MicroRNA Signature as Novel Biomarkers in Small Intestine Neuroendocrine Tumors

Aims
Identification of exclusive microRNA (miR) profiles of small intestine neuroendocrine tumors (SI-NETs) at different stage of disease. Furthermore, to study potential miR targets, which may have a significant role in the development, prognosis and progression of SI-NETs.

Background
MicroRNAs are well known post-transcriptional regulators, which control cell proliferation, differentiation and apoptosis in a variety of cells. However, miR expression is not fully characterized in SI-NETs.

Results & Conclusions
The expression of miR-96, -182, -183, -196a and -200a is significantly upregulated in microdissected SI-NET cells compared to microdissected normal enterochromaffin (EC) cells. MiR-31, -129-5p, -133a and -215 expression reveals significant downregulation in microdissected SI-NET cells compared to microdissected normal EC cells.

This genome-wide miRs expression analysis of SI-NETs at different stage of disease provides information about potential pivotal miRs. This may lead to further insights into tumorigenesis and progression mechanisms of these tumors.

Figure 1. MiRs expression of SI-NET specimens. 33 differentially expressed miRs were detected both in mesentery metastases (M) and liver metastases (L) compared to primary tumors (P).

Figure 2. MiR-182, -183, -31 and -133a expression by Northern blot analysis. Total RNA from P, M and L was hybridized with 32P radiolabeled RNA probes. RNU48 was used as internal control.

Figure 3. MiR-31, -96, -129-5p, -133a, -182, -183, -196a, -200a and -215 expression by QRT-PCR analysis. (A) Total RNA from frozen specimens (P, M and L) and microdissected normal enterochromaffin (EC) cells were used to verify miR arrays data. RNA from microdissected normal EC cells was used as a reference. (B) Total RNA from microdissected normal EC cells and SI-NET (P, M, and L) cells revealed specific miR expression levels in tumor cells. The internal control RNU48, from each individual sample set to 1 was used for normalization. Student’s t-test calculated experimental significance. * = p < 0.05, ** = p < 0.01 and *** = p < 0.001

Material & Methods
Fifteen SI-NET specimens at different stage of malignancy (5 primary tumors, 5 mesentery metastases and 5 liver metastases) were included in this study. Total RNA was hybridized onto Affymetrix GeneChip® miR arrays for genome-wide profiling. Quantitative real time PCR (QRT-PCR) and Northern blot analyses on total RNA of the tumor specimens and microdissected SI-NET cells validated our in silico data.