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Receptor for Hyaluron-Mediated Motility Isoform B Protects Pancreatic Neuroendocrine Tumors From Anoikis

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Background: More than 50% patients with pancreatic neuroendocrine tumors (panNETs) have developed metastasis at diagnosis. Treatment options for these patients are very limited. Metastatic panNETs represent incurable tumors that have continued to rise in recent decades. Understanding how metastasis of panNET occurs is critical for success in developing therapies that prevent dissemination of tumor cells and destroy metastatic tumor cells.

Method: Using a novel *RIP-Tag; RIP-tva* mouse model, we have identified the first gene that promotes liver-specific metastasis of panNET through somatic gene transfer. This gene encodes the Receptor for Hyaluronan-Mediated Motility isoform B ($RHAMM^B$) protein. However, the mechanism by which $RHAMM^B$ promotes metastasis of panNET remains to be determined.

Results: Here, we demonstrate that $RHAMM^B$-overexpressing mouse panNET cells are more resistant to cell detachment-induced anoikis by producing less reactive oxygen species (ROS). Anoikis resistance is vital during cancer progression and metastasis. Furthermore, we show that overexpression of $RHAMM^B$ in human panNET cell lines increases their metastatic ability in xenograft tumor models.

Conclusion: Hence, our results suggest that overexpression of $RHAMM^B$ confers survival advantage after cell detachment to promote metastasis of panNET.