MicroRNA-143 is a potential tumor suppressor targeting DNA methyltransferases 3A in colorectal cancer

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Background and Aims: The aim of this study was to elucidate the roles of microRNA deregulations in colorectal cancer (CRC) development.

Methods: Expression levels of 95 human mature microRNAs (miRNAs) were examined using real-time PCR based expression arrays on 10 paired colorectal carcinomas and normal tissues. Down-regulation of miR-143 was further evaluated in colon cancer cell lines and 30 paired CRC and normal tissues by quantitative PCR. Potential targets of miR-143 were defined. The functional effect of the miR-143 and its targets was performed in human colon cancer cell lines to confirm target association.

Results: We identified the most 10 down-regulated miRNAs in CRC including miR-30a-5p, miR-145, miR-137, miR-133a, miR-204, miR-143, miR-215, miR-26a, miR-125b, miR-125a. Down-regulation of miR-143 was further verified in both seven human colon cancer cell lines and 90% (27/30) of CRC tissues ($P < 0.0001$). Using *in-silico* predictions, *DNMT3a* was defined as a downstream potential target of miR-143. Restoration of miR-143 expression in colon cancer cell lines down-regulated expression of DNMT3a, decreased tumor cell growth by MTT assay ($P < 0.05$) and soft agar colony formation assay ($P < 0.05$). Expressions of *DNMT3a* and miR-143 were inversely correlated in CRC tissues. *DNMT3a* was further demonstrated to be a direct target of miR-143 by luciferase reporter activity assay.

Conclusions: Our findings demonstrated that down-regulation of miR-143 and up-regulation of DNMT3a are significant changes in the development of CRC. These findings point to a tumor suppressive role of miR-143 in epigenetic aberration of CRC, pointing to miRNA-based targeted approaches for colorectal cancer therapy.