Tumor suppressors miR-1 and miR-133a target the oncogenic function of prostate nucleoside phosphorylase (PNP) in prostate cancer

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Background:
Prostate cancer (PCa) is the most frequently diagnosed cancer and second leading cause of cancer deaths among men in developed countries. Our recent analyses of miRNA expression signatures showed that miR-1 and miR-133a were significantly reduced in several types of cancer. Interestingly, miR-1 and miR-133a are located on the same chromosomal locus in the human genome. We examined the functional significance of miR-1 and miR-133a in PCa cells and identified the novel molecular targets regulated by both miR-1 and miR-133a.

Aims:
1. To determined the expression levels of miR-1 and miR-133a in PCa, we performed real-time PCR to compare PCa and non-PCa prostate tissue that provided from prostate needle biopsy.
2. The function of miR-1 and miR-133a were examined in PCa cell line (PC3 and DU145) using XTT assay, invasion assay and migration assay.
3. Molecular targets were identified by genome-wide gene expression analysis and luciferase reporter assay.
4. Purine nucleoside phosphorylase (PNP), the target gene of miR-1 and miR-133a, was examined the expression levels in PCa by RT-PCR and Immunohistochemistry (tissue array).

Key findings:
1. Expression levels of miR-1 and miR-133a were significantly low in PCa compared to the benign prostate (non-PCa) tissue.
2. PNP is a novel target gene of miR-1 and miR-133a and potentially functions as an oncogene in PCa.

Conclusions:
Down-regulation of miR-1 and miR-133a was a frequent event in PCa and both function as tumor suppressors. PNP is a novel target gene of both miRNAs and potentially functions as an oncogene. Identification of novel molecular networks regulated by miRNAs may provide new insights into the underlying causes of PCa oncogenesis.

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