Procaine and procainamide inhibit the Wnt canonical pathway by promoter demethylation of WIF-1 in lung cancer cells.


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Abstract

Secreted Wingless type (Wnt) ligands have previously been shown to be involved in tumor developmental processes and oncogenesis. Aberrant promoter methylation of Wnt inhibitory factor-1 (WIF-1) is a fundamental mechanism of epigenetic silencing in human cancers. Procaine, a local anesthetic drug, and procainamide, a drug for the treatment of cardiac arrhythmias, have been reported as inhibitors of DNA methylation, causing demethylation and reactivation of methylation-silenced genes such as RARbeta and GSTP1. The promoter demethylation of WIF-1 has not previously been reported on. We demonstrated previously that WIF-1 is silenced due to promoter hypermethylation in lung cancer cell lines. In this study, we demonstrate promoter demethylation of WIF-1; restoration of WIF-1 expression, and underexpression of cytosolic beta-catenin protein and TCF reporter activity, after procaine and procainamide treatment in H460 and A549 cell lines. Our results provide the first evidence that procaine and procainamide reactivate WIF-1 in these cancer cells and downregulate the Wnt canonical pathway. These results further suggest that procaine and procainamide may have a potential use for preventing the development of lung cancer.

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