Procaína e procainamida diminuem a proliferação celular por efeito epigenético: inibem a metilação do DNA

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

Department of Cardiothoracic Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing, PR China.

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. Procaína, a local anesthetic drug, and procainamida, 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.

PMID: 19885602

Department of Cardiothoracic Surgery, Beijing Friendship Hospital, Capital Medical University, Beijing, PR China.

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. Procaína, a local anesthetic drug, and procainamida, 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.

PMID: 19885602