L-plastin phosphorylation is modulated by PI3K and promotes cancer cell invasiveness

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Video Byte

Keywords: L-plastin, Actin-bundling, PI3K, ERK/MAPK, SGK, RSK, Invasion, Invadopodia, Extracellular matrix degradation, Metastasis, cancer, Cell Communication and Signaling

Posted Date: February 26th, 2021

DOI: <https://doi.org/10.21203/rs.3.rs-276404/v1>

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Abstract

When intra- or extracellular changes occur, cells respond by triggering intracellular signaling pathways. Aberrant signaling can lead to a variety of diseases, including cancer. A recent study further investigated the link between aberrant signaling pathways and cancer metastasis. The actin-bundling protein L-plastin has been proposed as a marker of metastasis, and phosphorylation on Ser5 of the protein is known to increase its actin-bundling activity. To unravel the signaling network upstream of this phosphorylation event, researchers performed computational modeling based on immunoblot data. They found that in addition to ERK/MAPK, the PI3K pathway contributes to L-plastin phosphorylation at Ser5 through its downstream kinase SGK3. In addition, knocking down L-plastin significantly reduced cell invasion, while stably expressing a phosphomimetic L-plastin variant led to increased migration and invasion. Confocal imaging demonstrated that phosphorylation at Ser5 promotes L-plastin recruitment to invadopodia, as well as MMP-9 activity and extracellular matrix degradation. Although these results remain to be confirmed in vivo, they suggest that L-plastin phosphorylation at Ser5 increases breast cancer cell invasiveness, making L-plastin a potential target for therapeutic approaches aimed at blocking dysregulated signaling in both the ERK/MAPK and PI3K pathways to inhibit cancer cell metastasis.