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Unveiling Pancreatic Neuroendocrine Tumors through Plasma-Derived Small Extracellular Vesicles

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BACKGROUND

The global incidence of pancreatic neuroendocrine tumors (PanNETs) has witnessed a steady rise in the past three decades. Unfortunately, the survival rates remain low primarily due to late-stage diagnoses and a lack of specific and sensitive diagnostic markers. Therefore, there is an urgent need for improved and efficient early diagnostic biomarkers. Small extracellular vesicles (sEVs) have gained significant attention in the field of tumor growth and cancer metastasis, owing to their remarkable capacity to induce metastatic behavior and proliferation. This study pioneers the investigation of the relationship between sEV concentration and PanNET grades, as well as the presence of BIRC2/cIAP and the autophagy marker Beclin-1 as cargo within sEVs derived from plasma. By examining plasma-derived small extracellular vesicles, this research sheds new light on the potential role of these vesicles as diagnostic biomarkers for PanNETs, offering a promising avenue for early detection and improved patient outcomes.

METHODS

sEVs were extracted from the clarified plasma samples and subjected to morphological characterization using transmission electron microscopy. Furthermore, the presence of sEVs was validated through the expression of sEV markers CD63 and TSG101, while calnexin served as the negative control. Quantification of sEVs was conducted using nanoparticle tracking analysis (NTA), providing valuable insights into their abundance and size distribution. Subsequently, the presence of BIRC2 and Beclin-1 as cargo within sEVs derived from plasma was investigated through western blot analysis. Additionally, Immunohistochemistry (IHC) was employed to evaluate the expression of BIRC2 and Beclin-1 in both PanNET tissue and healthy control samples.

RESULTS

This study presents compelling evidence of elevated plasma secretion of sEVs in PanNETs (Grade I & II) individuals compared to healthy controls (HCs). Moreover, higher protein expression levels of BIRC2 and Beclin-1 were observed in PanNETs compared to HCs. Notably, the immunohistochemistry (IHC) analysis of PanNET tissue revealed a parallel expression pattern for both proteins.

CONCLUSIONS

The findings unveil a potential correlation between elevated plasma secretion of sEVs and PanNET pathogenesis. Heightened expression of BIRC2 and Beclin-1 proteins further highlights their potential as important PanNET biomarkers. This study provides valuable insights into PanNET biology, paving the way for new diagnostic and therapeutic approaches.

ABSTRACT ID 23470