Melanoma oncogene MITF integrates multiple signals to regulate cell identity

August 29, 2018 – Three key signalling pathways in development (MAPK, PI3K and WNT) are frequently deregulated in cancer and respond to complex microenvironmental cues to regulate the activity of transcription factors. Some transcription factors act as master regulators to integrate signals from multiple pathways to control the expression of cell fate-determining genes. In this article published in *PNAS*, Kao Chin Ngeow and colleagues from Prof. Colin Goding's lab characterise one such master regulator, MITF, a lineage survival oncogene with a central role in melanoma. In melanocytes, activation of GSK3 (downstream of the PI3K and WNT pathways) and BRAF/MAPK signalling results in dual phosphorylation of MITF. This exposes MITF's nuclear export signal to cause relocation to the cytoplasm and subsequent decrease in MITF activity. This work has implications for the understanding of melanoma progression and the control of cell identity in development and disease.