

KRAS activity improves overall survival and fosters an anti-tumor microenvironment in colorectal cancer

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INTRODUCTION & AIM

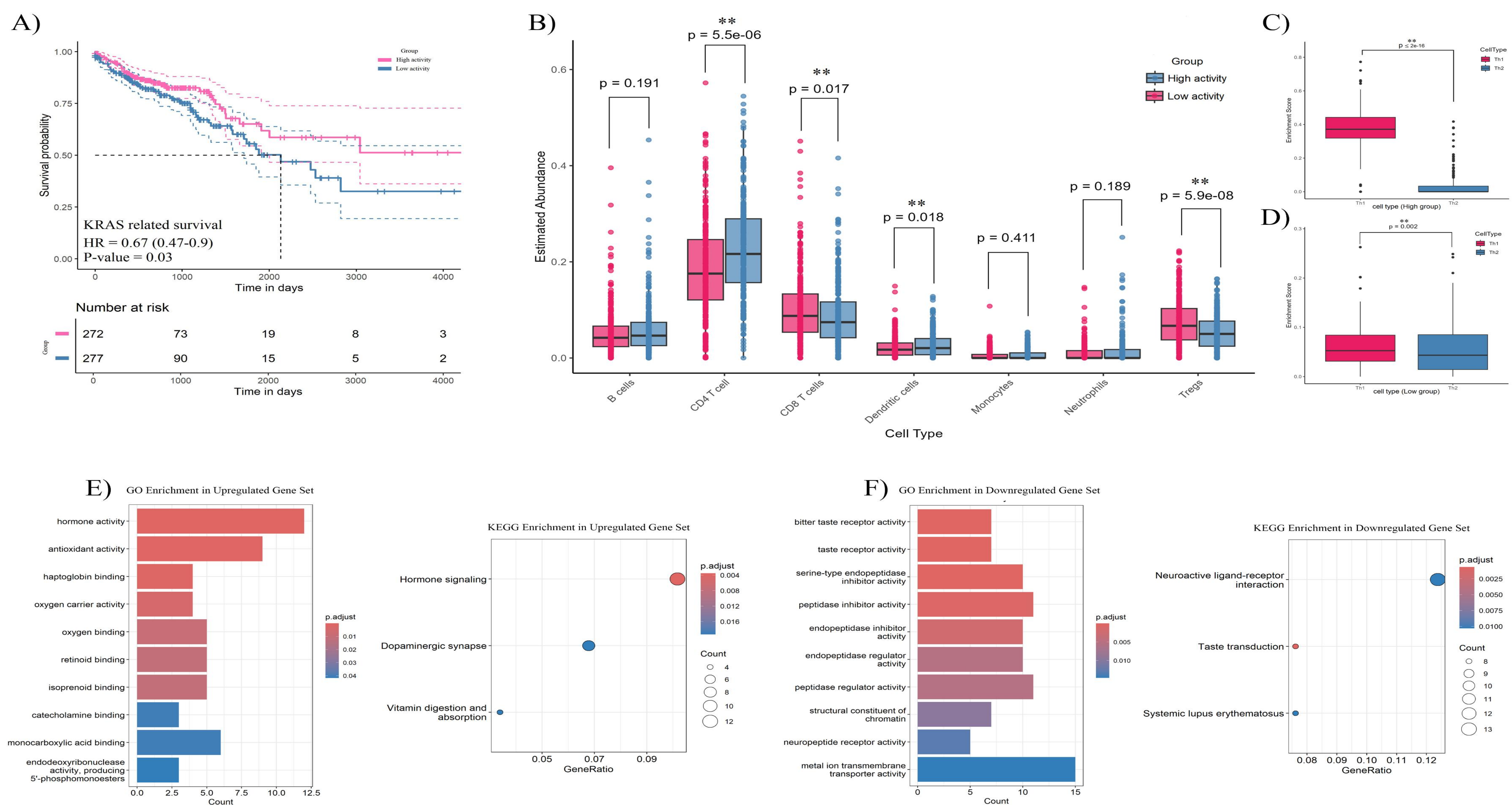
Although KRAS mutations are key drivers of colorectal cancer (CRC) progression and resistance to treatment, the prognostic and immunomodulatory impact of KRAS gene expression remains unclear. This study investigated KRAS activity to reveal links with tumor stage, survival, immune landscape and pathways in CRC.

METHOD

RNA-seq and clinical data from 549 TCGA-COAD/READ patients were downloaded via TCGAbiolinks. Samples were stratified by median KRAS TPM into high- and low-activity groups. Immune infiltration was estimated using CIBERSORTx and xCell, compared with Wilcoxon tests and Spearman correlations. Differentially expressed genes were identified using DESeq2 (FDR < 0.05, $|\log_2FC| > 1$), with GO/KEGG enrichment analysis via clusterProfiler. Overall survival was evaluated by Kaplan-Meier curves and log-rank tests.

RESULTS & DISCUSSION

High KRAS activity was significantly associated with earlier tumor stages (stage I-II: 53% vs. 46% in low KRAS activity; $P < 0.05$). Kaplan-Meier analysis demonstrated significantly improved overall survival in the high KRAS activity group ($P < 0.05$; HR < 1)(A). Immune profiling revealed elevated Th1 CD4+ T cells ($P = 2 \times 10^{-16}$) and dendritic cells ($P = 0.018$), but reduced Tregs ($P = 5.9 \times 10^{-8}$) and CD8+ T cells ($P = 0.017$) in high-KRAS-activity tumors. Correlations confirmed positive links with Th1 ($r = 0.6$) and DCs ($r = 0.08$), negative with Tregs ($r = -0.33$), CD8+ ($r = -0.15$) and Th2 ($r = -0.2$) cells ($P < 0.05$)(B-D). Enrichment analysis showed upregulated hormone/antioxidant functions ($P = 2.3 \times 10^{-7}$) and downregulated taste receptor pathways ($P = 4.2 \times 10^{-9}$) in the low-KRAS-activity group (E,F).



CONCLUSIONS

Elevated KRAS activity is associated with improved prognosis and Th1-skewed antitumor immunity in CRC, where Th1/DC surveillance compensates for reduced CD8+ T-cell infiltration. Thus, KRAS expression serves as a critical biomarker and immunotherapy target.

FUTURE WORK/ REFERENCES/ACKNOWLEDGMENT

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