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Rab37 Mediates Osteopontin Secretion to Promote Pancreatic Cancer Metastasis and Stemness

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Background: Pancreatic cancer (PC) is one of the most formidable malignancies in the world. The poor prognosis has been attributed to the high incidence of local invasion, distant metastasis, and chemoresistance. The cancer secretome has been linked to the hallmarks of cancer and may be the key to find novel therapeutic targets for cancers. Rab small GTPases are master regulators of secretory pathways. However, the role of Rab-controlled trafficking pathways in PC is less explored.

Material and Methods: Rab37 expression was determined in the tissue microarrays of 89 pancreatic tumors by IF and IHC staining using different primary antibodies. The correlation of the Rab37 expression with disease progression was calculated. Using cell line, animal, and clinical analyses, we identified the role of Rab37 in pancreatic cancer.

Results: We found that Rab37 is oncogenic in PC. Rab37 function was involved in cancer cell migration, invasion, and stemness. Osteopontin (OPN) was a major cargo of Rab37-associated vesicles. Rab37 overexpression enhanced OPN release to activate ERK signaling and thus promoted pancreatic cancer metastasis and stemness.

Conclusion: Rab37 plays an oncogenic role in PC and it acts as a cancer metastasis and stemness promoter through regulating OPN secretion engaging ERK signaling. Targeting the transport of Rab37-mediated OPN is an alternative modality in the treatment of PC.