Overexpression of miR-194 Incapacitates HMGA2-driven Colorectal Cancer

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Colorectal cancer (CRC) is one of the leading causes of cancer death worldwide with increasing incidence and mortality in developed countries. Oncogenes and microRNAs (miRNAs) are revealed to be deregulated and to regulate key signaling pathways in CRC. Oncogenic transcriptional regulator high-mobility group AT-hook 2 (HMGA2) participates in transformation of several cancers including CRC and exhibits strong correlation with poor prognosis and distal metastasis. Evidence of HMGA2 and its co-regulated miRs contributing to tumor progression remains to be clarified We performed gene-set enrichment analysis on expression of 70 CRC patients and revealed HMGA2 correlated miRs including upstream regulations. We reported that the expression of HMGA2 and miR-194 were negatively correlated and miR-194 functioned as a tumor suppressor in CRC by reducing the cell proliferation and tumor growth in xenograft model. Overexpression of HMGA2 reduced miR-194 expression and biological activity, whereas re-expressing miR-194 in cells with high level of HMGA2 compromised the cell survival, epithelial-mesenchymal transition process, and drug resistance. Our findings demonstrate that miR-194, as important as HMGA2, coordinately regulate the oncogenesis of CRC in inverted behaviors. Overexpression of miR-194 impairs the effects of HMGA2, demonstrating alternative molecular therapeutics for CRC patients with high expressed HMGA2.