MicroRNA expression profiling in endometrial adenocarcinoma

av

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Abstract


Endometrial cancer is the most common gynecological malignancy and the fourth most common cancer among women. In this thesis, the focus has been on studies of miRNA expression in endometrial cancer.

We have created the database miREC, which integrates available data about miRNAs and their target genes, specifically targets that are involved in the development of endometrial cancer. The database will be used to map linkages between miRNAs and their target genes in order to identify specific miRNAs that are potentially important for the development of EC.

The quantitative polymerase chain reaction (qPCR) is one of the most common methods used for microRNA expression analysis, since it is highly specific and allows quantitative detection of small changes in gene expression. Several factors influence the variability of qPCR expression values, such as the amount and quality of the starting material. Thus, it is important to apply a suitable normalization strategy in the data analysis, which can be the use of stably expressed endogenous control genes. The results showed that U87 and snoRNA were the most appropriate control genes for use in miRNA expression analyses.

In order to determine the expression profile of miRNA in endometrial adenocarcinoma, we have measured the expression levels of 742 miRNAs in human tumor and normal tissues. Among these, 138 miRNAs were identified as differentially expressed between cancer and normal endometrium samples. Validation of 25 differentially expressed miRNAs was confirmed by real-time quantitative PCR. Based on the result of the expression studies, we choose to further investigate the role of mir-34a as a potential marker for endometrial adenocarcinoma. We performed transfection studies, and from our data it appears that mir-34a inhibits cell proliferation by down-regulating the target genes NOTCH1 and DLL1.

Keywords: Endometrial cancer, microRNA, BDII rat model, normalization, endogenous controls.

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