βPix-Dynamin2 complex induced by Src kinase promotes colorectal cancer invasion by facilitating membrane dynamics

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Abstract

Dynamics of the plasma membrane involving cytoskeleton rearrangement is required for cancer cell migration and invasion. In this study, we demonstrated that upregulated βPix, a guanine nucleotide exchange factor of Rac1, promoted metastasis in colorectal cancer (CRC) cells. Pull-down assay with the Src homology 3 (SH3) domain of βPix revealed that Dyn2, a large GTPase, interacted with βPix via its proline-rich domain (PRD). The βPix-Dyn2 complex accumulated at the leading edge of the membrane, which induced Rac1 activation and membrane ruffling. We also found that the phosphorylation of tyrosine at the 442 position of βPix by Src kinase was critical for βPix-Dyn2 complex formation. Interestingly, application of SH3 antibodies targeting intracellular βPix with gold nanoparticles disrupted the βPix-Dyn2 complex, resulting in inhibited cell invasion. Taken together, the Src-βPix-Dyn2 axis may be essential for CRC cell invasion. The development of inhibitors disrupting the βPix-Dyn2 complex would be a useful therapeutic strategy for CRC treatment.