171 TUMOR MICROENVIRONMENT IMMUNE CELL LANDSCAPE VARIES AMONG MOLECULAR SUBTYPES IN GASTRIC CANCER

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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**[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[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 Prism9 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 $CD8^+$ cytotoxic T cells and $CD4^+$ 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^{56dim} and cytokine secreting immune modulating $NK^{56bright}$ cells were the lowest infiltrating the GS molecular subtype (figure 4). Intriguingly, $NK^{56bright}$ infiltration markers don't differ significantly between subtypes. It was worth observing that in general, there is more infiltration of NK^{56dim} over $NK^{56bright}$ cells in GC patients (figure 4).

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

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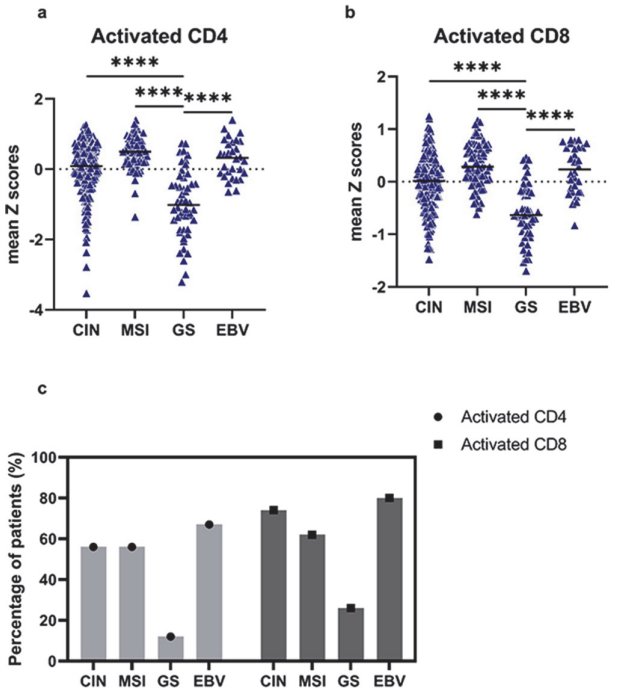
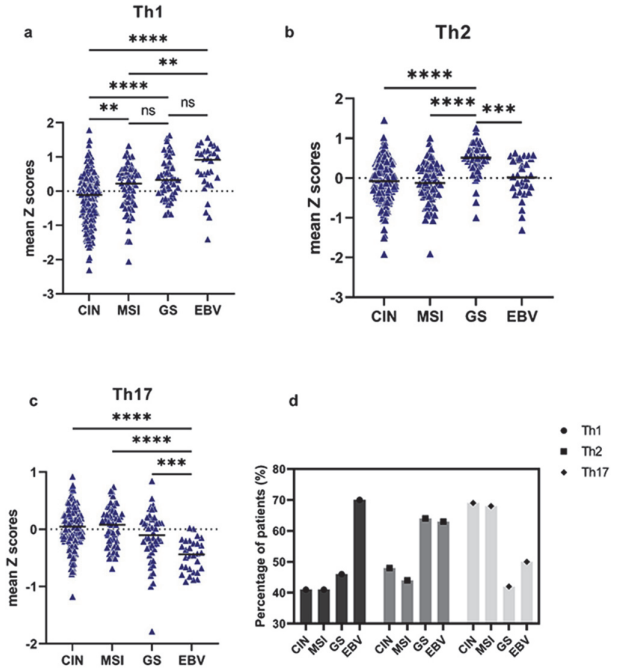


Abstract 171 Figure 1 Immune cell infiltration landscape of T cells (CD4+, CD8+) cells by GC molecular subtypes. Statistical significance was confirmed using one-way ANOVA, P-Value,**** <0.0001



Abstract 171 Figure 2 Immune cell infiltration landscape of Th1, Th2, and Th17 cells by GC molecular subtypes. Statistical significance was confirmed using one-way ANOVA, P-Value, **-0.0045, ***-0.0002, **** <0.0001

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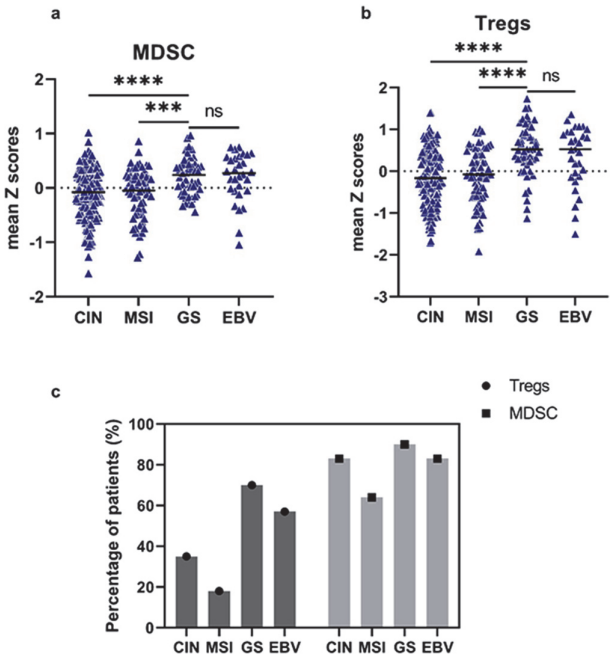
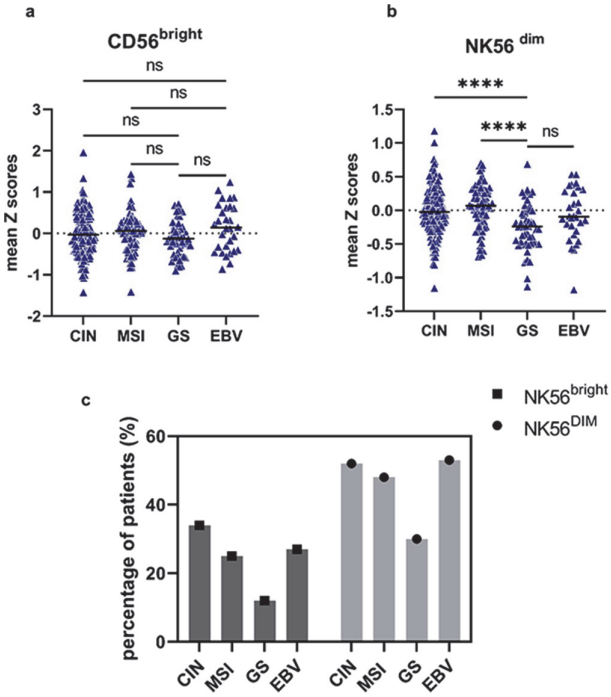


Abstract 171 Figure 3 Immune cell infiltration landscape of MDSC and Tregs by GC molecular subtypes. Statistical significance was confirmed using one-way ANOVA, P-Value, **-0.0045, ***-0.0002, **** <0.0001



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

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