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microRNA-mediated regulation of splicing factors SRSF1, SRSF2 and hnRNP A1 in context of their alternatively spliced 3'UTRs.

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Abstract:

SRSF1, SRSF2 and hnRNP A1 are splicing factors that regulate the expression of oncogenes and tumor suppressors. SRSF1 and SRSF2 contribute to the carcinogenesis in the kidney. Despite their importance, the mechanisms regulating their expression in cancer are not entirely understood. Here, we investigated the microRNA-mediated regulation of SRSF1, SRSF2 and hnRNP A1 in renal cancer.

The expression of microRNAs predicted to target SRSF1, SRSF2 and hnRNP A1 was disturbed in renal tumors compared with controls. qPCR, Western blot/ICC and luciferase reporter system assays identified microRNAs that contribute to the regulation of expression of SRSF1 (miR-10b-5p, miR-203a-3p), SRSF2 (miR-183-5p, miR-200c-3p), and hnRNP A1 (miR-135a-5p, miR-149-5p). Silencing of *SRSF1* and *SRSF2* enhanced the expression of their targeting microRNAs. miR-183-5p and miR-200c-3p affected the expression of SRSF2-target genes, *TNFRSF1B*, *TNFRSF9*, *CRADD* and *TP53*. 3'UTR variants of *SRSF1* and *SRSF2* differed by the presence of miRNA-binding sites.

In conclusion, we identified a group of microRNAs that contribute to the regulation of expression of SRSF1, SRSF2 and hnRNP A1. The microRNAs targeting SRSF1 and SRSF2 are involved in a regulatory feedback loop. microRNAs miR-183-5p and miR-200c-3p that target SRSF2, affect the expression of genes involved in apoptotic regulation.

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