

Bioinformatic discovery of microRNAs and their expression in human gastric cancers

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Abstract

MicroRNAs (miRNAs) are endogenous non-protein-coding RNAs of approximately 22 nucleotides. Due to their critical involvement in embryonic development, tissue formation and physiological functions, many research efforts have devoted to the discovery of miRNAs, including bioinformatic approaches. Our laboratory has applied mature miRNA sequence patterns to scan the genome sequences of more than fifty bilaterian animal species for identification of homologous miRNAs. The regions centered surrounding these candidate miRNAs were then extracted for folding and calculating the features of their secondary structure. Using a support vector machine as a classifier combined with these features, we identified more than 15,000 orthologous or paralogous candidate pre-miRNAs, as well as their corresponding candidate mature miRNAs. Stem-loop RT-PCR and Next Generation Sequencing methods were used to experimentally validate the prediction results. In addition, we have also examined expression alterations of miRNAs and isomiRs in human gastric cancer cells. We have analyzed the expression of miRNAs in gastric cancer cells following the treatment with de-methylation agents. These miRNAs silenced by tumor-specific methylation could play significant oncogenesis roles in gastric cancer progression. We further analyzed the expression levels of several selected altered miRNAs in clinical gastric cancer tissues. We found that poor clinical feature was significantly associated with low expression of miR-34b and miR-129-3p. In addition, we have demonstrated that miR-196 promotes cell migration and invasion, suggesting its oncogenic potential in gastric cancer progression. Furthermore, we observed that increased circulating miR-196 in serum is associated with cancer disease status and relapse. Our studies are beneficial to interrogate oncogenic miRNAs in the human cancers and their applications as novel cancer biomarkers.

Keywords: microRNA, bioinformatics, gastric cancer, biomarker