Supplemental Figure Legend

Fig. 1. Using mouse models to address the complexity of brain tumors. At the level of the organism, individual genomic variation determines how likely an individual is to develop cancer and affects how individuals with brain tumors respond to treatment. At the level of the organ, cells and growth factors in the tumor microenvironment can play important roles in brain tumorigenesis. These cells include reactive astrocytes, inflammatory cells, microglia, neurons, and endothelial cells. At the level of tumor cells, the different cells in the normal neural lineages, such as neural stem cells (NSC) or progenitor cells (PC) (and possibly differentiated brain cells; DC) may give rise to tumors that reflect the timing and location of the transforming events. At this time, the tumor initiating cell type (TIC) has not been clearly established for most brain tumors. Within brain tumors, cancer stem cells (CSC) are hypothesized to maintain the tumor and give rise to more differentiated cancer cells (DCC). At the molecular level, there is crosstalk and feedback inhibition between different signaling pathways important for tumor growth, survival, and migration. For example, blockade of the AKT signaling pathway using mTOR inhibitors may attenuate mTOR-mediated growth-promoting signals, but will also release mTOR negative feedback inhibition on AKT signaling pathway, and lead to unanticipated tumor growth.