

J Cell Biochem. 2018 Feb;119(2):2440-2449. doi: 10.1002/jcb.26407. Epub 2017 Oct 27.

Procaine is a specific DNA methylation inhibitor with anti-tumor effect for human gastric cancer.

Li YC1, Wang Y2, Li DD3, Zhang Y3, Zhao TC3, Li CF3.

Author information

Abstract

DNA hypermethylation and the silencing of tumor suppressor genes caused by DNA hypermethylation is considered as a molecular hallmark of many kinds of cancers. Procaine, a local anesthetic, has been shown as a potential DNA methylation inhibitor in some types of cancers. However, the influence of procaine on DNA methylation regulation as well as the biological function in gastric cancer is still unknown. We report here that procaine represses the DNA-methylation level and promotes the proliferation arrest and apoptosis of gastric cancer cells. Global DNA methylation measurement demonstrates that procaine significantly reduces the global DNA methylation level. Analyses of the DNMTs expression and activity show procaine represses the activity, but not the expression, of DNMT1/DNMT3A. Further evidence on specific genes shows that procaine reduces the DNA methylation level in the promoter regions of CDKN2A and RAR $\beta$  genes through abrogating the binding of DNMT1/DNMT3A toward these regions. This repression would not be reversed by the overexpression of DNMT1/DNMT3A. Moreover, RT-qPCR and luciferase report assays demonstrate that procaine leads to the upregulation of CDKN2A and RAR $\beta$  due to the activation of the promoter of these genes. In the end, we test the function of procaine toward gastric cancer cells and find that procaine has the growth inhibitory and apoptosis inducement effect toward gastric cancer cells. Collectively, our data not only uncovers the regulation mechanisms of procaine to DNA methylation but also suggests an anti-tumor potential of procaine specific to the gastric carcinoma and provides a new therapeutic strategy for gastric carcinoma