Genisteína é demetilador e acetilador no câncer cervical

Genistein induces alterations of epigenetic modulatory signatures in human cervical cancer cells.

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Abstract

Introduction Epidemiological studies indicate that diet rich in fruits and vegetables are associated with decreased cancer risk thereby indicating that dietary polyphenols can be potential chemo-preventive agents. The reversible nature of epigenetic modifications makes them a favorable target for cancer prevention. Polyphenols have been shown to reverse aberrant epigenetic patterns by targeting the regulatory enzymes, DNA methyltransferases (DNMTs) and histone deacetylases (HDACs). In vitro and in silico studies of DNMTs and HDACs were planned to examine genistein's role as a natural epigenetic modifier in human cervical cancer cells, HeLa. <P></P> Methods Expression of the tumour suppressor genes (TSGs) [MGMT, RARβ, p21, E-cadherin, DAPK1] as well the methylation status of their promoters were examined alongwith the activity levels of DNMT and HDAC enzymes after treatment with genistein. Expression of DNMTs and HDACs was also studied. In-silico studies were performed to determine the interaction of genistein with DNMTs and HDACs. <P></P> Results Genistein treatment significantly reduced the expression and enzymatic activity of both DNMTs and HDACs in a time dependent way. Molecular modeling data suggests that genistein can interact with various members of DNMT and HDAC families and supports genistein mediated inhibition of their activity. Time dependent exposure of genistein reversed the promoter region methylation of the TSGs and re-established their expression. <P></P> Conclusions In this study, we find that genistein is able to reinstate the expression of the TSGs studied by inhibiting the action of DNMTs and HDACs. This shows that genistein could be an important arsenal in the development of epigenetic based cancer therapy.

KEYWORDS:

DNA methyltransferases (DNMTs); chemoprevention; epigenetics; genistein; histone deacetylases (HDACs); methylation; tumor suppressor genes

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