Abstract

During the last two decades, the attention of many scientists has been attracted by a newly discovered group of regulatory molecules – RNA interference. These RNA molecules are capable of very efficient gene silencing. The main pathways of this mechanism are used by two major types of small noncoding RNAs – microRNA (miRNA) and small interfering RNA (siRNA). These RNAs are a direct product of genes and are able to bind to mRNA molecules and influence their activity. Due to this knowledge, scientists started examining the effect of RNAi in cancer cells and tried to find a way how RNAi can be applied in therapy.

The main topic of this thesis is the potential of miRNA replacement to harm cancer cell proliferation. In cancer cells, miRNA levels are downregulated or upregulated, depending on the nature of cancer and miRNA. Restoring levels of miRNAs can lead to elimination of cancer cell by apoptosis or stop cell in cell cycle arrest.

miRNA replacement was used first to examine the function of a single miRNA in HeLa cancer cells. The change in the expression level of miRNA treated cells was verified by reverse transcriptase quantitative PCR and the proliferation inhibition was examined using proliferation assays. The most potent miRNAs inducing significant proliferation inhibition were examined. In the second part of my work, miRNAs inducing significant effect were combined with oncogene targeted siRNAs and transfected to HeLa cells, in order to seek for possible synergistic effects.

By screening combinations of let7a, mir-16, and mir-145 and cancer-relevant siRNAs, a synergistic effect of some miRNA/siRNA combined treatments was identified. The most potent regimens were mir-16 and CDC 37-siRNA, and let7a with siRNAs targeted at CDK1 and PLCB1.