Niche Control of Germline Stem Cell Self-renewal and Differentiation

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Stem cells in adult tissues undergo self-renewal and generate differentiated cells that replenish the lost cells caused by natural turnover, injury, or disease. The molecular mechanisms regulating stem cells are also critical for regenerative medicine and fighting against cancer and aging. We have been using germline stem cells (GSCs) in the Drosophila ovary as a model system to study how the niche controls stem cell self-renewal, differentiation, and aging. In the Drosophila ovary, cap cells and anterior inner germarial sheath (IGS cells) form the niche for GSCs, whereas posterior IGS cells make up the differentiation niche for early GSC progeny. For the GSC niche, we show that Tet functions in cap cells as a scaffold protein independently of its enzymatic function to bring the chromatin remodeling complex PBAP to the transcription factor Stat92E to activate the transcription of dpp, which encodes a BMP niche signal for controlling GSC self-renewal. For the differentiation niche, we demonstrate that IGS cells form separate compartments to orchestrate cyst division, meiotic entry, and oocyte determination of early GSC progeny. Indeed, gap junction-transported cAMP from the niche is critical for controlling cyst division, meiotic entry, and oocyte determination. Currently, we are carrying out systematic genetic screens to identify additional key factors involved in stem cell-niche communication.