Roles of SRC family kinases in epithelial–mesenchymal transition

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Video Byte

Keywords: SRC family kinases, SFKs, epithelial-to-mesenchymal transition, epithelial-mesenchymal transition, EMT, treatment resistance, metastasis, invasion, unique domain, actin cytoskeleton, actin, cytoskeletal dynamics, tumor progression, cancer, cancer progression, aggressive cancer, tumorigenesis, adaptor protein, tumor microenvironment, immunomodulation, cell communication and signaling, SUNY Upstate

Posted Date: October 13th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-966203/v1>

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Abstract

Since the first SRC family kinase (SFK) was discovered in 1911, numerous SFKs have been identified in humans. SFKs are expressed in diverse tissues and cell types, where they regulate various biological processes. Posttranslational modification of these membrane-associated kinases can regulate their activity to affect cell signaling in different ways, but dysregulation of SFKs can promote cancer progression, invasion, and metastasis. In cancer cells, the kinases can promote epithelial-to-mesenchymal transition (EMT) to promote invasion. Specifically, they destabilize cell junctions, change cell polarity, and mediate invadopodia formation by influencing the actin cytoskeleton. SFKs also activate EMT-inducing molecules by influencing signaling pathways such as the TGF- β /SMAD, Wnt, NOTCH, and EGFR pathways. Given the roles of SFKs in cancer, SFK inhibitors have been developed as therapies for metastatic disease. However, the existing inhibitors lack specificity and can lead to activation of alternate oncogenic pathways and resistance. In addition, since SFKs also play important roles in normal cells, nonspecific inhibition can have unintended consequences. Development of treatment strategies that effectively target specific SFKs or even specific domains within SFKs could help pinpoint certain interactions to minimize off-target effects and reduce cancer spread related to these multifunctional proteins.