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, glucagonomas 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 HIF1α and IκBα. 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 decreased HIF1α 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 NFκB activity.

1. RSUME is down-regulated in PanNETs and regulates VEGF through HIF1α in PanNET cells

2. RSUME negatively regulates NF-κB activity by enhancing IκBα SUMOylation

3. RSUME enhances PTEN sumoylation, protein stability and increases its nucleus accumulation

4. RSUME knockdown decreases metastasis in vivo

5. Model

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RSUME KD reduces PTEN

RSUME is induced during hypoxia

RSUME negatively regulates NF-κB

RSUME is down-regulated in PanNETs

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