MiRNA profile associated with invasiveness in non-functioning pituitary adenomas

E. Nikolova[1], Silviya Klenderova – Valkova[1], Biliyana Georgieva[1], Atanaska Elenkova[2], Asen Hadzhiyanev [3], A. Todorova[1,4]

[1] Department of Medical Chemistry and Biochemistry, Medical University-Sofia, Sofia, Bulgaria; [2] Department of Endocrinology, Medical University-Sofia, USHATE "Acad. Iv. Penchev", Sofia, Bulgaria; [3] Department of Neurosurgery, University Hospital "St. Ivan Rilski", Medical University-Sofia, Sofia, Bulgaria; [4] Genetic Medico-Diagnostic Laboratory Genica, Sofia, Bulgaria

Corresponding author: nikolova.emily@gmail.com

Background

Non-functioning pituitary adenomas (NFPAs) are not associated with hormonal hypersecretion and are among the most common pituitary tumours. In some patients tumour recurrence and invasion have been observed. So far, the diagnosis and monitoring of NFPAs remains difficult due to the lack of clinical biomarkers. In the present study, microRNAs (miRs) expression profiles were analysed in patients with invasive and non-invasive NFPAs and their biomarker potential was evaluated.

Methods

MiRs profiles were analysed in 12 patients with non-invasive and 8 patients with invasive NFPAs using miRCURY LNA miRNA Cancer Focus PCR Panel (Qiagen). ROC curve analysis evaluated the diagnostic ability of the selected miRNAs. $P<0.05$ was assumed for statistically significant and was calculated using un-paired, 2-tailed Student's t-test.

- NFPA tissue collection
- RNA isolation

qPCR
- miRCURY LNA RT
- cDNA amplification on LC 480

Data analysis

Results

Four miRs were found differentially expressed related to invasion and recurrence of NFPAs. MiR-106a, miR-17 and miR-20a were up-regulated in patients with recurrent invasive NFPAs (fig. 1), while miR-210-3p was down-regulated in invasive NFPAs compared to patients with non-invasive NFPAs (fig. 2).
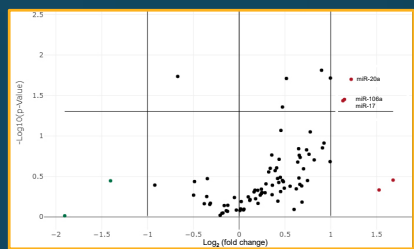

Figure 1. Volcano plot of up-regulated miR-106a, miR-17 and miR-20a in patients with recurrent invasive NFPAs
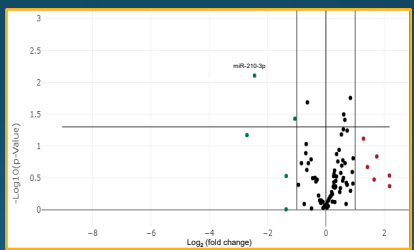

Figure 2. Volcano plot of down-regulated miR-210-3p in invasive NFPAs compared to non-invasive NFPAs

The average AUC was 0.943 (95% CI = 0.876-1) for miR-106a, miR-17 and miR-20a, and AUC = 0.915 (95% CI = 0.702-1) as markers for differentiating invasiveness.
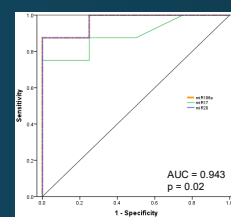

Figure 3. ROC curve analysis of miR-106a (AUC=0.969), miR-17 (AUC=0.891) and miR-20a (AUC=0.969) in invasive NFPAs
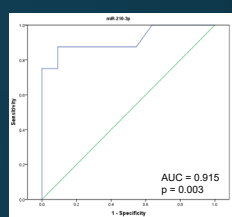

Figure 4. ROC curve analysis of miR-210-3p with AUC = 0.915 (95% CI = 0.768-1) in invasive compared to non-invasive NFPAs

Conclusion

The ability to predict tumour invasion and recurrence after the initial surgery will decrease morbidity and mortality rate in patients with NFPAs. The selected profile of miR-106a, miR-17, miR-20 and miR-210-3p showed biomarker potential. The next step is confirmation of the results in a larger patient cohort.

Funding