Regulation of novel breast cancer genes by PI3K/Akt pathway

PI3K/Akt 通路調控新型乳腺癌基因

PI: Dr. Rebecca Chin

Identification of novel Akt isoform-specific substrates which regulate TNBC pathogenesis: The role of Akt3 in cancer stemness remains unclear. Furthermore, an Akt3-specific substrate is yet to be identified. In this project, we discovered a key function of Akt3 in driving self-renewal of CSCs and tumor initiation in TNBC. Knocking out Akt3 suppresses CSC properties accompanied by reduced Snail/Slug expression, whereas overexpression of Akt3 promotes stemness. Analyses of clinical datasets revealed that Akt3 expression is positively associated with Snail/Slug expression, as well as phosphorylation of YB1 at Ser^{102}. We also identified YB1 as an Akt3-specific substrate. Importantly, phosphorylation of YB1 at Ser^{102} by Akt3 plays a critical role in the self-renewal of TNBC CSCs. These findings suggest that disrupting the Akt3-YB1 signaling axis may provide new therapeutic opportunity for TNBC. The work is currently under revision at *Genes & Diseases*.