



Figure 6. 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, for example, inflammation. These cell clones are those at risk of subsequent genetic and epigenetic events that could drive tumor progression. Abnormal epigenetic events, such as the aberrant gene silencing focused on in this chapter, could be the earliest heritable causes, in many instances, for a potential role in 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 to stabilize the heritable silencing. The gene silencing, in turn, disrupts normal homeostasis, preventing stem and progenitor cells from moving properly along the differentiation pathway for a given epithelial cell system (blue arrow) and channels them into the abnormal clonal expansion (red arrow).