Differences in the microRNA expression of G1 and G2 pancreatic neuroendocrine tumors

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Background:

In the past few years, it has been observed, that the number of registered **neuroendocrine tumors** (NET) considerably **increased** (from 3,9 (2001) to 7,9 (2012) / 100000 people) **(1,2,3)**. We have focused on **NETs of the pancreas (pNETs)**. The **therapy** of pNETs is **principally influenced by** their histological **grade**, which can change through the progression of the tumor. Currently, to determine the grade, it is inevitable to use invasive methods, such as biopsy and surgery, and it requires an experienced pathologist. According to the **WHO classification** pNETs are sorted into **3 grades** based on their KI-67 index, mitotic index, and differentiation. **MicroRNAs** are short, stable, non-coding RNAs that play a role in the posttranscriptional regulation of gene expression. Their **expression** is **tissue- and tumor-specific** and may be **characteristic of the grade**. MicroRNAs are actively secreted by cells into their environment, thus can be detected in body fluids as well. In this study we selected 4 microRNAs based on literature data **(4,5)**, and measured their expression in **FFPE** (formalin-fixed paraffin-embedded) **blocks of G1 and G2 samples**.

Aims:

Our aim was to find miRNAs that show significant differences in expression according to grade, thus could be suitable for grade determination. The significant miRNAs could be used to complement the histological approach.

Selected microRNAs for this study:

Based on literature search we have selected four miRNAs (**hsa-miR-96-5p, hsa-miR-130b-3p, hsa-miR-106b and hsa-miR-194-5p**). These miRNAs, were examined in pNETs from FFPE samples. The expression of **hsa-miR-106b** was shown to have prognostic relevance. Its expression is was found to be **upregulated** in G3 tumors compared to G1 and G2 tumors. **(4,6)** The **hsa-miR-96-5p** is an oncogenic microRNA. Its expression **increased** with PNET grade and in other tumors it is associated with tumor progression. It **inhibits FOXO1** and **activates AKT/GSK-3β/β-catenin signaling pathway**. **(4,5)** The expression of **hsa-miR-130b-3p** was found to **increase** with the grade, whereas the expression of **hsa-miR-194-5p decreased** with grade. For these miRNAs no specific function in PNET is determined yet. **(4,5)**

Materials and Methods:

We've collected **33 FFPE samples (16 G1, 17 G2)** from the two Departments of Pathology of Semmelweis University. From **80-80 µm sections** of the FFPE blocks we **isolated total RNA** with **Recover ALL Kit** (Thermo Fisher Scientific). The sections were from tumor tissue only, marked by a pathologist. The expression of ***hsa-miR-96-5p, hsa-miR-130b-3p, hsa-miR-106b and hsa-miR-194-5p*** was determined by **RT-qPCR**, using **TaqMan MicroRNA Assays**. We calculated the ΔCT values using **cel-miR-39** spike-in external control and **RNU48** internal control, and analyzed them with unpaired t-test, using **GraphPad Prism**.

The miR-130b and miR-194 have shown significant difference in expression in grade 1 and grade 2 pNETs.

pNET, grade1, grade2, FFPE, miRNA, miR-130b, miR-194, miR-96, miR-106b

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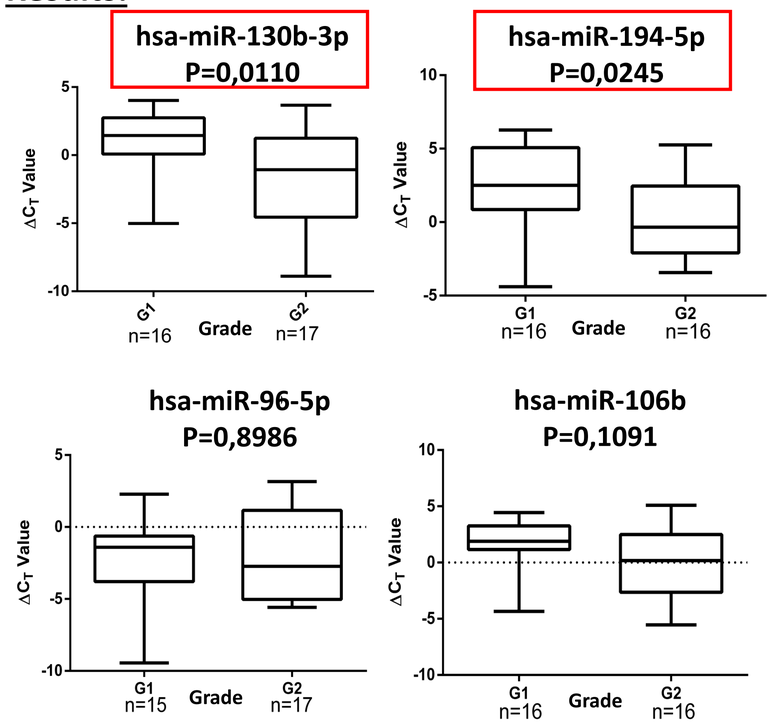
Results:



Conclusions:

In conclusion, two of the four miRNAs (***hsa-miR-130b-3p***, ***hsa-miR-194-5p***) have shown significant difference in expression in grade 1 and grade 2 pNETs. Both microRNAs showed lower expression in G2 compared to G1 pNETs.

References:

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