



**Figure 5.** The position of abnormal DNA methylation in tumor progression. This is depicted in the classic model (Kinzler and Vogelstein 1997) for genetic alterations during the evolution of colon cancer. Altered DNA methylation is shown to occur from very early on in tumorigenesis (red arrow), as discussed in the text, during the conversion of normal to hyperplastic epithelium, accruing during the progression from noninvasive to invasive and, ultimately, metastatic tumors. This places it in a strategic position for channeling stem cells into abnormal clonal expansion (illustrated in Fig. 6) by cooperating with key genetic alterations. These epigenetic abnormalities also have connotations for cancer treatment and markers of prognosis.