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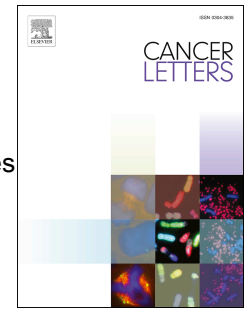

Overexpression of MIST1 reverses the epithelial-mesenchymal transition and reduces the tumorigenicity of pancreatic cancer cells via the Snail/E-cadherin pathway

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Abstract

The role of transcription factors in cancer has attracted significant attention. Although genetic models indicate MIST1 functions as a tumor suppressor in mice, its role in human pancreatic cancer is unclear. We explored the expression and function of MIST1 in pancreatic cancer. Analysis of three GEO datasets (GSE16515, GSE15471, and GSE62165) showed *MIST1* mRNA was significantly downregulated in human pancreatic cancer compared to normal pancreatic tissues. Moreover, MIST1 protein and mRNA expression were downregulated in pancreatic cancer cell lines compared to normal cells. Immunohistochemistry confirmed MIST1 was downregulated in human pancreatic cancer tissues (n=47) and associated with differentiation. *In vitro*, overexpression of MIST1 reduced pancreatic cancer cell growth, migration, and invasion. *In vivo*, overexpression of MIST1 retarded tumor xenograft growth and decreased tumor cell dissemination to the liver. Furthermore, MIST1 reversed the epithelial-mesenchymal transition by downregulating Snail and upregulating E-cadherin. Knockdown of E-cadherin promoted the migration and invasion of cancer cells overexpressing MIST1. In conclusion, this study indicates restoring the expression of MIST1 reversed the EMT and reduced the tumorigenicity of pancreatic cancer cells partly via the Snail/E-cadherin pathway.

Keywords: MIST1; PDAC; GEO; migration; invasion