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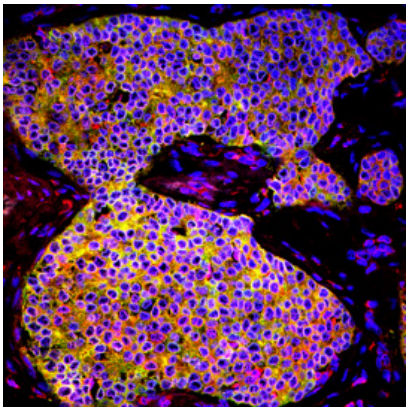
The major research direction of our group has been the characterization of the metabolic pathways that regulate phosphoinositide 3-kinase (PI3K) signalling, specifically concentrating on inositol polyphosphate 5-phosphatases, which exhibit altered expression and/or mutations in human disease and cancer. These include breast cancer, ciliopathy syndromes, diabetes/insulin signalling, neuronal disorders, leukaemia and developmental disorders. In addition, our group also investigates the functional role of inositol polyphosphate 3- and 4-phosphatases in various human diseases. Recently, our group identified PIPP, a PI(3,4,5)P_3 5-phosphatase, as a tumour suppressor in breast cancer which is downregulated in poor prognostic cases and these findings were published in the journal *Cancer Cell*. Furthermore, we have also identified and characterized a family of signal adaptor proteins called the four and a half LIM domain (FHL) proteins that play significant roles in muscle development and cancer, and we are currently exploring novel therapeutic agents for the treatment of different types of muscular dystrophy.

Research Projects

1. **The role of inositol polyphosphate phosphatases in cancer development.**
2. **PI3-kinase and development.**
3. **Mechanism of skeletal muscle disease and identification of novel therapies.**



Human Breast Cancer

Selected significant publications:

1. Conduit SE, Ramaswamy V, Remke M, Watkins DN, Wainwright BJ, Taylor MD, **Mitchell CA** and Dyson JM. 2017. A compartmentalized phosphoinositide signaling axis at cilia is regulated by INPP5E to maintain cilia and promote Sonic Hedgehog medulloblastoma. *Oncogene* (accepted)

2. Dyson JM, Conduit SE, Feeney SJ, Hakim S, DiTommaso T, Fulcher AJ, Sriratana A, Ramm G, Horan KA, Gurung R, Wicking C, Smyth I, **Mitchell CA**. 2017. INPP5E regulates phosphoinositide-dependent cilia transition zone function. Journal of *Cell Biology* 216(1):247-263

3. Ooms LM, Binge LC, Davies EM, Rahman P, Conway JR, Gurung R, Ferguson DT, Papa A, Fedele CG, Vieusseux JL, Chai RC, Koentgen F, Price JT, Tiganis T, Timpson P, McLean CA and **Mitchell CA**. 2015. The inositol polyphosphate 5-phosphatase PIPP regulates AKT1-dependent breast cancer growth and metastasis. *Cancer Cell* 28(2):155-169.

4. McGrath MJ, Binge LC, Sriratana A, Wang H, Robinson PA, Pook D, Fedele CG, Brown S, Dyson JM, Cottle DL, Cowling BS, Niranjan B, Risbridger GP, **Mitchell CA**. 2013. Regulation of the transcriptional coactivator FHL2 licenses activation of the androgen receptor in castrate-resistant prostate cancer. *Cancer Research* 73(16):5066-5079.

5. Fedele CG, Ooms LM, Ho M, Vieusseux J, O'Toole SA, Millar EK, Lopez-Knowles E, Sriratana A, Gurung R, Baglietto L, Giles GG, Bailey CG, Rasko JE, Shields BJ, Price JT, Majerus PW, Sutherland RL, Tiganis T, McLean CA, **Mitchell CA**. 2010. Inositol polyphosphate 4-phosphatase II regulates PI3K/Akt signaling and is lost in human basal-like breast cancers. *Proc. Nat. Acad. Sci. USA* 107(51): 22231-36.