AB067. P039. Rab37 mediates exosomal osteopontin secretion to promote pancreatic cancer metastasis and stemness

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Abstract: Pancreatic cancer is one of the most formidable malignancies in the world. The poor prognosis associated with pancreatic cancer 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 identifying novel therapeutic targets for cancers. Rab small GTPases are master regulators of secretory pathways. However, the role of Rab-controlled trafficking pathways in pancreatic cancer remains poorly defined. Using cell lines, *in vivo* experiments, and clinical analyses, we identified an oncogenic role of Rab37 in pancreatic cancer. Osteopontin (OPN) was identified as a major cargo of Rab37-associated vesicles, and Rab37 overexpression enhanced OPN release, mainly through the exosome pathway, to activate extracellular signal-regulated kinase (ERK) signaling, thereby promoting pancreatic cancer metastasis and stemness. Dysregulation of Rab37-mediated OPN secretion may result from KRAS mutation. Our findings have possible implications for prognosis evaluation and therapeutic strategies for pancreatic cancer.

doi: 10.21037/apc.2018.AB067

Cite this abstract as: Shan YS. Rab37 mediates exosomal osteopontin secretion to promote pancreatic cancer metastasis and stemness. Ann Pancreat Cancer 2018;1:AB067. doi: 10.21037/apc.2018.AB067