MiR-590-5p inhibits colorectal cancer angiogenesis and metastasis by regulating nuclear factor 90/vascular endothelial growth factor axis

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Abstract

Altered expression of microRNA-590-5p (miR-590-5p) is involved in tumorigenesis, however, its role in colorectal cancer (CRC) remains undetermined. In this study, we found that the expression level of miR-590-5p was lower in the human CRC cells and tissues than in the normal controls. Overexpression of miR-590-5p inhibited angiogenesis, tumor growth, and lung metastasis in a xenograft mouse model. On the contrary, miR-590-5p knockdown promoted CRC progression. Nuclear factor 90 (NF90), a positive regulator of vascular endothelial growth factor (VEGF) mRNA stability and protein synthesis, was shown to be a direct target of miR-590-5p. Overexpression of NF90 restored VEGF expression and rescued the loss of tumor angiogenesis caused by miR-590-5p. Conversely, the NF90-shRNA attenuated the increased tumor progression caused by the miR-590-5p inhibitor. Clinically, the levels of miR-590-5p were inversely correlated with those of NF90 and VEGF in CRC tissues. Furthermore, knockdown of NF90 leads to a reduction of pri-miR-590-5p and an increase of mature miR-590-5p, suggesting a negative feedback loop between miR-590-5p and NF90. Taken together, these data establish miR-590-5p as an anti-onco-miR that inhibits CRC angiogenesis and metastasis through a new mechanism involving NF90/VEGF signaling axis, highlighting the potential of miR-590-5p as a target for human CRC therapy.