Altered expression of EGF-induced claudins increases the tumorigenic potential in colorectal cancer cells

Souza, WF, Miranda, NF, Robbs, BK, Viola, JPB, Morgado-Díaz, JA

Cell Biology Program, Research Center, National Cancer Institute

Colorectal cancer represents the fourth most common cause of cancer-related death worldwide, which is closely linked to metastasis development. During process of malignancy, epithelial cells undergo cell-cell adhesion disassembly, increasing its ability to invade adjacent tissues. In this context, tight junctions (TJs) are one of the principal regulators of cell-cell adhesion system and claudins proteins, important components of TJs, regulate different events related with carcinoma progression. Previous studies have showed altered expression of these proteins in human colorectal cancer samples, nevertheless the molecular mechanisms underlying this event in this cancer type remain to be defined. In present study we evaluated the cellular and molecular events related with the altered expression of claudin in colorectal cancer cells. Cell lines derived of human colorectal cancer (HT-29 and Caco-2), which display different differentiation levels, were treated with 20 ng/mL epidermal growth factor (EGF) and the localization and protein levels were analyzed by immunofluorescence and immunoblotting. Our results showed that EGF induced differentially the expression of the protein levels of claudin-1, -2, -3, and caused redistribution of these proteins as evidenced by the discontinuous labeling at the cell-cell contacts. Also, increase of the cell motility, foci formation and anchorage-independent growth were observed after EGF treatment. Furthermore, we transduced HT-29 cells with retroviral-vectors containing claudin-1, -2 and -3 c-DNA to overexpress these proteins and showed that transduced HT/Cld2 and HT/Cld3 cells presented a increase of foci formation and anchorage-independent growth. Together, our findings indicate that EGF regulates claudins expression of a differential fashion dependent of the cell differentiation stage to increase the tumorigenic potential in colorectal cancer.

Keywords: colorectal cancer, cell adhesion, tight junction