

Global MicroRNA Profiling of Small Intestine Neuroendocrine Tumors (SI-NETs) and Establishment of a Method to Study Serum MicroRNA Expression from the Same Tumors

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Background: MicroRNAs (miRNAs) are important post-transcriptional regulators in biological processes and they function either as tumor suppressors or oncogenes. This study aims at providing exclusive miRNAs profile and identifying serum miRNA expression from SI-NET patients' serum.

Methods: We used frozen SI-NET specimens to perform Affymetrix miRNA-arrays. QRT-PCR analysis validated our in silico results. Moreover, human NET cells and serum samples were involved in the study.

Results: Global miRNA profile shows the expression of significantly altered nine miRNAs between primary tumors and metastases. Furthermore, QRT-PCR analysis from laser-capture microdissected (LCM) tumor cells detected upregulated miR-96, -182, -183, 196a and 200a expression in LCM tumor cells versus LCM normal enterochromaffin (EC) cells from two independent specimen sets. Whereas, miR-31, -129-5p, -133a and -215 were downregulated in LCM tumor cells versus LCM normal EC cells. In addition, the five upregulated miRNAs are significantly more expressed in LCM primary tumor cells than in LCM stroma cells. Whereas, two downregulated miRNAs out of four are significantly less expressed in LCM primary tumor cells than in LCM stoma cells. The nine deregulated miRNAs are expressed at different level on five human NET cell lines. Moreover, the potential miRNA target genes list is the results of miRNA online software programs search combined to our published results from SI-NETs microarray analysis by Leja et al., 2009. In addition, we established a technical method to isolate miRNAs from serum samples. Total RNA, which includes miRNAs, was isolated from 3 healthy donors, 3 primary SI-NETs, 3 lymph node metastases and 3 liver metastases. Then, QRT PCR analysis was used to prove method reliability by detecting miR-16, an internal control.

Conclusion: The SI-NET miRNA profile provides potential pivotal miRNAs, which may be involved in tumor progression and having a role to develop novel therapeutic targets. Moreover, we may implement the study using patient's serum.