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ABSTRACT

Copy Number Variation Analysis of a Pancreatic Neuroendocrine Tumor (NET) from a Patient with von Hippel-Lindau (VHL)

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von Hippel-Lindau disease (VHL) is an autosomal dominant syndrome that results from germline mutations in the VHL gene, predisposing to multiples tumors, including neuroendocrine tumor (NET) of the pancreas detected in 11% to 17% during lifetime. Little is known about the cytogenetic anomalies presented in pancreatic NETs, and the identification of commonly imbalanced genes may contribute for the understanding of the somatic steps of the carcinogenesis. The aim of this study was to detect chromosomal imbalances in a pancreatic NET of a patient with VHL disease. We used GeneChip Human Mapping 50K Set Xba240 (Affymetrix) to assess genomic CNVs; Genotyping Console Software (Affymetrix) was used for analysis. We detected three deletions in 3p25.3-p11.2, 3q26.33-qter, and 8q21.11-q24.3, and one duplication in 7q22.1- qter. All genes located in these regions were analyzed according to their biological processes using DAVID Functional Annotation Tool. This analysis revealed a duplication of the oncogene MET, and other genes involved in cell proliferation, resistance to apoptosis and angiogenesis. The PPARG gene, from the PTEN/PI3K/AKT/mTOR pathway, was deleted; BRAF gene, component of the RAS/RAF/MAPK pathway, was duplicated. The involvement of known pathways already described in other VHL-related tumors, as RCCs and hemangioblastomas, suggests common steps in the tumorigenesis and progression of pancreatic NETs related with VHL disease.