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MicroRNA-224 inhibits progression of human prostate cancer by downregulating TRIB1

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Our previous microarray data showed that microRNA-224 (miR-224) was downregulated in human prostate cancer (PCa) tissues compared with adjacent benign tissues. However, the underlying mechanisms by which miR-224 is involved in PCa remain unclear. In this study, we identified TRIB1 as a target gene of miR-224. Forced expression of miR-224 suppressed PCa cell proliferation, invasion and migration, and promoted cell apoptosis by downregulating TRIB1. Moreover, the expression level of miR-224 in PCa tissues was negatively correlated with that of TRIB1. miR-224 downregulation was frequently found in PCa tissues with metastasis, higher PSA level and clinical stage, whereas TRIB1 upregulation was significantly associated with metastasis. Both miR-224 downregulation and TRIB1 upregulation were significantly associated with poor biochemical recurrence-free survival of patients with PCa. In conclusion, these findings reveal that the aberrant expression of miR-224 and TRIB1 may promote PCa progression and have potentials to serve as novel biomarkers for PCa prognosis.

Carcinogenesis

Prostate cancer (PCa) is the most frequently diagnosed cancer in men,[1] which is a clinically heterogeneous-multifocal disease. Both genetic insults and changes in epithelial-stromal interactions are involved in its carcinogenesis and progression.[2] The incidence of PCa is increasing, especially in developed countries. One in six American males will develop PCa during their lifetime.[3] More than 900,000 new cases of PCa are diagnosed worldwide every year. More than a quarter of a million men will die of PCa this year throughout the world.[4] Highly variable in current diagnostic and prognostic criterions has led to failure in diagnosis and determination of its outcome. For example, Gleason score is frequently underestimated and serum prostate specific antigens (PSA) levels can be increased in other diseases, such as benign prostatic hyperplasia (BPH) and prostatitis.[5] Therefore, it is of great importance to understand the carcinogenic process and its corresponding molecular basis for PCa in order to enhance the diagnostic efficiency, to establish the effective therapeutic strategies, and to improve patients' survival.

MicroRNAs (miRs) are small, evolutionary conserved, noncoding RNAs that regulate a variety of gene expression at post-transcriptional level by pairing with complementary nucleotide sequences in the 3′-UTR of specific target genes.[6] miRs directly regulate gene expression at both subtype-specific and its abundance levels. They regulate diverse cellular processes, such as proliferation, differentiation, and apoptosis, and can either serve as a tumor suppressor or as an oncogene, depending on the genes they target.[7] miRs expression is highly cell type and location specific during embryonic development and adult stages. Dysregulation of miR expression plays important roles in the initiation and progression of cancers of various tissue origins. Therefore,

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