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Single-Nucleotide Polymorphisms Within MicroRNAs Sequences and Their 3' UTR Target Sites May Regulate Gene Expression in Gastrointestinal Tract Cancers

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Background: Esophageal, stomach, and colorectal cancers are commonly lethal gastrointestinal tract (GIT) neoplasms, causing almost two million deaths worldwide each year. some environmental risk factors are acknowledged; however, genetic defects can significantly contribute to predisposition to GIT cancers. Accordingly, recent works have shown that single-nucleotide polymorphisms (SNPs) within miRNAs coding sequence (miR-SNPs) and miRNA target sites (target-SNPs) may further contribute to increased risk of developing cancer.
Objectives: In this study, we comprehensively identified miRNA-target gene pairs implicated in GIT cancers and catalogued the presence of potentially functional miR-SNPs and target-SNPs that impair the correct functional recognition.
Materials and Methods: Using bioinformatics tools, manual literature review, and a highly accurate dataset of experimentally validated miRNA-target gene interactions, we compiled a list of miRNA-target genes pairs related to GIT cancers and prioritized them into different groups based on the levels of experimental support. Functional annotations (gene ontology) were applied to these pairs in each group to gain further information.
Results: We identified 97 pairs in which both miRNAs and target genes were implicated in GIT cancers. Several pairs, denoted as highly polymorphic pairs, had both miR-SNPs and target-SNPs. In addition, more than 5000 miRNA-target gene pairs were identified in which, according to the previous reports, either the miRNAs or the target genes had a direct involvement in GIT cancers. More than 800 target-SNPs are located in regulatory regions that were extracted from the ENCODE project through the RegulomeDB database. Of these, 20 were classified as expression quantitative trait loci (eQTLs).
Conclusions: Our work provided a comprehensive source of prioritized and annotated candidate polymorphisms inside miRNAs and their target sites in GIT cancers, which would facilitate the process of choosing right candidate miRNA-target genes and related polymorphisms for future association or functional studies.

*Keywords:*MicroRNAs; Gastrointestinal Neoplasms; Colorectal Neoplasms; Gastric Neoplasms; Esophageal Neoplasms; Single Nucleotide Polymorphisms