Targeting Hippo-Related Cell Polarity in Breast Cancer

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Severe loss of cell polarity is one of the signatures of triple negative breast cancer (TNBC), which is a current clinical challenge due to its aggressive malignancy and absence of therapeutic treatment. Cell polarity is a fundamental feature of cells. Loss of cell polarity in mammary gland epithelial cells leads to epithelial-mesenchymal transition (EMT), where cells lose attachment to each other as well as gain migratory and invasive properties that results in the tumor formation. The Hippo-pathway is thought to be critical in orchestrating cell polarity through regulating nuclear translocation of YAP/TAZ and therefore, dictating YAP/TAZ-mediated gene network. In the present work, using methods involving RNA interference, elevated gene-expression and immunofluorescence microscopy, I have examined the impact of deregulated YAP/TAZ through cell polarity that in turn promotes breast tumor initiation and invasion. In addition, we have assessed the clinical relevance of Verteporfin, a YAP/TAZ inhibitor, in anti-TNBC treatment. The results from my project indicate that knockdown of either YAP or TAZ in breast cancer cells helps to recover cellular polarity, whereas the elevation in nuclear expression of YAP or TAZ in normal breast cells leads to loss of cell polarity that in turn triggers tumorigenesis. Importantly, a blockade of YAP/TAZ function by the YAP/TAZ inhibitor alters cell polarity and further induces triple negative breast cancer cells to undergo apoptosis. Thus, information gained from my project provides a novel strategy to cure triple negative breast cancer through the blockade of YAP/TAZ-mediated Hippo- pathway.

Awards Won: