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# "**Basal Expression of ACK1 within Luminal Breast Cancer Subtypes compared to other Breast Cancer Subsets**"

**Background**: Breast cancer remains as one of the most common cancers in women globally, as well as one of the most significant contributors to total global cancer-related morbidity. Breast cancers present with a high rate of incidence of acquired resistance to first-line treatments such as CDK4/6 inhibitors and hormonal therapy, highlighting the need for novel therapeutic treatments and molecular targets. The non-receptor tyrosine kinase ACK1 has been found to be significantly overexpressed in both prostate and breast cancer, and has been significantly implicated in key molecular pathways present in breast cancer pathology. However, the relative expression levels in different subtypes of breast cancer is not well known or well-established.

**Objective:** We aimed to analyze basal ACK1 expression levels in various breast cancer cell lines and assess for variations by breast cancer subtype.

**Methods:** The METABRIC and TCGA breast cancer projects from the TCGA database were utilized for clinical data and for analysis of ACK1 expression in patient tumor samples. Quantitative reverse-transcriptase polymerase chain reaction (Q-RT-PCR) and western blot analysis were conducted to analyze ACK1 gene and protein expression in several breast cancer cell lines including MCF7, T47D, BT474, SKBR3, MDAMB231, and LM2-4175 cell lines. The software Graph Pad Prism was used for statistical analysis using a one-way ANOVA and unpaired two-tailed student's T-test.

**Results:** Clinical TCGA analysis of clinical patient breast tumor samples yielded significantly increased expression of ACK1 in luminal breast cancer subtypes ($p < 0.01$). Likewise, Q-RT-PCR analysis revealed increased expression of ACK1 in MCF7 (Luminal A), T47D (Luminal A), and BT474 (Luminal B) cell lines. We were also able to detect high levels of protein expression for TNBC subtypes.

**Conclusions:** The heterogeneous nature of the phenotypes of breast cancer have been shown to yield varied treatment outcomes and tumor responses to current therapies, posing a significant challenge for successful treatment. While further studies are needed to corroborate the increased expression of ACK1 across further breast cancer subtypes and in in-vivo models, understanding the variations in expression of ACK1 and subsequent changes in molecular activity within luminal breast cancer subtypes could potentially yield novel biochemical targets/pathways and more selective targeted therapies in the realm of breast cancer treatment.