ANALYSIS OF PROTEIN-PROTEIN INTERACTION NETWORKS OF TUMORS FROM PATIENTS WITH MULTIPLE ENDOCRINE NEOPLASIA TYPE 1 (MEN1)

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Multiple Endocrine Neoplasms (MEN) involve tumors in two or more endocrine glands and have two main types: MEN 1 and MEN 2. MEN 1 is an autosomal dominant disease with high penetrance, diagnosed clinically and with genetic testing. Early diagnosis and tumor screening reduce morbidity and increase survival of patients with MEN 1. Non-invasive screening methods that identify molecular biomarkers, with cost-effectiveness, high precision and ease of use, are necessary. Biomarkers are important not only for early detection, but also for prognostic stratification, surveillance and personalized treatment. The objective of this work was to identify proteins and protein signaling pathways in tumor tissues of patients with multiple endocrine neoplasia type 1 (MEN 1) who presented pituitary adenomas (group 1), parathyroid tumors (group 2) and enteropancreatic neuroendocrine tumors (group 3). For this, label-free shotgun proteomic analysis was performed by mass spectrometry using the LC-MS/MS Orbitrap Híbrido Quadrupole Q Exactive (Thermo Fisher Scientific) and interaction network analysis using String. In group 1, analyzing pituitary adenomas, the interaction network highlighted proteins involved in the altered metabolism of tumor cells, a common feature in neoplasms that require energy and rapid proliferation. Proteins such as ALCAM and CD59 suggest changes in cell adhesion and migration, facilitating tumor invasion and metastasis. The presence of proteins such as CD59 indicates mechanisms by which tumor cells can evade the immune system. In group 2, parathyroid tumors, the network interaction demonstrates the ability of individuals to reprogram their metabolism to meet high demands for energy and biosynthesis. The presence of PHGDH and UGP2 reflects this metabolic adaptation, crucial for the growth and survival of tumor cells. Adhesion and motility proteins such as DSP and CTNNA1 suggest that MEN1 tumor cells may have enhanced mechanisms for invading adjacent tissues. The presence of multiple Rab proteins indicates a potential increase in vesicular secretion activity. This is particularly relevant for endocrine tumors, which can secrete excess hormones, causing severe clinical symptoms. The high expression of ribosomal components suggests an increased need for protein synthesis to support the rapid cell growth observed in MEN1 tumors. In group 3, analyzing enteropancreatic neuroendocrine tumors, interactions between mitochondrial proteins and fatty acid metabolism indicate an altered energy metabolism. Interactions between cytoskeletal and adhesion proteins (TLN1) suggest structural adaptations that may facilitate cell invasion and migration. The proteins involved in vesicular transport and secretion reflect the dysregulation of hormone production, characteristic of endocrine tumors. Possible mechanisms of immune evasion were also observed, with the presence of HLA-E and HLA-G. Analysis of the protein interaction network of multiple endocrine neoplasia type 1 (MEN 1) tumors suggests that these proteins play crucial roles in the metabolic adaptation of tumor cells. Understanding these interactions provides valuable information for developing targeted therapies that disrupt these critical processes in neoplastic cells.

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