



High KRAS signaling is associated with favorable tumor immune microenvironment and better survival in triple negative (TN) breast cancer patients

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Background

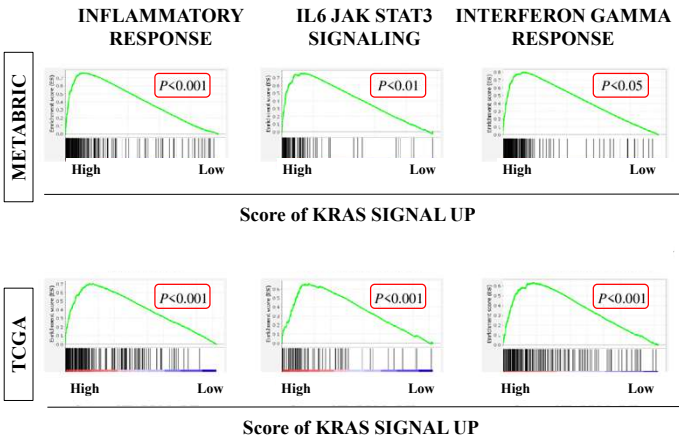
KRAS is one of the best known oncogenes and frequently altered in various cancers. Mutation of KRAS is frequently observed with pancreatic cancer, colorectal cancer, and non-small cell lung cancer. Within those cancers, mutated KRAS functions as immune suppressor. In the current study, we try to elucidate the role of KRAS signaling and tumor immune microenvironment (TIME) in breast cancer. We hypothesized that the upregulation of KRAS signaling associate with better tumor immune microenvironment in triple negative (TN) breast cancer patients.

Material & Methods

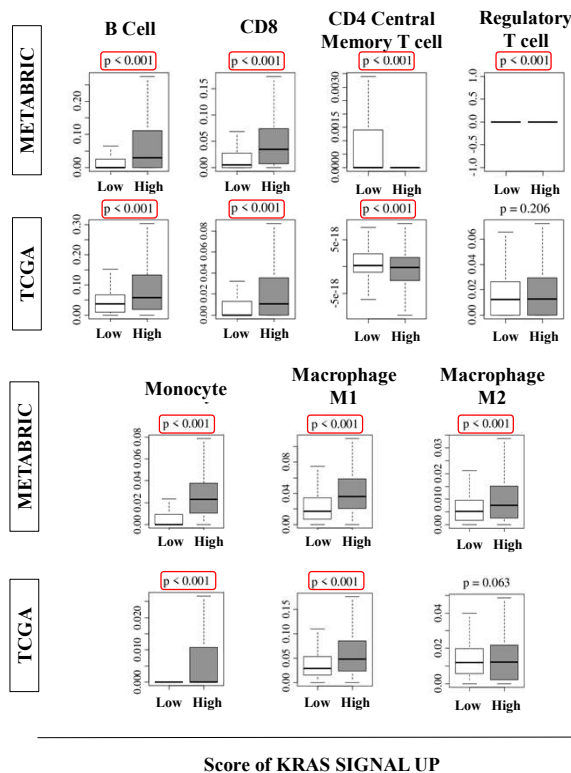
The clinicopathological and survival information of 755 breast cancer patients from The Cancer Genome Atlas (TCGA) database and 1904 breast cancer patients with METABRIC (Molecular Taxonomy of Breast Cancer International Consortium) database. To investigate the association of KRAS signaling and the tumor immune microenvironment, the intratumoral immune cell compositions were calculated by performing xCell and other immunological scoring. Also, gene set enrichment analysis (GSEA) was performed between high and low groups. Survival analysis of Overall Survival (OS) and Disease Free Survival (DFS) were conducted comparing high and low groups.

Results

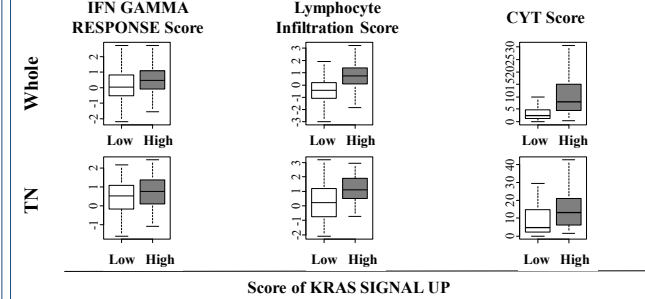
The tumors with KRAS-high scores enriched immune related gene sets in TNBC



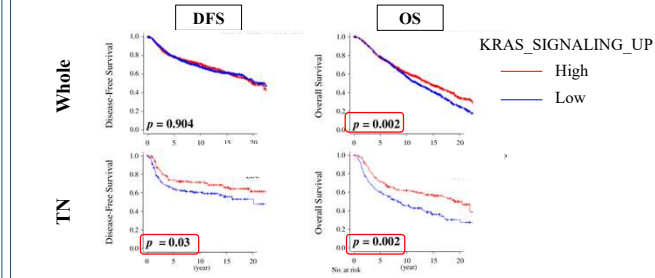
The tumors with KRAS-high scores were associated with anti-tumor immune microenvironment in TNBC



The tumors with KRAS-high scores were associated with anti-immune scoring



KRAS-high score was associated with improved disease-free survival (DFS) and overall survival (OS) in TNBC



Conclusion

Enrichment of genes related with KRAS signaling is associated with improved DFS and OS in TNBC patients. KRAS_SIGNALING_UP high TNBC was found to be associated with anti-tumor immune microenvironment, which was demonstrated by immune cell composition analysis, GSEA, CYT, interferon gamma response score as well as lymphocyte infiltration signature score.

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