PhD in Biotechnology (2011) at the University of Queensland. He then did a postdoc with Professor Wolfram-Hubertus Zimmermann in Goettingen, Germany. James returned to Australia and became a group leader in 2014. James' lab focusses on the development and use of human cardiac tissues for discovery of new heart failure therapeutics. His lab has developed and utilises one of the most advanced human organoid platforms, and publishes original research in leading international journals including: Cell, Circulation (x5), Cell Stem Cell (x2), PNAS, Biomaterials (x2), Development (x2), Nature Communications (x3), and Science Translational Medicine. James is an inaugural recipient of the very prestigious Snow Medical Fellowship, has won The Metcalf Prize (2019), American Heart Association Paul Dudley White Award (2018), The Centenary Institute Medical Innovation Award (2017), and The Paul Korner Award (2016).

Abstract: Cardiac injury and dysfunction occur in COVID-19 patients and increase the risk of mortality. Causes are ill defined, but could be direct cardiac infection and/or inflammation-induced dysfunction. To identify mechanisms and cardio-protective drugs, we use a state-of-the-art pipeline combining human cardiac organoids with phosphoproteomics and single nuclei RNA sequencing. We identify an inflammatory 'cytokine-storm', a cocktail of interferon gamma, interleukin 1β and poly(I:C), induced diastolic dysfunction. Bromodomain-containing protein 4 is activated along with a viral response that is consistent in both human cardiac organoids and hearts of SARS-CoV-2 infected K18-hACE2 mice. Bromodomain and extraterminal family inhibitors (BETi) recover dysfunction in hCO and completely prevent cardiac dysfunction and death in a mouse cytokine-storm model. Additionally, BETi decreases transcription of genes in the viral response, decreases ACE2 expression and reduces SARS-CoV-2 infection of cardiomyocytes. Together, BETi, including the FDA breakthrough designated drug apabetalone, are promising candidates to prevent COVID-19 mediated cardiac damage.

All welcome!

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