Abstract citation ID: bvac150.1211

Neuroendocrinology and Pituitary
RF25 | PMON147
Plasma MicroRNA Expression in Phenocopy of Multiple Endocrine Neoplasia Type 1 Compared to Patients with Acromegaly and Primary Hyperparathyroidism: Potential Biomarkers of Multiple Endocrine Tumor Growth
Diana Trukhina, MD, Elizaveta Mamedova, MD, PhD, Alexey Nikitin, PhD, Philipp Koshkin, PhD, Zhanna Belaya, MD, PhD, and Galina Melnichenko, MD, PhD
**Introduction:** Changes in the expression of microRNA facilitate in the formation of various tumors. MEN1 is a rare disease caused by mutations in MEN1 gene encoding the menin protein and characterize by the occurrence of parathyroid, pituitary, gastroenteropancreatic and other tumors. If a patient with the MEN1 phenotype carry no mutations in the MEN1 gene, the condition considers a phenocopy of syndrome (phMEN1). We hypothesize that the pathogenic link among the above sporadic tumors might be represented by molecular pathways involving the MEN1 gene and epigenetic regulations — particularly microRNAs.

**Materials & methods:** Single-center, case-control study: assessment of plasma microRNA expression in patients with phMEN1, acromegaly (AM), primary hyperparathyroidism (PHPT) and healthy controls. Morning plasma samples were collected from fasting patients and age- and sex-matched controls and stored at −80°C. Total RNA isolation: miRNeasy Mini Kit with QIAcube. The libraries were prepared by the QIAseq miRNA Library Kit following the manufacturer. Circulating miRNA sequencing was done on Illumina NextSeq 500 (Illumina). Subsequent data processing was performed using the DESeq2 bioinformatics algorithm.

**Results:** We enrolled 36 consecutive patients (12 patients in each group) with phMEN1, AM, PHPT, along with 12 age and gender matched controls. Median age of phMEN1 group — 59 [52; 60.5]; AM — 59 [52; 63]; PHPT — 60.5 [54; 62.5]; control — 59 [51.5; 62.5]. The groups did not differ in age (p=0.88) and gender – in all groups were 11 women and 1 man (p=1.00).

We divided all assessed microRNAs into 3 groups based on the significance of the results; the first group consisted of samples with the highest levels of detected microRNAs (>50), the second group — moderate (10–50), the third group — the lowest (<10).

The microRNA expression pattern was almost the same between AM and phMEN1 groups (15 microRNAs upregulated, 10 — downregulated), we found slightly decreased hsa-miR-4301 (padj=0.038); it is interesting that phMEN group when compared to PHPT and control groups showed decline in hsa-miR-4301 too. PHPT and control groups had also quite similar expression profile (4 microRNAs upregulated, 19 — downregulated).

607 microRNA were differently expressed in groups phMEN1 and PHPT (473 upregulated microRNAs, 134 — downregulated). We found increased expression of some microRNAs that interferes with menin: hsa-miR-24-1-5p (padj=0.0008), hsa-miR-24-3p (padj=0.034), hsa-miR-26a-5p (padj=0.0005), hsa-miR-421 (padj=0.018), hsa-miR-762 (padj=0.027). In addition, we found decreased microRNAs with oncogene potential: miR-3182 (padj=0.007), hsa-miR-875-5p (padj<0.001), hsa-miR-6749-5p (padj<0.001).

173 microRNA differed in phMEN1 and control groups (11 microRNAs upregulated, 162 — downregulated). We detected several decreased microRNAs in phMEN1 that participate in tumor genesis: hsa-miR-625-3p (padj<0.005), hsa-miR-3168 (padj=0.028), hsa-miR-302b-3p (padj<0.001).

**Conclusion:** We found microRNAs, which could potentially become biomarkers in phMEN1 diagnosis. The results need to be validated using different measurement method with larger sample size. Likewise further assessment of plasma microRNA expression in genetically confirmed MEN1 patients is needed.

**Presentation:** Monday, June 13, 2022 12:30 p.m. - 12:35 p.m., Monday, June 13, 2022 12:30 p.m. - 2:30 p.m.