Deconstructing breast cancer from a developmental perspective

Synopsis

In order to understand the intratumoral heterogeneity evident in many forms of breast cancer, and especially in triple negative breast cancer (TNBC), we have used a variety of single cell approaches to investigate development of the mammary gland in the mouse from embryogenesis through adulthood. I will discuss the results from our and other studies that use a variety of lineage tracing, molecular, and bioinformatic strategies that provide more detailed understanding of the lineage relationships in the mammary gland than we have had previously. I will summarize our results showing that cells in the early embryo exhibit characteristics expected of bipotential mammary stem cells, and basal-like TNBC exhibits many features of such cells, suggesting that some of the mutations in TNBC may enable mammary cells to reprogram to a primitive, developmentally plastic state. As an example, I will describe how one gene we found to be important in cell state transitions enables reprogramming to a motile, invasive neural crest-like state when it is expressed at elevated levels in mouse mammary cancer models, and this is also found in human breast cancers. This finding offers targets for molecular intervention.