

ASYMMETRIC LOCALIZATION OF Dlc1 DEFINES TRUNK NEURAL CREST POLARITY FOR DIRECTIONAL DELAMINATION AND MIGRATION

WEDNESDAY
21 JUNE 2017

10:30AM – 11:30AM

ANATOMY SEMINAR ROOM
L2, MD10, DEPARTMENT
OF ANATOMY, NUS.

DR MARTIN CHEUNG

School of Biomedical Sciences
University of Hong Kong
Hong Kong

Multipotent neural crest cells (NCCs) originate in the dorsal neural tube and implement a transcriptional programme to initiate an epithelial-mesenchymal transition (EMT) that involves alteration of cytoskeletal structure, loss of cell-cell adhesion and apical-basal polarity to convert an epithelial cell into a mesenchymal motile phenotype. After EMT, these unpolarized NCCs acquire front-back polarity that is prerequisite for directional delamination and migration into the periphery where they form neurons and glia of the periphery nervous system. It has been unclear how this polarization is established and regulated. Using fluorescence biosensory in emigrating NCCs, we show that the breaking of cell symmetry is accompanied with distribution of highly active RhoA small GTPase to the cell rear and fluctuating RhoA activity at the protrusive front. This differential localization and level of RhoA activity predicts the future back-front polarity axis and the direction of movement. Strikingly, the RhoGAP, Deleted in liver cancer 1 (Dlc1), is asymmetrically localized to the cell front and its level of activity determines polarized NC morphology and motility by restricting spatial RhoA activation to the cell rear. We also found that the association of Dlc1 with Nedd9 is crucial for its asymmetric localization and polarized RhoA activity. Moreover, Nedd9 and Dlc1 are subject to the transcriptional regulation of NC specifiers, Sox9 and Sox10, respectively. Thus, we reveal a novel SoxE-Dlc1/Nedd9-RhoA regulatory axis to govern NC migratory polarization.

Speaker Biographies:

Dr Martin Cheung received his BSc in Biochemistry from the Chinese University of Hong Kong and PhD in the Division of Genetics from the University of Nottingham in UK. He then went on to carry out his Medical Research Council postdoctoral fellowship under the mentorship of Dr James Briscoe at the National Institute for Medical Research, where he unraveled the importance of SoxE family transcription factors in neural crest development. He then joined the University of Hong Kong as a Research Assistant Professor in the former Department of Biochemistry and became Assistant Professor in the School of Biomedical Sciences since Nov 2013. His lab's research focuses on deciphering the molecular regulatory circuitry that orchestrates cell migration in both neural crest development and neural crest-derived melanoma.

Address enquiries Dr Hu Qidong at 66013730 or Ms Carolyne Ang at 65163200. All are welcome.