On Thursday the 21st of October 2021 at 11 am

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Canther
- Team ”Cell plasticity and Cancer” –

Therapeutic potential of targeting TrkA/CD44 interaction in triple negative breast cancer

Even though breast cancer therapies have been considerably improved thanks to target therapies, triple negative breast cancers is still a clinical challenge. In fact, standard of TNBC treatment remains surgery and chemotherapy and currently results in locoregional or distant relapses. Design of new specific therapy is still needed. Hence, Nerve growth factor (NGF) induces growth tumor and metastases in breast cancers. However, the NGF pro-tumoral effects results not only of the phosphorylation of TrkA but increases TrkA/CD44 [1]. To target TrkA/CD44 association, we have investigated the nature of this association. Using plasmids of expression of a mutated TrkA or deleted CD44, by Proximity Ligation Assay and by microscale thermophoresis we have validated TrkA/CD44 interaction and it molecular determinants. Then, using a mimetic petide of CD44 that impedes TrkA/CD44 we investigated the biological role of TrkA/CD44 in breast cancer cells in vitro and in vivo. In vitro, we shown that inhibition of TrkA/CD44 decreased survival and abolished NGF-induced migration/invasion. We also confirm by FRET the involvement of RhoA activation. At least, in vivo inhibition of TrkA/CD44 decreased tumor growth and metastasis of breast cancer cells xenografted in SCID mice. To conclude, our study demonstrates the potential of targeting direct interaction TrkA/CD44 in triple negative breast cancer.

See you all in zoom!
For the ONCOLille Animation Committee
Chann Lagadec

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