

SLITS FUNCTION AS TUMOR SUPPRESSORS IN MOUSE MAMMARY GLAND. **Milana PeBenito**, Dr. Lindsay Hinck, Dr. Rebecca Marlow. Department of Molecular, Cell, & Developmental Biology, University of California, Santa Cruz.

The mammary gland is a ductal structure with a bilayer of luminal cells surrounded by a myoepithelial layer. The interaction of the secreted guidance protein, SLIT, with its receptor, ROBO1, is crucial in maintaining adhesive contacts between this bilayer, as loss-of-function mutations in either the *Slit2* or *Robo1* genes result in a loss of adhesion between these two cell layers. Moreover, histological and immunohistochemical analyses on *Slit2*^{-/-};*Slit3*^{-/-} glands have revealed that the lumens are filled with disorganized cells. I have identified three processes that are deregulated in *Slit2*^{-/-};*Slit3*^{-/-} glands and likely contribute to lumen occlusion. First, using the marker of cell proliferation, Ki67, in immunohistochemistry, I find elevated cell proliferation in the lumens of *Slit2*^{-/-};*Slit3*^{-/-} compared to wildtype glands. This suggests that the filled lumens are at least partially due to deregulated growth control in the knock-out tissue. Second, using the myoepithelial cell marker, smooth muscle actin (SMA), in immunohistochemistry, I observe the presence of SMA-positive cells in the lumens. This suggests that a subset of myoepithelial cells have inappropriately migrated into the luminal space. Additionally, cells within these occluded lumens show an elevated expression of the metastasis marker CXCR-4. Together these data suggest that SLITs may function as tumor suppressors to control cell proliferation and migration, and that the neoplasias observed in *Slit*-null tissue may be a precursor to breast cancer.