

# RSUME regulates tumorigenesis and metastasis in pancreatic neuroendocrine tumors



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**INTRODUCTION:** Pancreatic neuroendocrine tumors are rare and represent only about 1 to 2% of all neoplasias of the pancreas. They derive from hormone producing cells of the pancreas and are correspondingly designated as insulinomas, gastrinomas, VIPomas, glucagoninomas etc. The pathogenesis of this heterogenous family of tumors is largely unknown. RSUME was previously identified as sumoylation enhancer protein to stabilize target genes such as HIF1 $\alpha$  and I $\kappa$ B $\alpha$ . We found that RSUME is highly expressed in pancreas but loss of expression in PanNETs. Therefore the (patho-) physiological consequence due to RSUME absence was studied using PanNET derived BON1 cells. We found that RSUME knockdown in BON cells led to decrease HIF1 $\alpha$  expression and vascular density and increased the liver metastasis tested in an orthotopic tumor model and the molecular mechanisms are partly attribute to decreased PTEN expression and increased NF $\kappa$ B activity.

