MUC20 overexpression predicts poor prognosis and enhances EGF-induced malignant phenotypes via activation of the EGFR-STAT3 pathway in endometrial cancer

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Abstract

Objective. Mucins play a critical role in the malignancy of various tumors and have been identified as diagnostic markers and as attractive therapeutic targets. However, the role of mucin (MUC) 20 in endometrial cancer (EC) is still unknown.

Methods. The relationship between MUC20 expression and clinical characteristics of EC was analyzed in 97 EC tumors and 16 normal tissues by immunohistochemistry. Effects of MUC20 on EC cells, HEC-1A and RL95-2, were examined by \textit{in vitro} cell growth, migration, and invasion assays, as well as \textit{in vivo} tumor growth in SCID mouse model. Western blotting was performed to analyze signaling pathways modulated by MUC20.

Results. MUC20 expression was significantly higher in EC tumors compared with the normal tissue. High levels of MUC20 expression in EC tumors were correlated with an unfavorable histologic subtype. Furthermore, MUC20 was an independent prognostic factor for poor survival as evaluated by multivariate analyses. Overexpression of MUC20 in EC cells significantly enhanced cell growth, migration, and invasion, as well as tumor growth \textit{in vivo}. The MUC20-enhanced invasive behavior was significantly blocked by erlotinib, an EGFR inhibitor. Moreover, MUC20 overexpression enhanced EGF-mediated migration and invasion, suggesting a critical role of EGFR in MUC20-mediated effects. We found that MUC20 overexpression could enhance EGF-induced phosphorylation of EGFR and STAT3. Inhibition of the STAT3 activity by its inhibitor Stattic significantly suppressed the MUC20-enhanced invasive behavior.

Conclusions. MUC20 is novel prognostic factor for EC and its overexpression enhances EGF-triggered invasive behavior through activation of EGFR-STAT3 pathway.