

Changes in MicroRNAs Expression and Clinical Associations in Patients with Neuroendocrine Pancreatic Tumors

Francesca Tavano¹, Fabio F di Mola¹, Francesca P Burbaci¹, Lucia Lombardi², Massimiliano Copetti⁴, Ada Piepoli³, Angelo Andriulli³, Evaristo Maiello², Pierluigi di Sebastiano¹

¹Department of Surgery, ²Division of Oncology, ³Division of Gastroenterology and
⁴Unit of Biostatistics, IRCCS “Casa Sollievo della Sofferenza”. San Giovanni Rotondo, FG, Italy

Context In a previously study, we analyzed associations between altered expression of 13 microRNAs (miR-145, miR-23a, miR-455-3p, miR-708, miR-151-5p, miR-30c, miR-let-7i, miR-199a-5p, miR-30a, miR-143, miR-21, miR-155*, and miR-31) and clinical variables in patients with pancreatic adenocarcinoma. **Objective** Here, expression levels of these miRNAs were analyzed to evaluate their possible associations with clinical-pathological features in patients underwent surgical resection for pancreatic neuroendocrine tumors (PETs). **Methods** miRNAs expression levels in tumors compared to matched-pairs non-cancerous tissue samples, were analyzed by using TaqMan MicroRNA Assay. Association analysis was performed by means of Spearman correlation coefficient and Mann-Whitney U-test. **Results** No significant association was found between miR-145, miR-23a, miR-455-3p, and miR-708 levels and patients sub-phenotypes. Conversely, miR-151-5p expression

was inversely correlated with age at diagnosis ($r_s = -0.77$, $P = 0.009$), both miR-30a and miR-let-7i levels were positively associated with tumor size ($r_s = 0.69$, $P = 0.027$ and $r_s = 0.67$, $P = 0.034$), while over-expression of either miR-199a-5p and miR-30c was associate with male gender ($P = 0.046$ and $P = 0.003$). Further original finding was the association between miR-143, miR-21 and miR-155* levels and tumor mitotic index ($P = 0.04$, $P = 0.0002$, and $P < 0.0001$, respectively), while expression of both miR-31 and miR-30c was associated with tumor proliferation index ($P = 0.003$ and $P = 0.01$, respectively). In addition, miRNAs expression levels were also found to be correlated with each others in PETs tissue samples. **Conclusions** These data suggest a prognostic significance for specific miRNAs in PETs. Understanding the associations between miRNAs expression levels could help identify novel regulatory network involved biology of PETs.