

Activation of the Ras-ERK signaling cascade is associated with increased metastasis risk in breast cancer. In the present study, 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.

Stimulus dependent ERK dimerization

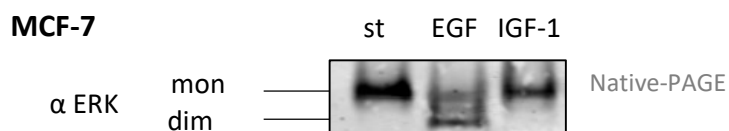


Figure 1.-Identification of ERK dimerization upon different stimulation in MCF-7 cell line.

ERK dimers promote migration upon EGF stimulation

MCF-7 migration ability

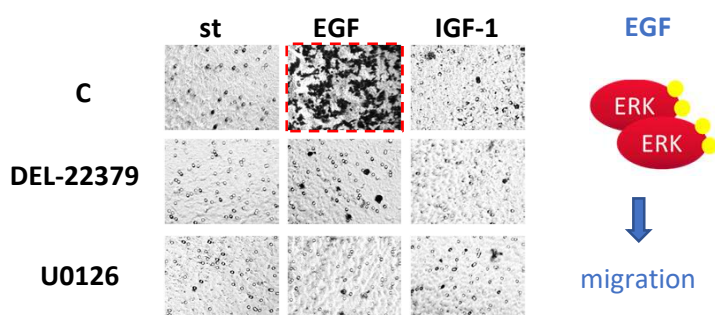


Figure 2.- ERK dimers might be responsible for transmigration ability. $p=0.009$

Overexpressed KSR1 promotes migration upon agonist stimulation

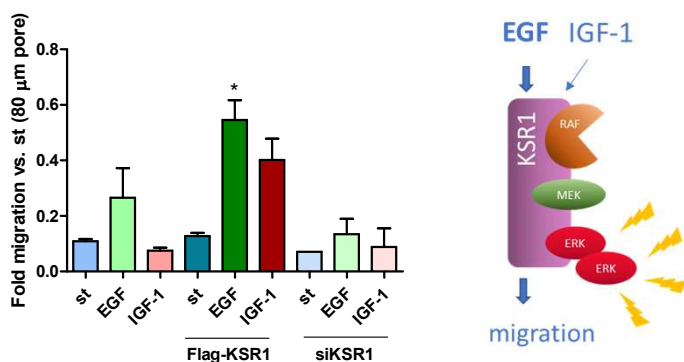


Figure. Transmigration of MCF-7-KSR1 cells into migration assay upon different stimulation (EGF and IGF-1; 50 ng/ml). *, $p < 0.05$.

ERK dimers are involved in metastasis

MDA-MB-231

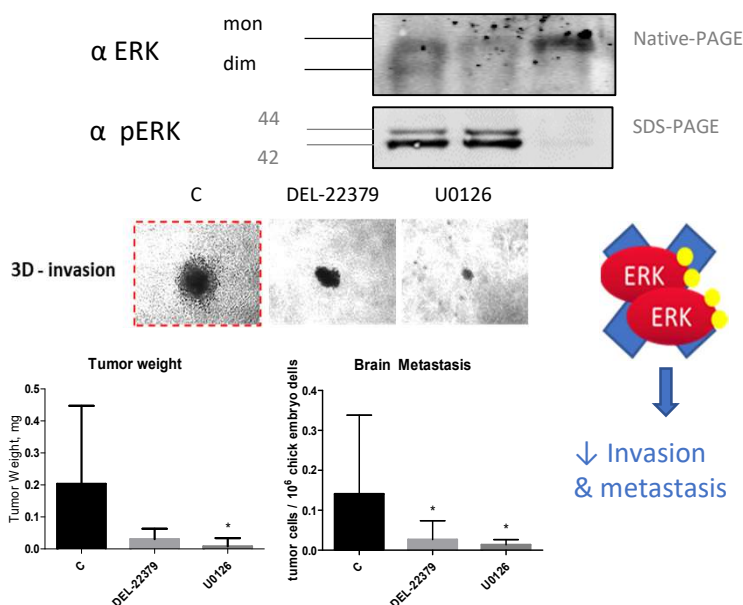


Figure 4. ERK dimers inhibition upon treatment, DEL-223879 and U0126, decrease invasion in 3D-spheroids, and tumour weight and organ metastasis in chicken embryo xenografts.

CONCLUSIONS

- 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.

→ Targeting ERK dimerization could emerge as a valid therapeutic strategy for the treatment of breast cancer.

REFERENCES

- Herrero, A. et al. Small Molecule Inhibition of ERK Dimerization Prevents Tumorigenesis by RAS-ERK Pathway Oncogenes. *Cancer Cell* (2015) doi:10.1016/j.ccell.2015.07.001.
- Casar, B., Pinto, A. & Crespo, P. Essential Role of ERK Dimers in the Activation of Cytoplasmic but Not Nuclear Substrates by ERK-Scaffold Complexes. *Mol. Cell* (2008) doi:10.1016/j.molcel.2008.07.024.