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RHBDF1 regulates APC-mediated stimulation of the epithelial-to-mesenchymal transition and proliferation of colorectal cancer cells in part via the Wnt/β-catenin signalling pathway

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Abstract

The human rhomboid family-1 gene (RHBDF1) is an oncogene in breast and head and neck squamous cancers. Here, we show that RHBDF1 plays a significant role in colorectal cancer (CRC) formation and that the RHBDF1 expression level is higher in CRC than in corresponding normal tissues. Moreover, RHBDF1 promotes cell proliferation, invasion and migration in vitro. Furthermore, through overexpression and silencing of RHBDF1 and the mediator complex, our study demonstrates that RHBDF1 may positively regulate adenomatous polyposis coli (APC) in the Wnt/β-catenin signalling pathway to increase the expression levels of MMP-14 and Twist, which act as important epithelial-to-mesenchymal transition (EMT) stimulating factors. Additionally, RHBDF1 may regulate c-myc and CyclinD1 expression to influence cell proliferation. Finally, RHBDF1 overexpression and silencing influence CRC growth in BALB/c nude mice. In summary, our findings demonstrate that the regulatory effects of RHBDF1 on EMT and on cell proliferation are partially attributable to the Wnt/β-catenin signalling pathway.

Keywords: RHBDF1; Colorectal cancer; Wnt/β-catenin; APC; EMT

Introduction

Colorectal cancer (CRC) is a common human malignancy that is a leading cause of cancer-related mortality worldwide, and statistics suggest that over 1.2 million people are affected by CRC annually [1]. Previously, the incidence in western countries was

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