FCGR1A Serves as a Novel Biomarker and Correlates With Immune Infiltration in Four Cancer Types

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Primary research

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Abstract

Background: FCGR1A encodes a protein that plays an important role in the immune response. The prognosis and tumor immune infiltration of FCGR1A in heterogeneous tumors remains unclear.

Methods: Differential expression analysis of FCGR1A between tumor and normal tissues and the difference in overall survival (OS) among different cancer types were performed by Gene Expression Profiling Interactive Analysis (GEPIA). The correlation between FCGR1A and cancer immune infiltration or immune gene markers was completed through Tumor Immune Estimation Resource (TIMER) site.

Results: FCGR1A exhibited high expression in various cancer types. FCGR1A was significantly correlated with the overall survival (OS) of cervical and endocervical cancer (CESC), cholangiocarcinoma (CHOL), kidney renal clear cell carcinoma (KIRC) and skin cutaneous melanoma (SKCM) ($P < .05$). High expression of FCGR1A meant a better prognosis except for KIRC. FCGR1A showed significant differences at different stages of KIRC and SKCM ($P < .05$). Furthermore, FCGR1A was notably associated with immune infiltrating levels of CD4+ T cell, CD8+ T cell, B cell, macrophage, neutrophil, and dendritic cell in the four cancers ($P < .05$). FCGR1A also showed close relevance with different immune gene markers. The copy number variation (CNV) of FCGR1A significantly influenced the abundance of immune infiltration in KIRC and SKCM.

Conclusion: FCGR1A may be a potential prognostic biomarker and related to immune infiltration levels in diverse cancers, especially in CESC, CHOL, KIRC, and SKCM. Besides, FCGR1A may be involved in the activation, regulation or induction of immune cells.

Background

FCGR1A (CD64) is a transmembrane glycoprotein (72-kDa) with the CD32 and CD16 receptors, comprises large immunoglobulin (Ig) superfamily[1-2]. It locates on chromosome 1 which is often expressed on the surface of monocytes, macrophages, dendritic cells, and regulated by cytokines[3]. It is also a gene that encodes a protein which is a high-affinity Fc-gamma receptor and plays an important role in the immune response. CD64 is rarely expressed on the surface of neutrophils (PMN) under normal conditions. When the body is infected, CD64 expression on the surface of neutrophils can be rapidly increased under the stimulation of bacterial cell wall lipopolysaccharide, interleukin-12, γ -interferon, and granulocyte colony-stimulating factor[4]. Neutrophils have the function of phagocytosis and killing microorganisms, and play a key role in the defense of the body against cell infection. Increased CD64 expression is one of the markers of PMN activation and can be used as a good diagnostic indicator of infectious diseases[5]. Some studies had reported that FCGR1A (CD64) was of great significance in the diagnosis of leukemia[6]. The AML of type M4 and M5 morphology significantly correlates with the expression of CD64 [7].

Cervical cancer is the fourth most common cancer among women worldwide and has a high mortality rate, especially in developing countries[8]. High-risk types of human papillomavirus (HPV) lead to the most occurrence of cervix cancers, thus HPV vaccination and screening are necessary[9]. Immunotherapy offers hope for women with recurrent and metastatic cervical cancer[10]. Cholangiocarcinoma (CHOL) is a malignant tumor of epithelial cells, which occurs in different parts of the biliary tree. The latest classification includes intrahepatic, periportal, and distal cholangiocarcinoma based on anatomical location[11]. CHOL accounts for approximately 3% of all gastrointestinal malignancies and has difficulty in diagnosing and treating[12]. Previous studies have pointed out that the polarization of macrophages to the pro-tumor M2 state in CCA is related to poor prognosis and metastasis[13-15]. And the significant correlation between TAM and TAN infiltration and adverse clinical outcomes has also been confirmed, but they have not been tried as a treatment target for CCA[16-18]. Kidney renal clear cell carcinoma (KIRC) is the most common subtype of renal cell carcinoma (80%) and nearly 25% of patients were diagnosed with regional advanced or distant metastasis[19-20]. Immunotherapy greatly improves the difficulty of RCC treatment. Studies have reported that tumor patients with high expression of CTLA4, LAG3, and TIGIT have worse OS, while high expression of TIM-3 was associated with better prognosis[21]. Up to now, PD-1 inhibitors (Nivolumab) have been approved by the FDA for the treatment of RCC. CTLA-4 (Ipilimumab) and PD-L1 inhibitors (Avelumab) are also being investigated [22]. Melanoma is one of the most aggressive cancers, accounting for 4 percent of all skin cancers, but 75 percent of deaths, and has an extremely high metastatic potential [23]. So far, nivolumab[24] and Pembrolizumab[25] have been approved by the FDA as the first choice for immunotherapy in advanced melanoma patients and have yielded superior overall response rate[26].

In this study, we comprehensively analyzed the relationship between the expression of FCGR1A and the prognosis of various cancers using the Gene Expression Profiling Interactive Analysis (GEPIA) database. Besides, tumor immune Estimation Resource (TIMER) was utilized to study the correlation between FCGR1A and tumor-infiltrating immune cells. We also elucidated the important role of FCGR1A in CESC, CHOL, KIRC, and SKCM, as well as providing a potential relationship between FCGR1A and tumor-immune interactions.

Methods

2.1 Gene Expression Profiling Interactive Analysis (GEPIA) analysis

The expression level of the FCGR1A gene in distinct cancer types was analyzed via the GEPIA (<http://gepia.cancer-pku.cn/index.html>). GEPIA is an open web that contains 9736 tumor and 8587 normal samples from TCGA and GTEx projects[27]. This web focused on the analysis of RNA sequence expression. We utilized GEPIA to plot survival curves with different FCGR1A gene expression in 33 cancer types including OS and disease-free survival (DFS) and compared their log-rank test. Boxplot and stage plot were also depicted by GEPIA.

2.2 TIMER Database Analysis

TIMER is a public resource dedicated to tumor immune infiltrates across 32 cancer types incorporating 10897 samples from The Cancer Genome Atlas (TCGA) (<https://cistrome.shinyapps.io/timer/>)[28]. This web server provides a variety of immune deconvolution methods to estimate the abundance of immune infiltration and explores tumor immunity or genomic characteristic comprehensively[29]. The differential expression levels of FCGR1A in different

cancer types were shown by the box plot via TIMER. Cancers with significant differences in FCGR1A expression would be selected for further analysis. The relevance of FCGR1A expression with the abundance of immune infiltrates, containing CD4+ T cell, CD8+ T cell, B cell, macrophages, neutrophils, and DCs. Tumor purity was used as a comparison at the left of each result. Furthermore, the association between FCGR1A and gene markers of tumor-infiltrating immune cells which was reported in the published researches was described by TIMER[30-31]. The gene markers mainly included T cells, CD8+ T cell, B cell, monocyte, tumor-associated macrophages (TAMs), neutrophils, natural killer (NK) cells, dendritic cells (DCs), T-helper 1 (Th1) cells, regulatory T lymphocytes (Treg), and exhausted T cell. Besides, the relationship between the copy number variation of FCGR1A and tumor immune infiltrating level can also be analyzed easily. We placed FCGR1A and relevant marker genes on x and y-axis respectively to depict scatter plots and obtain correlation coefficient as well as P-value. The expression level was exhibited with log2 TPM.

2.3 Statistical Analysis

The expression difference of FCGR1A in diverse tumor types and immune infiltrating levels among distinct immune cells, immune marker genes, and copy number variation were generated in the TIMER database. The web server drew the expression scatterplots together with the Spearman's rho value and estimated statistical significance based on tumor purity. The box plots based on FCGR1A expression tumor tissue and paired normal tissue were performed by GEPIA. Meanwhile, expression violin plots were generated according to the patient pathological stage. GEPIA performed overall OS and disease-free survival (DFS) analysis on the basis of FCGR1A expression and used the Log-rank test for hypothesis. In addition, the strength of the correlation should abide by the following criterion: 0.00-0.19 (very weak or none), 0.20-0.39 (weak), 0.4-0.59 (moderate), 0.6-0.79 (strong), 0.8-1.0 (very strong). P-value <0.05 was regarded as statistically significant.

Results

3.1 The FCGR1A expression levels in different cancer types

In order to determine FCGR1A expression in various tumor locations, we used RNA-seq data of multiple cancers from TCGA to explore FCGR1A expression via TIMER. The results of FCGR1A expression between tumor and normal tissue were shown in Figure 1A. To obtain more comprehensive and accurate conclusions, we also analyzed FCGR1A in the "general" module of GEPIA, and the results were exhibited in Figure1B. Combined with the above two results, FCGR1A was significantly higher in bladder urothelial carcinoma (BLCA), breast invasive carcinoma (BRCA), cervical and endocervical cancer (CESC), cholangiocarcinoma (CHOL), colon adenocarcinoma (COAD), esophageal carcinoma (ESCA), glioblastoma multiforme (GBM), head and neck cancer (HNSC), kidney renal clear cell carcinoma (KIRC), kidney renal papillary cell carcinoma (KIRP), acute myeloid leukemia(LAML), lower grade glioma (LGG), ovarian serous cystadenocarcinoma (OV), pancreatic adenocarcinoma (PAAD), prostate adenocarcinoma (PRAD), rectum adenocarcinoma (READ), skin cutaneous Melanoma (SKCM), stomach adenocarcinoma (STAD), testicular germ cell tumors (TGCT), thyroid carcinoma (THCA), Uterine Corpus Endometrial Carcinoma (UCEC) and Uterine Carcinosarcoma (UCS). Conversely, FCGR1A was markedly lower in Lung adenocarcinoma (LUAD), Lung squamous cell carcinoma (LUSC), and Thymoma (THYM).

3.2 A potential prognostic biomarker for CESC, CHOL, KIRC and SKCM: FCGR1A

We utilized GEPIA for survival analysis of all the cancers mentioned above with different FCGR1A expression. Finally, the results showed that FCGR1A was significantly associated with prognosis in 4 cancer types, which were CESC, CHOL, KIRC, and SKCM, respectively (Figure 2). Based on this result, we further developed box plots to more visually represent the difference in FCGR1A expression between the tumor tissue and the adjacent normal tissue (Figure 3). In addition, high FCGR1A expression exhibited a superior OS in CESC (HR: 0.55, $p=0.012$), CHOL (HR: 0.3, $p=0.016$) and SKCM (HR: 0.53, $p=3.2e-06$), and also showed better DFS of CHOL (HR: 0.29, $p=0.010$). The difference was that the low expression of FCGR1A in the KIRC was more conducive to survival (HR: 1.9, $p=5.3e-05$). We also analyzed whether there was a discrepancy in the expression of FCGR1A at different stages of the four cancers. Significant differences in FCGR1A expression at diverse stages were found in KIRC ($P=4.76e-10$) and SKCM ($P=0.00141$). However, no conspicuous distinction was observed in CESC and CHOL (Figure 4). Thus, although these results determined the prognostic ability of FCGR1A in CESC, CHOL, KIRC, and SKCM, the specific effect varied among 4 tumor sites.

3.3 FCGR1A expression and somatic copy number variation related with immune infiltration level in CESC, CHOL, KIRC and SKCM

To pinpoint the relation of FCGR1A with different immune infiltrated cells including CD4+ T cells, CD8+ T cells, B cells, macrophages, neutrophils, and DCs, we used TIMER to find out the correlation between FCGR1A and various immune cells of CESC, CHOL, KIRC, and SKCM (Figure 5A). All immune cells were significantly associated with FCGR1A expression levels in the four cancers ($P<0.05$). However, the correlation between FCGR1A and diverse immune cells varied greatly in different cancer types. FCGR1A had the highest correlation with dendritic cells among CESC, KIRC, and SKCM, which was 0.682, 0.704, and 0.754, respectively. In CHOL, FCGR1A was more closely related to neutrophils ($cor=0.778$). We also analyzed the correlation between FCGR1A and immune marker genes of various immune cells. After the correlation adjustment by purity, the results have shown that the FCGR1A was notably related to most immune marker genes in CESC, CHOL, KIRC, and SKCM (Table 1). It was not difficult to find that FCGR1A was strongly correlated with immune marker genes of some immune cells, mainly concentrated in T cells, monocytes, M2 macrophages, and dendritic cells. To be more specific, CD3E, CD2, CD86, CD115, CD163, VSIG4, MS4A4A, HLA-DPB1, HLA-DRA, HLA-DPA1, and ITGAX were all strongly associated with FCGR1A expression in four cancers ($Cor\geq 0.6$). We also validated the relationship between immune marker genes of these immune cells and FCGR1A expression in GEPIA and obtained similar results (Table 2). In addition, we also discovered that the strong correlation between FCGR1A and immune marker genes mainly focused on CESC, KIRC, and SKCM including T cell, CD8+ T cell, monocyte, tumor-associated macrophage (TAM), M2 macrophage, dendritic cell, T-helper 1 cell (Th1) and T cell exhaustion. Particularly, we found that TIM-3 of the T cell exhaustion was strongly correlated with CESC ($cor=0.887$) and SKCM ($corr=0.934$). Meanwhile, CD86 also showed an extremely close association with all four cancers, while B cells, M1 macrophages, and natural killer (NK) cells represented only weak or even no correlation in these four cancers. The study explored that exceeding strong relevance tended to occur in SKCM as well ($cor\geq 0.8$).

The analysis between somatic copy number variation and immune infiltration by the SNCA module in TIMER differed among four cancers. Studies showed that Arm-level deletion in KIRC was significantly associated with infiltration of B cell, CD8+ T cell, CD4+ T cell, macrophage, neutrophil, and dendritic cell ($P < .05$). Moreover, high amplification was related to the infiltration level of macrophage ($P < .05$). In SKCM, Arm-level Gain was prominently correlated with the infiltration level of the six immune cells, while Arm-level Deletion was only allied to B cell, CD4+ T cell, macrophage and dendritic cell ($P < .05$). No association was observed between copy number variation and immune cell infiltration in other two cancer types ($P > .05$) (Figure 5B).

Discussion

FCGR1A (CD64) is a transmembrane glycoprotein with a relative molecular weight of 72,000. It is encoded by A, B, and C3 genes on the long arm of chromosome 1 and belongs to the immunoglobulin superfamily. Although CD64 has not been studied extensively and systematically, it has high sensitivity and specificity for the diagnosis of sepsis and systemic infection, with a sensitivity of over 90% and specificity of 90%~100% in adults and children[32]. FCGR1A gene is the encoding gene of CD64, and the FCGR1A gene is up-regulated to make CD64 highly expressed. CD64 plays a role in the resistance to pathogen invasion through antibody-dependent cell-mediated cytotoxicity (ADCC), cell phagocytosis, and clearance of immune complexes. In the normal state, CD64 is mainly expressed in monocytes, macrophages, and dendritic cells, while the expression of neutrophils and lymphocytes is low. During bacterial infection, the body is stimulated by endotoxin or immune factors, the expression of neutrophil CD64 is increased, and the FCGR1A gene is up-regulated. Here, we studied that the expression of FCGR1A can affect the prognosis of different cancers. High expression of FCGR1A exhibited a superior survival in CESC, CHOL, and SKCM, while associated with a poorer prognosis in KIRC. Moreover, our research showed that tumor cell immune infiltration level and various immune marker genes were closely related to the FCGR1A expression. Thus, we can infer that FCGR1A can be regarded as a potential biomarker of cancers and play a role in tumor immunology.

We tested the expression levels of FCGR1A in 33 cancer types using TCGA data in GEPIA. The significant differential expression of FCGR1A was observed in many cancer categories. Compared to the normal tissue, FCGR1A expressed highly in BLCA, BRCA, CESC, CHOL, COAD, ESCA, GBM, HNSC, KIRC, KIRP, LAML, LGG, OV, PAAD, PRAD, READ, SKCM, STAD, TGCT, THCA, UCEC, and UCS, but lower in LUAD, LUSC, and THYM. By depicting box plots and survival curves of each tumor type, we found that the OS of CESC, CHOL, KIRC, and SKCM were significantly correlated with the expression level of FCGR1A. Meanwhile, box plots of these four cancers all showed that FCGR1A had notable differences between tumor and normal tissue. Besides, the expression of FCGR1A in KIRC and SKCM showed conspicuous differences at different stages. Combined with the above evidence, FCGR1A was strongly confirmed as a prognostic biomarker in CESC, CHOL, KIRC, and SKCM.

This study also indicated that FCGR1A was associated with multiple levels of immune infiltration in cancers. FCGR1A had the highest correlation with DCs among six primary tumor-infiltrating immune cells in CESC, KIRC, and SKCM, while had higher relevancy with neutrophils in CHOL. Moreover, significant positive relevance between FCGR1A expression and six immune cells was discovered in four cancers. We found that CD3E, CD2, CD86, CD163, VSIG4, MS4A4A, HLA-DPB1, HLA-DRA, HLA-DPA1, and TIM-3 which mainly gathering in T cell, monocyte, macrophage, and DCs were significantly correlated with FCGR1A through TIMER. We also obtained similar results via GEPIA. Therefore, the association of FCGR1A with diverse immune cell marker genes suggested its role in regulating tumor immunology of CESC, CHOL, KIRC and SKCM. M1 macrophage gene markers (such as NOS2 and IRF5) have weak or no correlation with FCGR1A expression, while M2 macrophage markers CD163, VSIG4, and MS4A4A have strong correlations. These consequences indicated that the potential regulatory role of FCGR1A in the polarization of tumor-associated macrophages (TAM). The increased expression of FCGR1A was positively correlated with the expression of Tregs and T cell exhaustion markers (FOXP3, CCR8, PD-1, Tim-3, and LAG3), suggesting that FCGR1A may play a role in the activation of Tregs and induction of T cell exhaustion. The FCGR1A was moderately or strongly associated with most immune marker genes in DCs and DCs can induce immune memory responses in cancer and promote antitumor immunity. Thus, the relationship if FCGR1A and the infiltration level of dendritic cells may imply the prognosis of the disease and the response to cancer treatment. TIM-3 is a vital surface protein on T cell exhaustion[33] and is highly correlated with LAYN expression in CESC and SKCM. Research had pointed out that patients with high expression of TIM-3 had significant metastatic potential, advanced cancer grades, and shorter overall survival than those with lower expression in cervical cancer[34]. And some literature had ever reported that TIM-3 is an immunomodulatory molecule in melanoma cells[35]. Besides, FCGR1A was positively correlated with T helper cells (such as Th1), indicating that FCGR1A may be involved in the regulatory role of T cells. Taken together, the evidence above suggests that FCGR1A plays a crucial role in the activation and regulation of immune cells in CESC, CHOL, KIRC, and SKCM.

There are few systematic studies on FCGR1A (CD64), mainly focusing on the diagnosis and distinction of infectious diseases, but rarely in cancer. However, an experimental study published in 2013 pointed out that hFcRI (CD64) could mediate the protective effect of anti-tumor antibodies on melanoma metastasis, and may also have a protective effect on solid tumors[36]. In addition, CD64 is often used in combination with C-reactive protein (CRP), procalcitonin (PCT), and other inflammatory markers for diagnosis[37]. The study showed that high CRP was 1.3 times higher than low CRP in all types of cancer, especially up to 2 times higher in lung cancer, and increased approximately 80 percent risk of early mortality[38]. Moreover, elevated CRP at diagnosis is associated with a poor prognosis in breast cancer[39]. A study proposed that procalcitonin was closely related to the diagnosis and outcome of lung cancer[40]. Therefore, infectious indicators are also of great value in cancer diagnosis and prognosis prediction and might be a promising new biomarker. However, the evidence of the FCGR1A gene at moment is insufficient, which still needs to be further verified in more clinical and basic experiments.

Conclusion

Generally speaking, high expression of FCGR1A results in different outcomes in diverse cancers. It is associated with better prognostic in CESC, CHOL, and SKCM except for CHOL. Meanwhile, FCGR1A is positively or even strongly correlated with immune cells in four cancer types and is also related to a variety of immune cell marker genes, such as CD2, CD3E, CD86, CD163, VSIG4, MS4A4A, HLA-DPB1, HLA-DRA, HLA-DPA1, ITGAX, TIM-3 in T cell, monocyte, M2 macrophage, DC, Th1 and T cell exhaustion. Thus, FCGR1A may contribute to the activation and regulation of the before-mentioned immune cells in varying degrees. LAYN may play an important role in immune cell infiltration and may serve as a prognostic biomarker for four cancers, especially SKCM.

Declarations

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable

Availability of data and materials

The dataset(s) supporting the conclusions of this article is(are) available in the TCGA repository

Competing interests

The authors declare that they have no competing interests

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Authors' contributions

Ji-Hi Xu: Conceptualization, Formal analysis and investigation, Writing-original draft preparation

Yong Guo: Conceptualization, Methodology, Writing-review and editing, Supervision

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Tables

Table 1
Correlation between FCGR1A and related gene markers of immune cells in TIMER

Description	Gene markers	CESC				CHOL				KIRP			
		None		Purity		None		Purity		None		Purity	
		Cor	P	Cor	P	Cor	P	Cor	P	Cor	P	Cor	P
T cell	CD3D	0.678	***	0.627	***	0.525	***	0.417	**	0.648	***	0.579	***
	CD3E	0.675	***	0.628	***	0.599	***	0.503	***	0.631	***	0.576	***
	CD2	0.710	***	0.666	***	0.596	***	0.501	***	0.668	***	0.623	***
CD8+ T cell	CD8A	0.672	***	0.623	***	0.542	***	0.45	***	0.613	***	0.561	***
	CD8B	0.408	***	0.348	***	0.380	***	0.287	0.094	0.596	***	0.549	***
B cell	CD19	0.408	***	0.285	***	0.391	**	0.250	0.147	0.413	***	0.364	***
	CD79A	0.436	***	0.311	***	0.374	**	0.238	0.169	0.463	***	0.412	***
Monocyte	CD86	0.813	***	0.777	***	0.772	***	0.729	***	0.847	***	0.831	***
	CD115 (CSF1R)	0.775	***	0.732	***	0.552	***	0.471	**	0.775	***	0.748	***
TAM	CCL2	0.392	***	0.302	***	0.497	***	0.454	***	0.078	0.073	0.030	0.5
	CD68	0.507	***	0.454	***	0.605	***	0.561	***	0.634	***	0.655	***
	IL10	0.525	***	0.445	***	0.411	**	0.230	0.184	0.646	***	0.596	***
M1 Macrophage	IRF5	0.199	***	0.193	***	0.291	0.086	0.291	0.200	0.385	***	0.385	***
	INOS (NOS2)	-0.127	**	-0.164	***	-0.228	0.180	-0.249	0.148	-0.037	0.400	-0.106	**
	COX2 (PTGS2)	-0.228	***	-0.342	***	0.387	**	0.287	0.095	0.131	***	0.089	0.0
M2 Macrophage	CD163	0.827	***	0.801	***	0.669	***	0.600	***	0.682	***	0.673	***
	VSIG4	0.794	***	0.772	***	0.783	***	0.742	***	0.782	***	0.772	***
	MS4A4A	0.858	***	0.836	***	0.733	***	0.686	***	0.738	***	0.714	***
Neutrophils	CD11b (ITGAM)	0.606	***	0.539	***	0.425	**	0.370	**	0.711	***	0.702	***
	CCR7	0.410	***	0.316	***	0.516	**	0.395	***	0.490	***	0.440	***
Natural killer	KIR2DL1	0.319	***	0.239	***	-0.043	0.802	-0.107	0.539	0.036	0.405	-0.006	0.9

cell	KIR2DL3	0.465	***	0.401	***	0.05	0.771	0.006	0.971	0.058	0.178	0.047	0.3
	KIR2DL4	0.390	***	0.340	***	0.236	0.165	0.168	0.334	0.279	***	0.247	***
	KIR3DL1	0.400	***	0.303	***	0.210	0.219	0.170	0.330	0.040	0.361	0.052	0.2
	KIR3DL2	0.497	***	0.435	***	0.331	**	0.346	**	0.108	**	0.088	0.0
	KIR3DL3	0.323	***	0.226	***	-0.189	0.270	-0.262	0.128	0.084	0.051	0.057	0.2
	KIR2DS4	0.371	***	0.318	***	0.116	0.499	0.066	0.708	0.041	0.341	0.018	0.6
Dendritic cell	HLA-DPB1	0.628	***	0.580	***	0.644	***	0.573	***	0.755	***	0.732	***
	HLA-DQB1	0.502	***	0.447	***	0.486	**	0.425	0.088	0.442	***	0.394	***
	HLA-DRA	0.570	***	0.524	***	0.654	***	0.581	***	0.775	***	0.764	***
	HLA-DPA1	0.597	***	0.549	***	0.696	***	0.634	***	0.736	***	0.710	***
	BDCA-1 (CD1C)	0.176	***	0.113	0.061	0.417	**	0.300	0.080	0.241	***	0.162	***
	BDCA-4 (NRP1)	0.229	***	0.176	***	0.587	***	0.529	**	0.059	0.173	0.003	0.9
	CD11c (ITGAX)	0.672	***	0.617	***	0.587	***	0.496	***	0.572	***	0.561	***
Helper T cell 1 (Th1)	T-bet (TBX21)	0.721	***	0.684	***	0.562	***	0.453	***	0.297	***	0.245	***
	STAT4	0.491	***	0.388	***	0.007	0.970	-0.123	0.482	0.410	***	0.348	***
	STAT1	0.562	***	0.512	***	0.245	0.149	0.198	0.253	0.614	***	0.579	***
	IFNG	0.699	***	0.644	***	0.440	***	0.322	0.059	0.587	***	0.545	***
	TNF	0.106	0.064	0.042	0.482	0.374	**	0.337	**	0.402	***	0.378	***
Regulatory cell (Treg)	FOXP3	0.583	***	0.517	***	0.543	***	0.437	***	0.577	***	0.532	***
	CCR8	0.494	***	0.434	***	0.505	**	0.416	**	0.564	***	0.525	***
	TGFB1 (TGFB β)	0.161	***	0.080	0.184	0.387	**	0.314	0.067	0.222	***	0.160	***
T cell exhaustion	PD-1 (PDCD1)	0.715	***	0.665	***	0.376	**	0.306	0.074	0.586	***	0.547	***

CTLA4	0.684	***	0.625	***	0.426	**	0.345	**	0.516	***	0.467	***
LAG3	0.734	***	0.689	***	0.364	**	0.26	0.131	0.614	***	0.573	***
TIM-3 (HAVCR2)	0.887	***	0.867	***	0.677	***	0.612	***	0.294	***	0.243	***
GZMB	0.607	***	0.537	***	0.484	**	0.382	***	0.291	***	0.214	***
***: P<.01 ***: P<.05												

Table 2
Correlation between FCGR1A and related gene markers of immune cells in GEPIA

Description	Gene markers	CESC		CHOL		KIRP		SKCM	
		Cor	P value	Cor	P value	Cor	P value	Cor	P value
T cell	CD3D	0.627	***	0.417	***	0.597	***	0.63	***
	CD3E	0.628	***	0.503	***	0.576	***	0.628	***
	CD2	0.666	***	0.501	***	0.623	***	0.697	***
CD8+ T cell	CD8A	0.623	***	0.45	***	0.561	***	0.718	***
	CD8B	0.348	***	0.287	***	0.549	***	0.649	***
Monocyte	CD86	0.770	***	0.750	***	0.760	***	0.860	***
	CD115 (CSF1R)	0.690	***	0.63	***	0.69	***	0.800	***
Macrophage	IRF5	0.12	0.039	0.58	***	0.27	***	0.62	***
	CD163	0.840	***	0.24	0.110	0.700	***	0.800	***
	VSIG4	0.740	***	0.742	***	0.700	***	0.830	***
	MS4A4A	0.810	***	0.570	***	0.660	***	0.780	***
Dendritic cell (DC)	HLA-DPB1	0.580	***	0.730	***	0.710	***	0.790	***
	HLA-DQB1	0.440	***	0.440	**	0.510	***	0.650	***
	HLA-DRA	0.530	***	0.700	***	0.700	***	0.820	***
	HLA-DPA1	0.540	***	0.700	***	0.670	***	0.770	***
	BDCA-1 (CD1C)	0.120	**	0.410	***	0.120	***	0.430	***
	BDCA-4 (NRP1)	0.140	**	0.660	***	0.130	***	0.340	***
	CD11c (ITGAX)	0.550	***	0.650	***	0.600	***	0.610	***
Helper T cell 1 (Th1)	T-bet (TBX21)	0.680	***	0.370	**	0.480	***	0.780	***
	STAT4	0.460	***	0.260	0.083	0.540	***	0.650	***
	STAT1	0.490	***	0.520	***	0.420	***	0.640	***
	IFNG	0.690	***	0.420	***	0.690	***	0.790	***
	TNF	0.098	0.084	0.530	**	0.290	***	0.610	***
T cell exhaustion	PD-1 (PDCD1)	0.700	***	0.490	***	0.680	***	0.770	***
	CTLA4	0.680	***	0.560	***	0.630	***	0.480	***
	LAG3	0.730	***	0.150	0.31	0.720	***	0.820	***
	TIM-3 (HAVCR2)	0.840	***	0.760	***	0.350	***	0.900	***
	GZMB	0.640	***	0.560	**	0.520	***	0.780	***
	CTLA4	0.680	***	0.560	***	0.630	***	0.480	***
***: P<.01 ** P<.05									

Figures

Figure 1

FCGR1A expression in different cancers types. (A) FCGR1A expression levels in different cancer types from TCGA database were performed by TIMER (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$). (B) Increased or decreased FCGR1A expression of different cancers compared with normal tissues in GEPIA

Figure 2

Kaplan-Meier survival curves comparing the high and low expression of FCGR1A in four cancer types in GEPIA A: CESC, B: CHOL, C: KIRC, D: SKCM

Figure 3

Box plots of FCGR1A expression between tumor and normal tissue in four cancer types

Figure 4

Violin plots pf FCGR1A expression in different stages of four cancers A: CESC, B:CHOL, C:KIRC, D: SKCM

Figure 5

Correlation of FCGR1A expression with immune infiltration level in CESC, CHOL, KIRC and SKCM A: CESC, B: CHOL, C: KIRC, D: SKCM

Figure 6

Correlation between somatic copy number variation and immune infiltration levels of 6 immune cells in four cancers. A: CESC, B:CHOL, C: KIRC, D:SKCM (*P <0.05, **P <0.01, ***P <0.001)