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Causal Relationship between the Loss of *RUNX3* Expression and Gastric Cancer

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The human *runt*-related gene *RUNX3/PEBP2aC*, located on chromosome 1p36, is a major mediator of signals elicited by members of the transforming growth factor-b (TGF-b) superfamily. Here we show that 45-60% of gastric cancer cell lines and surgically resected specimens do not significantly express *RUNX3* due to a combination of hemizygous deletion and hypermethylation of the *RUNX3* promoter region. Tumorigenicity of gastric cancer cell lines in nude mice was inversely related to their level of *RUNX3* expression, and one gastric tumor associated mutation (R122C), occurring within the conserved Runt domain completely abolished the tumor suppressive effect of *RUNX3*. The results suggest that a lack of *RUNX3* function is causally related to the genesis and progression of human gastric cancer.