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Autophagy Suppresses Tumorigenesis through Upregulation of MiR-449a in Colorectal Cancer

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Abstract : Autophagy is an essential mechanism to maintain cellular homeostasis through its degradation function, and the autophagy deficiency is related various diseases including tumorigenesis in several cancers. MicroRNAs (miRNAs) are small none coding RNAs, which regulate gene expression through degradation of mRNA or inhibition of translation. However, the relationship between autophagy deficiency and dysregulated miRNAs is still unclear. We revealed a mechanism that autophagy up-regulates miR-449a expression at the transcriptional level through activation of forkhead transcription factor family member FoxO1 and then suppresses tumorigenesis in CRC. Our data showed that the autophagic activity and miR-449a expression were lower in colorectal cancer (CRC) and has a positive correlation. We further reveal that autophagy degrades p300 expression and then suppresses acetylation of FoxO1. Under autophagic induction conditions, FoxO1 is transported from the cytoplasm to the nucleus and binds to the miR-449a promoter and then promotes miR-449a expression. In addition, either miR-449a overexpression or amiodarone-induced autophagy inhibits cell cycle progression, proliferation, colony formation migration, invasion, and tumor formation of SW480 cells. Our findings indicate that autophagy inducers may have the potential to be used for prevention and treatment of CRC through upregulation of miR-449a expression.

Keywords : autophagy, MiR-449a, FoxO1, colorectal cancer
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