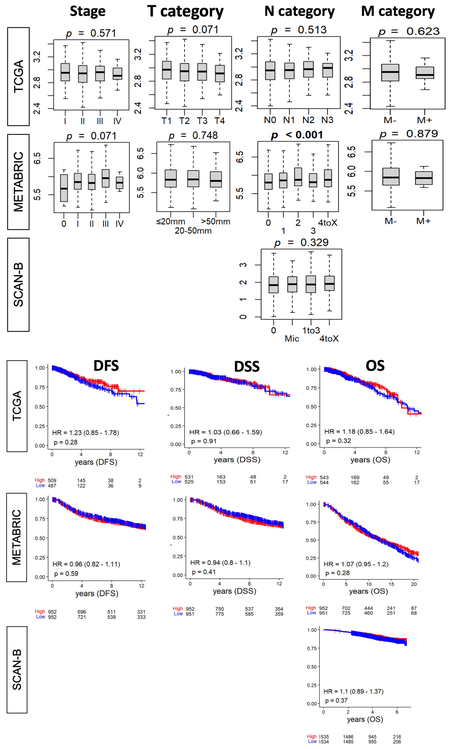
Expression of Burton's tyrosine kinase (BTK) in breast cancer associates with tumor immune microenviroment but lacks predictive value for clinical outcome

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Background & Methods

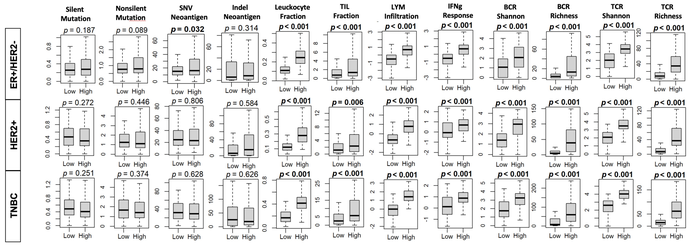
Background: Bruton's tyrosine kinase (BTK), a downstream mediator of the B-cell receptor (BCR) signaling pathway, is known to be essential in differentiation and proliferation of B-cell. Thus, BTK inhibitors are used to treat refractory mantle cell lymphoma and chronic lymphocytic leukemia. Recent discoveries have revealed the expression of BTK in myeloid-derived suppressor cells, known to worsen breast cancer (BC) outcomes. To this end, it was of interest to investigate the clinical relevance of BTK expression in BC. **Methods:** Total of 9297 BC patients from 23 independent cohorts with tumor transcriptome and clinical data were analyzed.

Tumor BTK expression is not associated with AJCC cancer staging or survival in BC

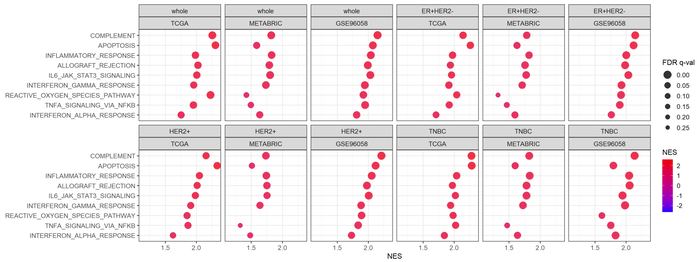


High tumor BTK expression is associated with activation of immune pathways but not with mutation or neoantigen burden

Molecular/immune features estimated from tumor DNA/RNA seq. data for TCGA cohort by Thorssen et al.

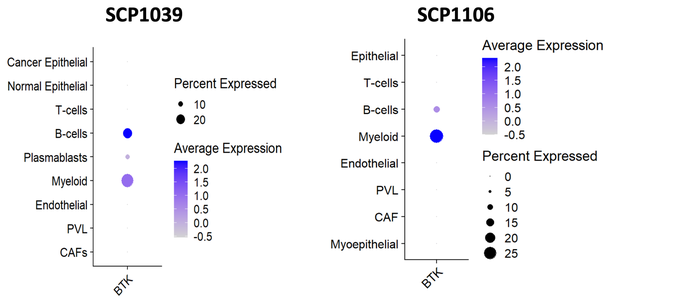


Gene set enrichment analyses – Hallmark gene set collection

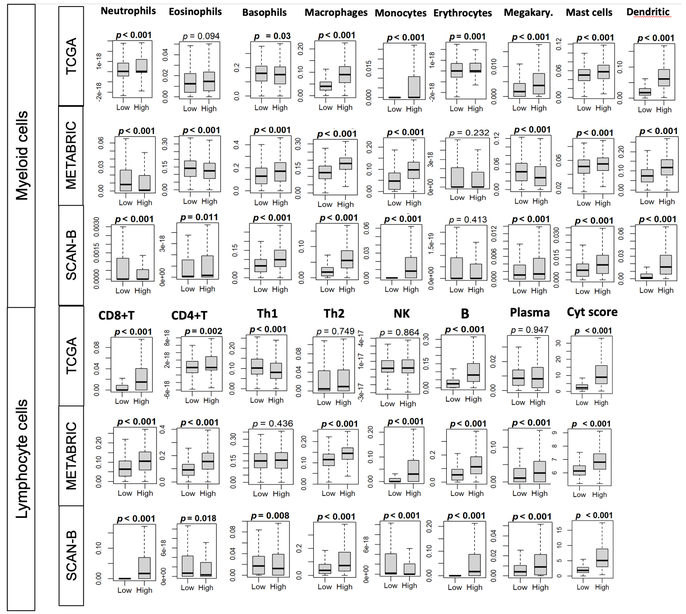


Single-cell RNA sequencing data shows BTK expression is mainly in tumor myeloid & B cells

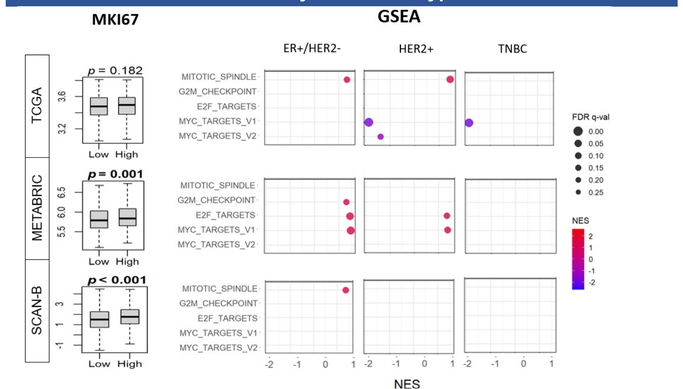
Two breast cancer tumor single-sequencing datasets



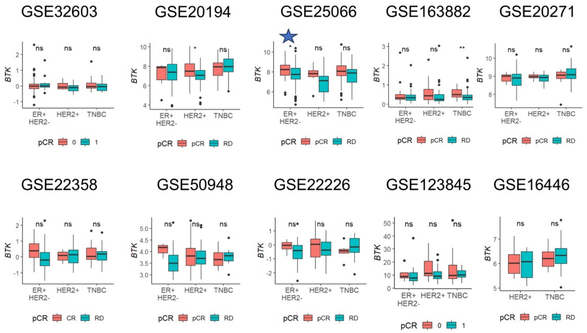
High BTK expression is associated with myeloid & lymphocyte enriched immune microenvironment & elevated cytolytic activity



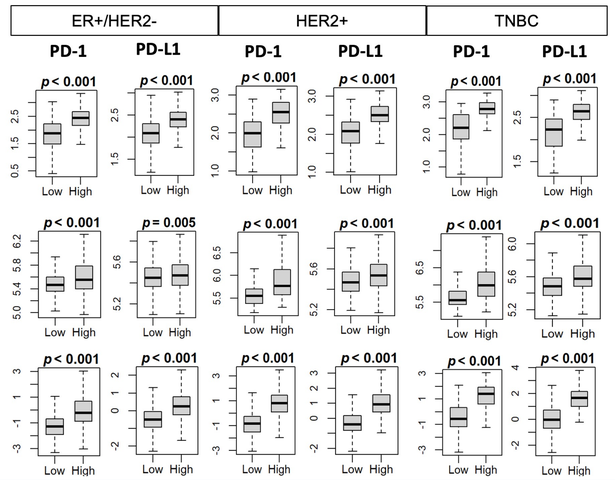
BTK level is correlated with cell proliferation in breast cancer, which differs by cancer subtype



Tumor BTK expression is not associated with response to neoadjuvant chemotherapy



Tumor BTK expression is associated with tumor immune checkpoint molecule expression



Conclusion

Myeloid cells and B-cells were the source of BTK expression, and it was associated with macrophage regulation and infiltration of various types of immune cells and proteins including PD1 & PD-L1 and enriched immune related gene sets. However, BTK expression was not associated with response to neoadjuvant chemotherapy or Impact on survival, regardless of BC subtypes.

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