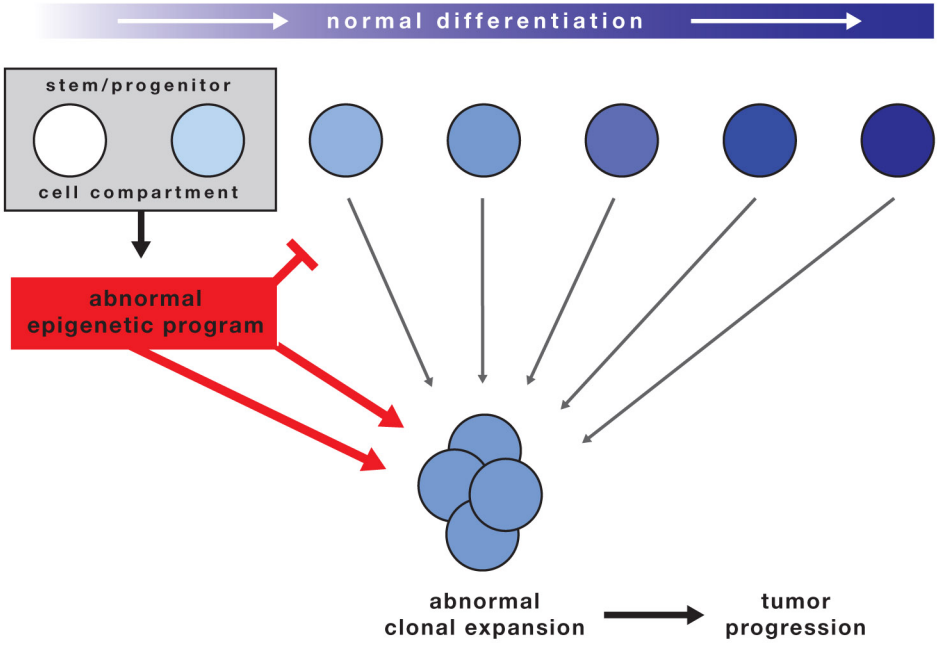

Figure 5. Epigenetic Gene Silencing Events and Tumorigenesis

The earliest steps in tumorigenesis are depicted as abnormal clonal expansion, which evolves during the stress of cell renewal. This is caused by factors such as aging and chronic injury, from, e.g., inflammation. These cell clones are those at risk of subsequent genetic and epigenetic events that would drive tumor progression. Abnormal epigenetic events, such as the aberrant gene silencing focused upon in this chapter, could be the earliest heritable causes, in many instances, for inducing the abnormal clonal expansion from within stem/progenitor cell compartments in a renewing adult cell system. The gene silencing is triggered by chromatin modifications that repress transcription, and the DNA hypermethylation of this chromatin serves as the tight lock, as discussed in the text, to stabilize the heritable silencing. The gene silencing, in turn, disrupts normal homeostasis, which prevents stem and progenitor cells from moving properly along the differentiation pathway for a given epithelial cell system (*top cells with deepening blue colors*) and channels them (*large red arrows*) into the abnormal clonal expansion.