

ARMI SPECIAL SEMINAR

2022



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Transient Induction of Cytokinesis in Cardiomyocytes as a strategy for Heart Regeneration

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Abstract

Cytokinesis is the last step in the eukaryotic cell cycle which physically separates a mitotic cell into 2 daughter cells. Shortly after birth in mouse cardiomyocytes, DNA synthesis occurs without cytokinesis leading to the majority of cardiomyocytes becoming binuclear resulting in cell cycle arrest and the heart is no longer able to regenerate. We generated transgenic mouse models to determine whether forced induction of cardiomyocyte cytokinesis generates mononuclear cardiomyocytes and restores the endogenous regenerative properties of the myocardium. We focused on two complementary regulators of cytokinesis, Polo-like kinase 1 (Plk1) and epithelial cell-transformation sequence 2 (Ect2). Here we report that cardiomyocyte-specific overexpression of constitutively active Plk1(T210D) promotes mitosis and cytokinesis in adult hearts, while overexpression of Ect2 promotes cytokinesis. Intriguingly, cardiomyocyte-specific overexpression of both Plk1(T210D) and Ect2 concomitantly prevents binucleation of cardiomyocytes postnatally and results in robust cardiomyocyte proliferation. Similarly, doxycycline-inducible cardiomyocyte-specific transient overexpression of both Plk1(T210D) and Ect2 in the adult heart results in cardiomyocyte proliferation and improves left ventricular systolic function following myocardial infarction. These results demonstrate that induction of cytokinesis in multinuclear cardiomyocytes is a viable strategy for regenerating the heart.

Bio

Dr Nicholas Lam obtained a BBiomedSc from the University of Melbourne, and BSc(Honours) and PhD degrees from Monash University. His PhD was in cardiac regeneration co-supervised by Prof David Kaye at the Baker Heart & Diabetes Institute and Prof Nadia Rosenthal at ARMI. Nick undertook postdoctoral training with Prof Hesham Sadek, a pre-eminent leader in cardiac regeneration at The University of Texas Southwestern Medical Center, where he is now an Assistant Instructor. His research has focused on cardiac regeneration by promoting proliferation of pre-existing cardiomyocytes in the adult mouse heart with first author publications in *Circulation*, *Nature Metabolism* and *Nature Cardiovascular Research*. His research vision will extend into promoting cardiac regeneration by inducing cytokinesis in multinuclear cardiomyocytes as a novel strategy.



EVENT DETAILS

DATE:

December 06, 2022

TIME:

11.00 – 12.00p.m.

VENUE:

G19, 15 Innovation Walk

Zoom:

<https://monash.zoom.us/j/82177912758?pwd=Q2RkNGJzeEgxckkzdmV5aVQwRGc5QT09>

Password: 975628

HOST:

Peter Currie



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