

ERK dimerization promotes migration in breast cancer

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Introduction

Activation of the Ras-ERK signaling cascade is associated with increased metastasis risk in breast cancer. However, the mechanisms of ERK promoting tumorigenesis in breast cancer remain unclear. In the present study, we demonstrated that ERK dimers enhanced the invasion and migration of breast tumors cells.

Material and method

ERK dimers were detected by western blot in native-PAGE after using ERK dimer inhibitor and MEK inhibitor in breast cell lines, MCF-7 and MDA-231-MB. ERK dimers downstream targets were determined by mass spectrometry and confirmed by co-immunoprecipitation assays. The role of ERK dimers, KSR1, and actin filaments cytoskeleton in migration and invasion of breast cancer cells were analyzed by transwell and 3D-spheroid assay. KSR1-ERK dimers and actin colocalization were measured by immunofluorescence.

Results and discussion

ERK regulation is dependent on its dimerization in response to stimulation. The worst prognosis is associated with ERK dimerization upon EGF in comparison with ERK monomers upon IGF-1 stimulation in the MCF-7 cell line. We found that ERK dimerization upon EGF stimulation increased migration and invasion of breast tumor cells. Moreover, KSR1 overexpression induced ERK dimerization in the cytoplasm enhancing migration and invasion. In contrast, ERK dimers inhibition blocked invasion of MDA-231-MB cells.

Conclusion

ERK dimerization plays a crucial role in the migration and invasion of breast tumor cells. ERK dimers bind to the scaffold protein KSR1 to enhance migration. Blocking ERK dimers formation reduced invasion capacity of MCF-7 and MDA-231-MB tumors cells. Thus, targeting ERK dimerization could emerge as a valid therapeutic strategy for the treatment of breast cancer.