



**Figure 2. How DNA Methylation Can Contribute to the Inactivation of Tumor Suppressor Genes**

Two active alleles of a tumor suppressor gene are shown as the two blue boxes at the top. The first step of gene inactivation is shown as a localized mutation (*left*) or gene silencing by DNA methylation (*right*). The second hit is shown as either a loss of heterozygosity (LOH) or transcriptional silencing by additional epigenetic events. In this way, DNA methylation can contribute as one of the pathways to satisfy Knudson's hypothesis.