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1386PD Longitudinal increase in Ki67 and high-grade transformation in pancreatic neuroendocrine tumours (PNETs)

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Background: Tumor proliferation and grade are important prognostic factors at diagnosis of PNETs. Little is known about how these factors change over time and if longitudinal increase in Ki67-index is associated with prognosis. The purpose of this work was to describe longitudinal changes in Ki67-index and tumor grade, as well as its impact on overall survival, in PNETs.

Methods: Platelet free plasma from 68 GEP-NET patients was collected. Whole miRNOME NGS analysis was performed on exome enriched small-RNAs fraction of 24 patients: 12 ^{18}PET/FDG+ and 12 ^{18}PET/FDG-. MiRNAs significantly associated with ^{18}PET/FDG outcome has been identified and validated by RT/qPCR on overall case series. Target miRNAs fold enrichment were then combined to create predictors (pAB, pAC, pBC and pABC). Man-Whitney test was applied and validated target miRNAs had been correlated with clinical outcome and clinical parameters (ki-67, grading, tumor burden and ^{68}Gallium-PET SUV_{max}).

Results: NGS whole miRNOME analysis revealed 10 target miRNAs able to distinguish ^{18}FDG/PET positive from negative Pancreatic-NETs (PNETs). Subsequently, mir-A, mir-B, mir-C (*patent pending*) have been validated on overall case series by multiplex RT/qPCR ($p < 0{,}0047$ and $p < 0{,}0001$, respectively), on PNETs case series and pBC and pABC resulted to be the best predictors ($p < 0{,}0001$). All validated miRNAs and derived predictors, especially mir-B, result significantly increased in small intestine (SINETs) and in PNETs patients when compared to healthy controls. Correlation analysis between target miRNAs and clinical parameters also revealed that mir-B negatively correlates with ^{68}Ga-PET SUV_{max} ($p < 0{,}04$), suggesting interference with SSTR expression.

Conclusions: We defined a 3 miRNAs *signature* able to correlate with ^{18}FDG/PET status. Over expression of mir-A, mir-B, mir-C or combined predictors in PNETs can provide prognostic information on tumor aggressiveness and might help to identify PRRT non-responders. In addition mir-B negatively correlates with clinical outcome and ^{68}Ga-PET SUV_{max}. We are investigating if mirB interfere with SSTR expression, affecting PRRT efficacy.

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