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FOXP3 in di erent genders of certain tumors, including BLCA, KIRC, LUSC, and PAAD. In Figure 3, there is a signi cant positive correlation between the expression of *FOXP3* in CESC, HNSC, OV, SKCM, and UCEC and overall survival. ere is a negative correlation between the expression of *FOXP3* in ACC, GBM, KIRC, and THYM and overall survival. Figure 4 shows that in UCEC, the expression of *FOXP3* is positively correlated with disease-free survival, disease-speci c survival, and progression-free survival. e expression of *FOXP3* is positively correlated with disease-free survival in BLCA. In disease-speci c survival and progression-free survival, the expression of CESC, HNSC and *FOXP3* are positively correlated, and GBM and KIRC are negatively correlated.

a **b** ***FOXP3*** **a**

a **a**

Figure 5 shows the relationship between the expression level of *FOXP3* and the content of stromal cells and immune cells. ere is a positive correlation in BLCA, CESC, CHOL, COAD, ESCA, HNSC, KICH, LUAD, LUSC, PAAD, READ, SKCM, THCA and UVM (Figure 6). In terms of immune cell in ltration, *FOXP3* expression

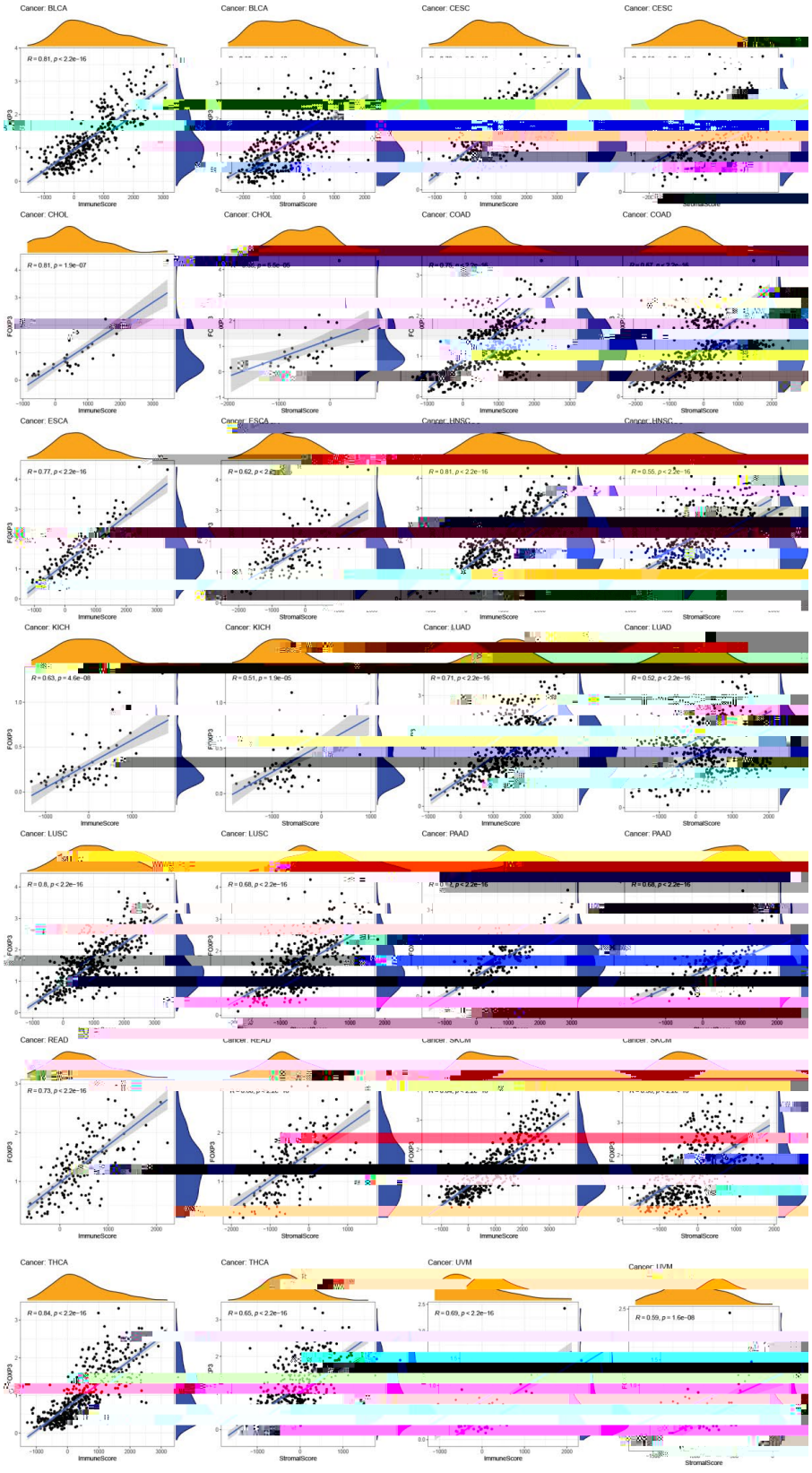

Figure 5: *FOXP3* expression and ESTIMATE score. ESTIMATE score includes matrix score (indicating whether there are stromal cells in tumor tissue) and immune score (indicating the inýltration of immune cells in tumor tissue).

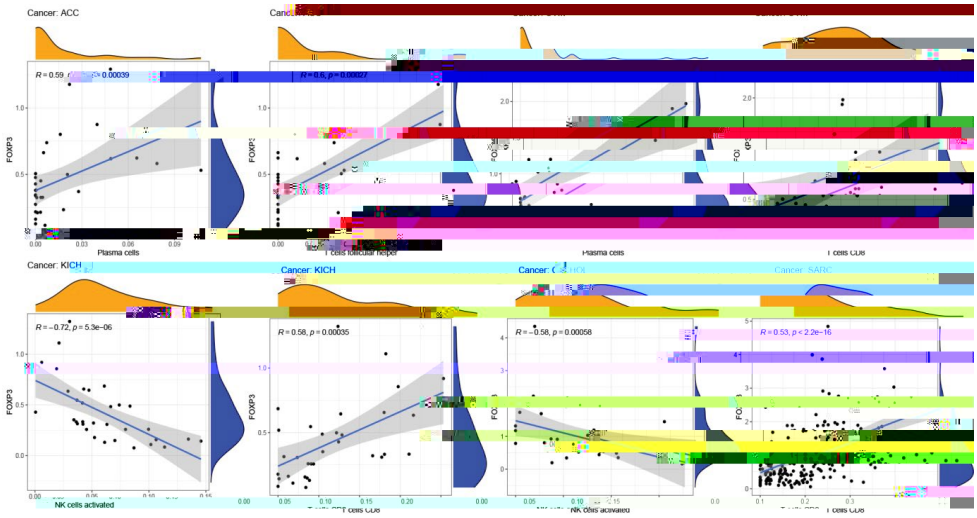

Figure 6: Correlation between *FOXP3* expression and immune cell inýltration. The CIBERSORT algorithm was used to calculate the immune cell inýltration, and the results of R>0.5 and p<0.05 were retained.

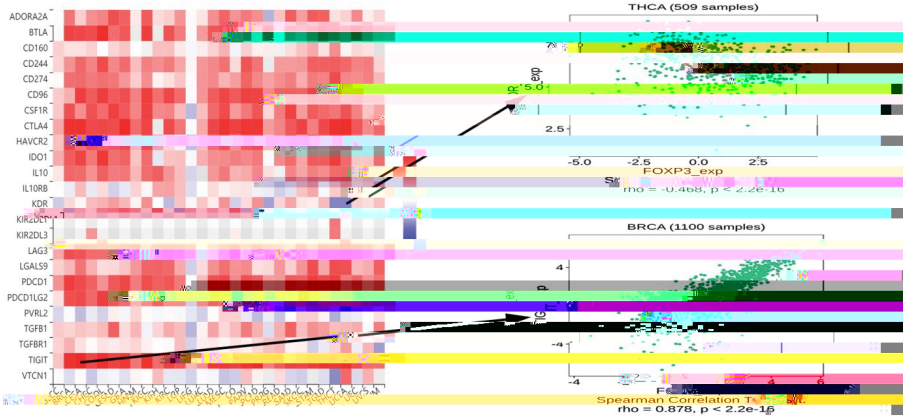

Figure 7: The correlation between *FOXP3* and the expression of immunosuppressive agents. Red indicates positive correlation, and blue indicates negative correlation. Take the top 2 strongest associations and display them through dot diagrams.

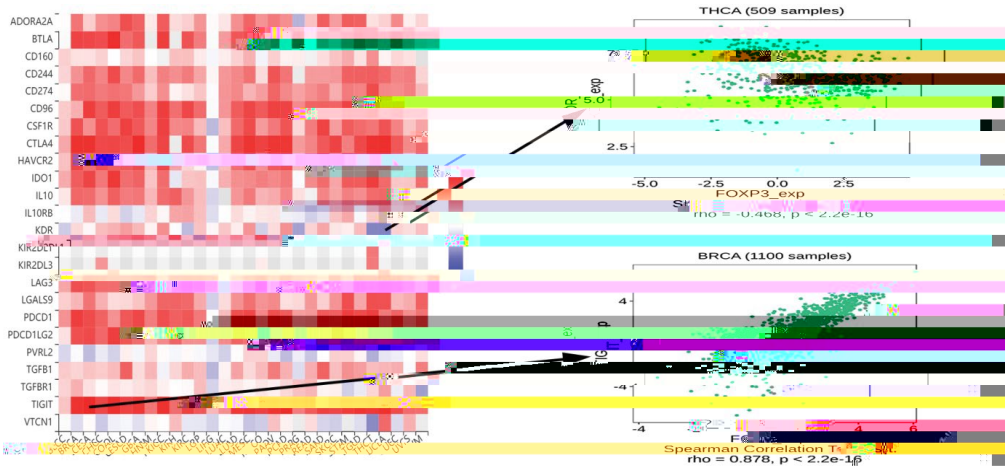

Figure 8: The correlation between *FOXP3* and the expression of immunostimulants. Red indicates positive correlation, and blue indicates negative correlation. Take the top 2 strongest associations and display them through dot diagrams

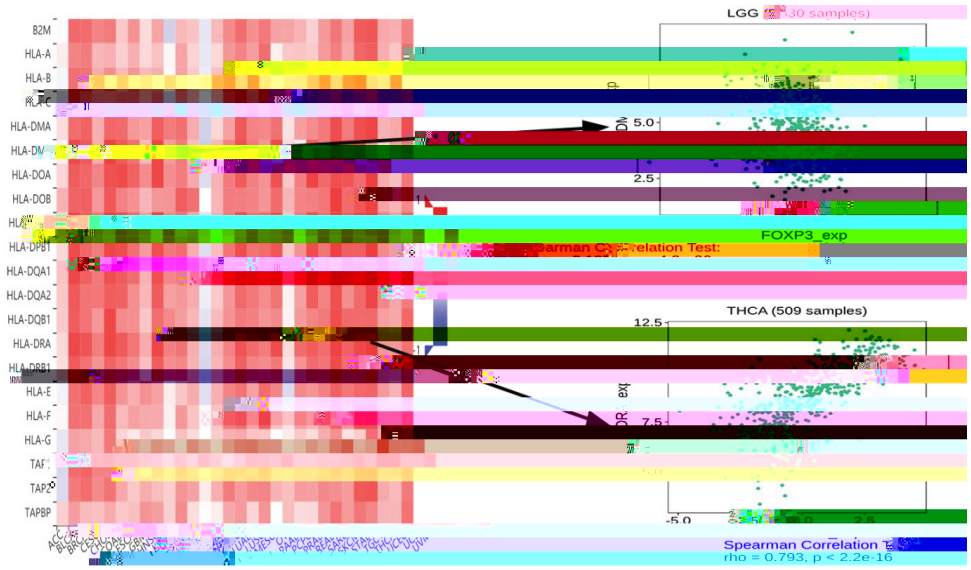

Figure 9: The correlation between *FOXP3* and MHC molecule expression. Red indicates positive correlation, and blue indicates negative correlation. Take the top 2 strongest associations and display them through dot diagrams.

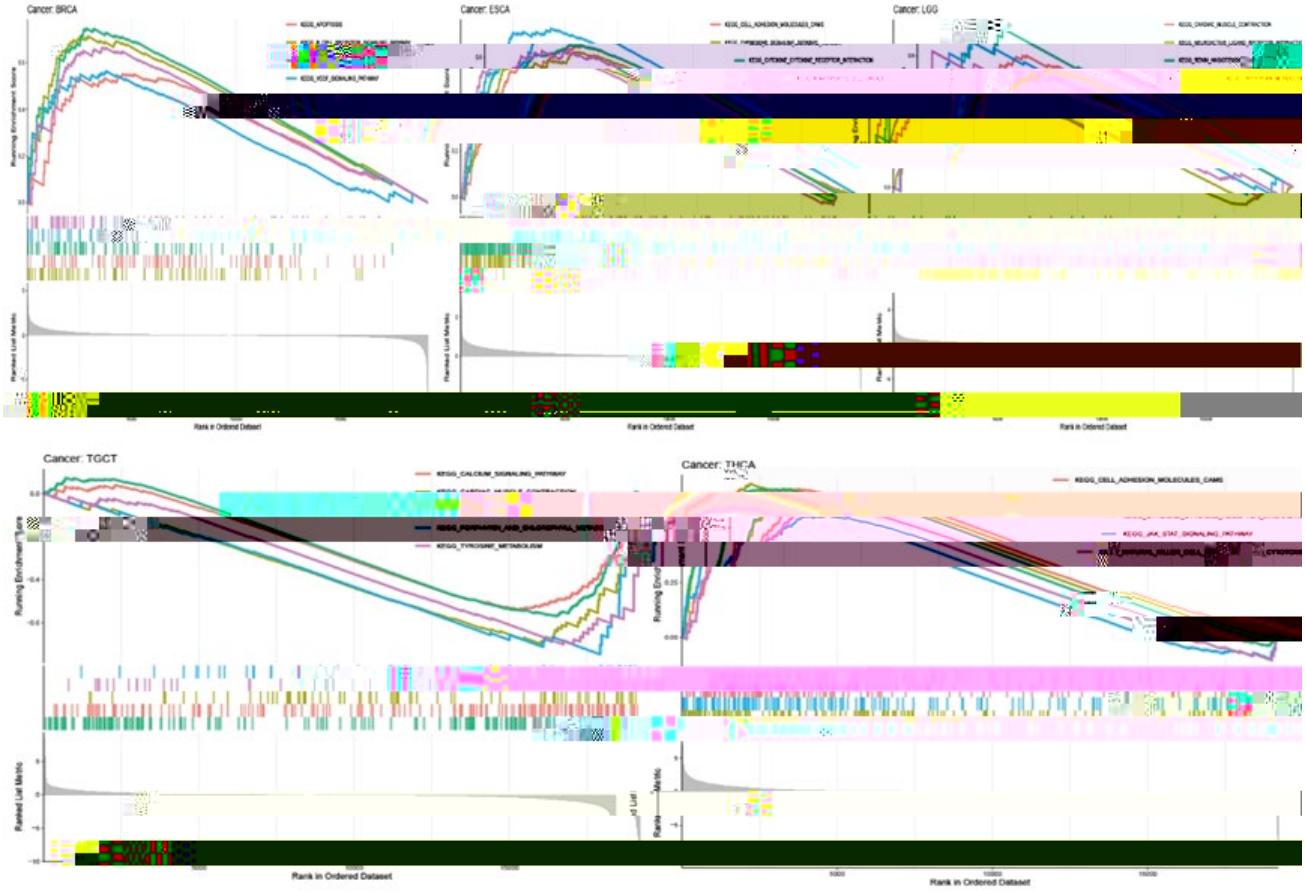

Figure 10:

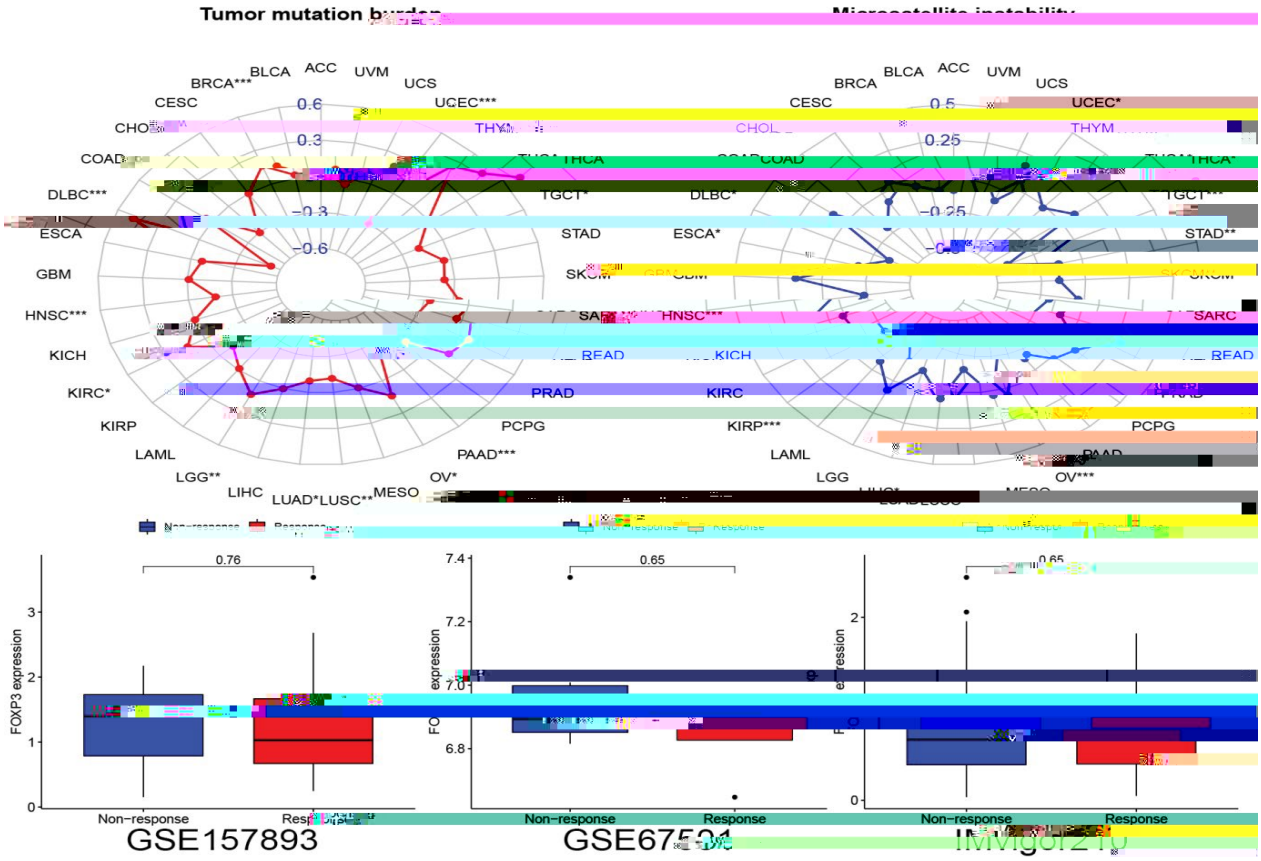

Figure 11: Correlation between *FOXP3* and immunotherapy markers and immunotherapy response.
Note: *means p<0.05, **means p<0.01, and ***means p<0.001.

Note: Non-response Response.

33 types of cancers, normal tissues and tumor tissues, has found the potential immunotherapy value of *FOXP3*. *FOXP3* not only participates in the regulation of tumor microenvironment, but also participates in the regulation of tumor local immunity. erefore, we have conducted related research including tumor microenvironment, immune cells, and immunomodulatory and immunotherapy response. In this study, our goal is to gain a deeper understanding of the potential immunological association between *FOXP3* and 33 human cancers. First, we studied the correlation between *FOXP3* and clinical parameters and found that only a small number of cancers have signi cant di erences in *FOXP3* expression with gender, age, and tumor stage, including CESC, CHOL, COAD, HNSC, KIRC, LUAD, PRAD, SKCM, UCEC. Amaral MGD found that the age di erence between *FOXP3* expression and oral tongue squamous cell carcinoma was not signi cant [15]. Another study showed that in colorectal cancer, the expression of *FOXP3* is related to gender and Dukes staging [16], which is consistent with the results of this study. *FOXP3* has a certain prognostic value in certain cancers, and related studies have also shown that the high density of *FOXP3* in tumor tissues is a powerful independent prognostic marker related to mortality [17]. Many previous studies have considered *FOXP3* as an independent factor a ecting the poor prognosis of various cancers. For example, in patients with tongue squamous cell carcinoma and Oropharyngeal squamous cell carcinoma, high expression of *FOXP3* is associated with low overall survival rate [18,19]. In breast cancer, the expression of *FOXP3* in breast cancer tissue is signi cantly higher than that in normal breast tissue, and the increase in *FOXP3* expression in tumor tissue is related to poor prognosis [20,21]. e above content illustrates the usefulness of *FOXP3* in the prognosis of cancer. erefore, we hypothesize that the regulation of *FOXP3* expression in various types of cancer may be clinically bene cial.

In order to further study the potential value of *FOXP3*, the correlation between *FOXP3* and immune cell in ltration was discussed. In terms of immune cell in ltration, *FOXP3* expression is positively correlated with plasma cell content in ACC and UVM. *FOXP3* expression is positively correlated with the content of T cells follicular helper in ACC; *FOXP3* expression is positively correlated with T cells CD8 in KICH, SARC and UVM. Previous studies have shown that CD8 and TGF-β1 are the two main factors in the tumor immune microenvironment. $CD8^+$ T cells are the most important e ector executive cells in the tumor immune microenvironment. Inhibiting their activity will a ect the body's immune defence function. *FOXP3* can help tumor cells escape by inhibiting or killing $CD8^+$ T cells [22]. In KICH and CHOL, we observed that *FOXP3* expression is negatively correlated with NK cells activated. In the analysis of various immunosuppressive agents, we found that the expression of *FOXP3* was correlated with the TIGIT of TGCT, and negatively correlated with the KDR of TGCT. TIGIT is

an immunosuppressive receptor of T cell immunoglobulin, which is mainly expressed in T cells and natural killer cells, and can inhibit the function of immune cells through a variety of mechanisms to a ect the prognosis of cancer patients [23,24]. Based on these data, we propose that there may be potential mechanisms for *FOXP3*, TIGIT and T cells,