EGFR *N*-glycosylation Affects Downstream Signaling and Stability of Tight Junctions in Colorectal Cancer Cells

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INTRODUCTION: Colorectal cancer (CRC) is an important public health problem in Brazil and worldwide. During the progression of epithelial tumors, such as CRC, the disruption of the apical junctional complex, composed of tight junctions (TJ) and adherens junctions (AJ), is frequently observed. The increased expression of different claudin isoforms, major integral transmembrane protein constituents of TJ, induces the loss of barrier function and increases malignant potential in CRC cells. Although more and more studies are contributing to a better understanding of the molecular aspects governing the destabilization of TJ, the role played by *N*-glycans in this process remains poorly understood. **OBJETIVE:** The aim of the present study is to investigate the role of the *N*-glycans in the regulation of estability of the TJ. **MATERIALS AND METHODS:** The human colorectal adenocarcinoma cell line HCT-116 was obtained from the American Type Culture Collection. To investigate the involvement of *N*-glycans with the stability of the TJ we examined, by western blot and immunofluorescence, the effects of treatment with two *N*-glycan biosynthesis inhibitors, swainsonine and tunicamycin. **RESULTS:** In this work, we demonstrate that inhibition of the *N*-glycan biosynthesis by tunicamycin, which blocks epidermal growth factor receptor (EGFR) *N*-glycosylation, decreases claudin-3 expression levels and promotes reorganization of its cellular localization. In addition, deglycosylation of EGFR decreases both, the activation of this receptor and phosphorylation levels of downstream proteins ERK and AKT. Our preliminary results also have shown that malignant tumors from patients with CRC, exhibit increased protein expression of claudin-3 and a greater degree of *N*-glycosylation of EGFR as compared to adjacent normal tissue. **CONCLUSION:** Altogether, these results demonstrate that *N*-glycosylation of EGFR plays a role in the regulation of TJ protein claudin-3, contributing to a better understanding of the biology of CRC. Our results also suggest a potential clinical significance of changes in *N*-glycosylation pattern of EGFR.

Keywords: colorectal cancer, epidermal growth factor receptor, tight junctions.

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