School of Medical Sciences Seminar Series

Wednesday the 8th of July 2020

3:00 – 4:00pm on Microsoft Teams

We ask all attendees to mute and turn off their video

Professor Melissa Little BSc PhD GAICD, FAAHMS, FAAS
Theme Director of Cell Biology at the Murdoch Children's Research Institute in Melbourne, Australia.

"Recreating human kidney tissue based on our understanding of kidney development"

Bio: Professor Melissa Little, is internationally recognised for her work on the systems biology of kidney development. For more than two decades, her work has investigated the molecular and cellular basis of kidney development and disease. This fundamental research has underpinned her pioneering studies into potential regenerative therapies for kidney disease. As a result, her team have developed approaches for directing the differentiation of human pluripotent stem cells to human kidney organoids. Her group are applying this knowledge to disease modelling, drug screening, cell therapy and tissue engineering. Professor Little is an NHMRC Senior Principal Research Fellow at MCRI, Program Leader of Stem Cells Australia and Professor, Faculty of Medicine, Dentistry and Health Sciences, University of Melbourne. Melissa is also Vice-President of the International Society for Stem Cell Research and immediate past President of Australasian Society for Stem Cell Research. A Fellow of the Australian Academy of Science and the Australian Academy of Health and Medical Sciences, Professor Little's work has been recognised by many awards, including the GlaxoSmithKline Award for Research Excellence (2005), AAS Gottschalk Medal in Medical Sciences (2004), Eisenhower Fellowship (2006), ANZSCDB Presidents Medal (2015), Boerhaave Professorship, Leiden University (2015), UNSW Eureka Prize (2016) and the NHMRC Elizabeth Blackburn Fellowship Biomedical (2018), Honorary Doctorate, Leiden University (2019), the prestigious Alfred Newton Richards Award (2019), and the Julian Wells Medal (2020).

Talk: Mammalian kidney development has historically been studied in the mouse given the availability of the genetic and transgenic tools for interrogating the morphogenesis of this complex organ across time and space. While there is evidence of significant congruence in many genetic pathways between mouse and human, there are temporal, anatomical, physiological and genetic distinctions between the two species. We have demonstrated that kidney organoids, generated via the stepwise differentiation of such pluripotent cells, form complex, multicellular 3D organoids representative of the Trimester 1 human kidney. It is hoped that such stem cell-derived human tissue will drive personalised disease modelling, toxicity and screening, cell therapy and even tissue bioengineering. All this will depend upon how reliably these models mirror normal human development at the level of cellular identity, multicellular complexity and functional maturation. We have shown at the level of transcriptional profile and anatomical structure that kidney organoids do represent a credible model of the Trimester 1 human kidney. Via single cell transcriptional profiling, we have examined the cellular complexity of kidney organoids, identifying the underlying sources of batch variation and the identity of potential off target cell types. Using CRISPR-Cas9 editing, we have developed a suite of reporter lines that is now allowing us to query the accuracy of patterning within the organoids, the lineage relationships during organoid formation and the transcriptional (bulk and single cell) profiles of individual cell types. We are also applying CRISPR-Cas9 gene editing to patient stem cell lines to test the capacity of organoids to model human kidney disease. Finally, the use of fluorescent reporter lines is facilitating real-time imaging after *in vivo* transplantation to assess the degree to which we can mature these organs. Together these approaches are informing us of where an organoid is useful, what limitations exist to their application and what improvements are required.

More info: Dr John Lock at john.lock@unsw.edu.au, Dr Nicola Smith at nicola.smith@unsw.edu.au, Greta Spies at g.spies@unsw.edu.au