Maspin subcellular localization control via the PI3K-AKT, JAK2-STAT3 pathways and cell-cell contact

Mariana Tamazato Longhi
Luiz Eduardo Silva
Mariane Pereira
Magna Magalhães
Jeffrey Reina
Francisca NL Vitorino
Barry M Gumbiner
JPC da Cunha
Nathalie Cella

Video Byte

Keywords: Cell Communication and Signaling, maspin, SERPINB5, EGFR, epidermal growth factor receptor, EGF, PI3K-AKT, JAK2-STAT3, cell-to-cell contact, interactome, Proteome, MCF-10A cells, immunofluorescence

Posted Date: October 14th, 2021

DOI: https://doi.org/10.21203/rs.3.rs-969325/v1

Abstract

Maspin is a protein with many diverse functions, found in many different cellular compartments. In breast cancer cells, maspin in the nucleus is correlated with a favorable prognosis, but if it is located in the cytoplasm, alone or in addition to the nucleus, it is associated with aggressive tumors. However, the mechanisms controlling maspin localization are not well understood. Previously, a research team found that EGFR (epidermal growth factor receptor) activation in a mammary cell line led to maspin nuclear localization and now they examined the pathways downstream from EGFR. They found that PI3K-Akt and JAK2-STAT3 pathways regulate the effects of activated EGFR on maspin localization. The researchers observed that cell density also affects maspin localization. In sparsely cultured cells, maspin is predominantly in the nucleus, but in densely cultured cells, it is in the cytoplasm and is resistant to EGFR activation. Proteomic and interactome analysis suggested that maspin plays a role in post-transcriptional and translational regulation, protein folding and cell-cell adhesion. These results suggest that nuclear accumulation of maspin is determined by an interplay between cell-cell communication and EGFR activation via PI3K-Akt and JAK2-STAT3. This study also identified potential maspin ligands, which could lead to new therapeutics or prognostic tools.