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"Investigating crosstalk between HER3 and EphA2 in triple negative breast cancer"

HER3 (Human Epidermal Growth Factor Receptor 3) is overexpressed in approximately 50-70% of breast cancers, significantly contributing to the second leading cause of cancer deaths among women. Despite lacking intrinsic kinase activity, HER3 forms heterodimers with other receptors, activating crucial signaling pathways implicated in tumor progression and resistance to therapies in triple negative breast cancer (TNBC). EphA2 (ephrin type-A receptor 2), another key player in cancer biology, functions as a transmembrane receptor involved in ligand binding and downstream signaling via its intrinsic kinase activity. EphA2 is often overexpressed in various cancer types, including TNBC correlating with aggressive tumor characteristics such as enhanced metastasis and therapy resistance.

In this study, we used the HCC1806 and MDA-MB-468 TNBC cell lines to investigate potential crosstalk between HER3 and EphA2, hypothesizing that increased phosphorylation of HER3 would correlate with increased phosphorylation of EphA2 upon HRG (heregulin) treatment. We employed a Receptor Tyrosine Kinase (RTK) array to analyze the phosphorylation status of EphA2 and HER3 and conducted immunofluorescence (IF) experiments to assess their co-localization.

Our results showed that HRG stimulation led to increased phosphorylation of both EphA2 and HER3 in the RTK array, and immunofluorescence demonstrated co-localization of the two receptors, suggesting functional interaction. However, co-immunoprecipitation (co-IP) failed to detect a direct physical interaction between EphA2 and HER3 under the conditions tested. This suggests that their interaction may be transient, indirect, or reliant on additional cofactors not present in our in vitro system.

This study suggests a cooperative interaction between HER3 and EphA2 based on their phosphorylation status, indicating potential crosstalk in their signaling pathways. Future studies will employ Proximity Ligation Assay (PLA) to determine whether HER3 and EphA2 are in close spatial proximity in situ, offering deeper insights into their functional interactions. Further research will focus on elucidating the underlying mechanisms of this interaction and exploring it's in vivo implications, with the aim of developing novel treatments for TNBC.