Background Immune interactions in the tumor microenvironment (TME) are a major factor in deciding the fate of immunotherapy. Heterogeneity and molecular subtypes, especially in solid tumors like gastric cancer (GC), involve substantial modification in TME. Hence understanding the immune cell populations infiltrating the TME of different molecular subtypes will help to develop more effective and targeted therapies.

Methods CBioPortal\textsuperscript{1,2} was used to extract and analyze The Cancer Genome Atlas (TCGA) Stomach Adenocarcinoma Pan-Cancer Atlas Data (STAD). Immune Metagene signatures from previous publications\textsuperscript{3} were used to analyze the immune infiltration landscape in different GC molecular subtypes—chromosomal instability (CIN) (n=223), microsatellite instable (MSI) (n=73), genomically stable (GS) (n=50), Epstein–Barr virus (EBV) associated (n=30). GraphPad Prism\textsuperscript{9} and MS Excel were used to analyze the data and generate the figures.

Results We analyzed the infiltration landscape of Natural Killer (NK) cells, T cells (CD4+, CD8+, Th1, Th2, Th17), immune suppressive Myeloid-derived suppressor cells (MDSC), and Regulatory T cells (Tregs) in GC molecular subtypes. The results showed that CD8\textsuperscript{+} cytotoxic T cells and CD4\textsuperscript{+} helper T cells were highly downregulated in the GS subtype in comparison to other molecular subtypes (figure 1). Cytokine secreting T helper cell subsets, Th1, Th2, and Th17 demonstrate a dissimilar infiltration pattern among subtypes (figure 2). Th1 cells were highly expressed in the EBV subtype as compared to Th1 infiltration in the other subtypes (figure 3). GS and EBV both depict higher infiltration of Th2 cells and lower infiltration of Th17 cells in comparison to CIN and MSI subtypes (figure 2). GS subtype along with EBV has a superior infiltration of immune suppressive MDSC and Tregs (figure 3). Both cytotoxic NK\textsuperscript{6dim} and cytokine secreting immune modulating NK56\textsuperscript{bright} cells were the lowest infiltrating GS molecular subtype (figure 4). Intriguingly, NK56\textsuperscript{bright} infiltration markers don’t differ significantly between subtypes. It was worth observing that in general, there is more infiltration of NK56\textsuperscript{dim} over NK56\textsuperscript{bright} cells in GC patients (figure 4).

Conclusions TME of the GS molecular subtype of GC contains less cytotoxic cells (NK56\textsuperscript{dim} and CD8\textsuperscript{+} T) and higher infiltration of immune suppressive cells (Tregs and MDSCs).

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REFERENCES


Abstract 171 Figure 3  Immune cell infiltration landscape of MDSC and Tregs by GC molecular subtypes. Statistical significance was confirmed using one-way ANOVA, P-Value, **-0.0045, ***-0.0002, **** <0.0001

Abstract 171 Figure 4  Immune cell infiltration landscape of NK56bright and NK56dim cells by GC molecular subtypes. Statistical significance was confirmed using one-way ANOVA, P-Value, **** <0.0001