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Identification of *ST7* Alteration Profile, Frequency of Alteration and Correlation with *ST7*-Related Genes using TCGA Data[†]

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Abstract

ST7 (Suppression of Tumorigenicity 7) was reported as a protein playing a role in maintaining cellular structure. This study aims to investigate the *ST7* alteration profiles and frequency of alteration in different cancers using data from The Cancer Genome Atlas (TCGA). The correlation between alterations of *ST7* and angiogenesis-related genes, *SERPINE1*, *MMP13*, and *VEGFA,* was determined and the relation between *ST7* and genes involved in suppression of *ST7* transcription, *PRMT5* and *SMARCA4*, were also analyzed. Data of 6 cancer groups from The Cancer Genome Atlas (TCGA) including ovarian serous cystadenocarcinoma (OSC), liver hepatocellular carcinoma (LHC), bladder urothelial adenocarcinoma (BUA), stomach adenocarcinoma (SC), prostate adenocarcinoma (PRAD) and glioblastoma multiforme (GBM) were downloaded for this study. The results indicated that 3 alteration patterns including amplification, missense mutation, and deletion were observed in 6 cancer studies. Gene pair between *ST7* and *SERPINE1* indicated the co-occurrent alteration in BUC, OSC and SC ($p < 0.05$). However, no association between alterations of these 2 genes and survival events in our study was observed. Shorter overall survival rate and disease-free survival were found in BUC patients with *ST7*, *PRMT5*, and *SMARCA4* alterations. These findings suggest that using TCGA data can target the potential genes involved in carcinogenesis. Combining *ST7* with *PRMT5* and *SMARCA4* could be used as indicators for analyzing the patient survival in BUC patients and may serve as the potential therapeutic target for cancer in the future.

Keywords: Co-occurrence, Gene alteration, *ST7*, TCGA

Introduction

Suppression of Tumorigenicity 7 (*ST7*) was first identified as a tumor suppressor gene in 2001 [1,2]. Previous studies suggest that *ST7* mediates tumor suppression through the regulation of the genes involved in maintaining the structure of the cell and involved in oncogenic pathways [3]. *ST7* protein differential expression in either normal tissues throughout the body or in cancer cell lines was identified [1]. Mutations in this gene were rarely observed among series of cell lines and primary cancers studied, implying that direct mutation was not a target mechanism in affecting *ST7* expression and function in cancer cells [4-8]. Aberrant histone acetylation, epigenetic modulations, has been proposed as a possible mechanism for controlling *ST7* expression since significant hypermethylation of the *ST7* promoter has not

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been observed in primary breast cancer [3]. However, alteration patterns of this gene in primary cancers have remained unclear.

The Cancer Genome Atlas (TCGA) Project, launched by the National Institutes of Health in 2005, is the largest cancer genomics data collections by gathering research data from the multi-institutional innovative research program. The main objective of this database was to facilitate the comprehensive understanding of the cancer genetics using genomic technologies and analysis tools to catalogue all of the potential cancer genes, identify prognostic and predictive biomarkers as well as novel cancer drug targets [9,10]. TCGA datasets include more than 11,000 patients, representing 33 cancers, and over 500,000 files. This information is publicly available and has been used by many researchers. TCGA currently collects and contain many different genome-wide data including expression of coding and non-coding RNA, somatic mutations, copy-number alteration, and epigenomic data such as promoter methylation. In addition to genomic and epigenomic data, it collects proteomic data by using reverse phase protein arrays (RPPA) technology. There were new oncogenes and tumor suppressor genes identified through analysis of TCGA data. Using data from TCGA has gained obvious achievements in prediction of cancer prognosis and found cancer therapeutic biomarker since integrated gene expression data and clinical outcome data have provided the potential events to correlate the expression pattern with the survival.

In this study, we identified the alteration patterns of *ST7* gene by downloading mutation and CNA (DNA copy-number alterations) data type from 21 TCGA cancer groups and 5 TCGA cancer groups including ovarian serous cystadenocarcinoma, liver hepatocellular carcinoma, bladder urothelial adenocarcinoma, stomach adenocarcinoma, and glioblastoma multiforme, encountered high percentage of *ST7* alteration (data not shown), were selected for further analyzing. Moreover, prostate adenocarcinoma group was also included in this study due to PC-3 prostate cancer cell line expresses the lowest *ST7* mRNA level [3]. *ST7* alteration patterns were identified and alteration frequencies were then compared across 6 types of cancer. In addition, we used TCGA datasets on a web-based genomic analysis platform to investigate the correlation between *ST7* and other genes including *SERPINE 1*, *MMP13* and *VEGFA*, angiogenesis-related genes, in those selected cancer groups since *ST7* function has been reported playing some role in cellular matrix maintenance [3] and involving in angiogenesis regulation via suppressing *in vivo* tumor growth in nude mice [2]. *SERPINE1*, also known as *PAI-1*, is a gene that its-translated protein plays an important role in inhibiting extracellular matrix (ECM) degradation [11] while *MMP13*, a gene in a family of zinc-dependent proteinases, plays a role in promotion of tumor invasion and metastasis by degrading ECM components such as collagens and proteoglycans [12]. A previous study by Hooi *et al.* showed an increase in *SERPINE1* expression and decrease in *MMP-13* expression in *ST7*-transfected PC-3 cells when compared to empty vector-transfected cells [3]. *SERPINE1* was also found to be expressed in a similar level to *ST7* expression, while the opposite pattern was observed with *MMP-13* expressions [3,13]. We also investigated the correlation between *ST7* and *VEGFA*, a proangiogenic protein secreted by tumor [14], to determine the potential effect of *ST7* expression on a gene involved in promoting angiogenesis process. In addition, we also analyzed the relation between *ST7* and *ST7*-associated genes (*PRMT5* and *SMARCA4*) since the association of protein arginine methyltransferase 5 (*PRMT5*) with the *BRG1* (*SMARCA4*) chromatin remodeling protein has been reported to be directly involved in the repression of *ST7* transcription by regulating chromatin accessibility [15]. The results from integrated 6 gene expression were used to identify cancer survival and disease-free status compared with those which no alteration detected. These data suggest a role for *ST7* as a biomarker for cancer progression detection in some cancers.

Materials and methods

Genetic alterations and gene expression databases

Data regarding *ST7*, *SERPINE 1*, *MMP13*, *VEGFA*, *PRMT5,* and *SMARCA4* in 6 cancer types were obtained from The Cancer Genome Atlas (TCGA) database, a free-access databases publicly available at http://www.cbioportal.org [8,9]. The cancers analyzed were: ovarian serous cystadenocarcinoma (OSC; TCGA provision), liver hepatocellular carcinoma (LHC; TCGA provision), bladder urothelial adenocarcinoma (BUA; TCGA provision), stomach adenocarcinoma (SC; TCGA provision), prostate

adenocarcinoma (PRAD; TCGA provision) and glioblastoma multiforme (GBM; TCGA provision). Several options in the web interface of cBioPortal were selected for analyzing and visualizing alterations in *ST7* across all of the selected samples in the TCGA data. Briefly, as mentioned above, we selected 6 cancer studies and data types which were "Mutation and CNA (DNA copy-number alterations)". For the gene set of interest, a term of "*ST7*" was entered into the input box. In addition, for visualizing the relationship of *ST7* genetic alterations with *SERPINE 1*, *MMP13*, *VEGFA*, *PRMT5* and *SMARCA4* alteration events in 6 cancer studies, we selected cancer samples with sequencing, CNA and mRNA data (RNA Seq V2) and entered all 6 queried genes into the input box. Types of alterations and a comparison of the alteration frequencies in given genes across all 6 studies were illustrated in an OncoPrint tab. The statements of approval or informed consent were not required for our study as we obtained data from an open-access database [16].

Genomic alterations summary

An OncoPrint obtained from genomic alterations analysis step was used to summarize the genomic alterations of *ST7* and its-related genes through cancer samples. On the table, rows represented genes and columns represented samples. Genomic alterations including mutations, CNA (amplifications and homozygous deletions), and changes in gene expression were summarized by graphs and color coding. This was a preliminary way to know about the alteration patterns of *ST7* in different types of cancer. In this section, mutual exclusivity and co-occurrence between *ST7* and its-related genes were analyzed. Moreover, only one genetic event existed in each cancer sample were analyzed as mutually exclusive while co-occurrence was the situation that multiple genes are altered in the same cancer sample. This was a preliminary way to gather information about the different alterations and expressions of given genes in each 6 cancer studies.

Survival analysis

From survival analysis, overall survival and disease/progression free survival rate was compared between samples with alteration of *ST7* only as well as *ST7* with 5 given genes and samples without alteration. The results were shown if the survival data in each type of cancer were available.

Statistics

A scatter plot of mRNA expression in each sample was presented. Expression data were log2 transformed and median centered per sample. For correlation analysis, co-occurrence and mutual exclusivity analysis were performed. Odds Ratio and p-values for each pair of significant aberrations were reported. For survival analysis, Kaplan-Meier plots with a logrank test were performed to compare the overall survival and disease/progression free survival rate of each cancer type with at least one alteration or without alteration in query genes. All kind of analyses mentioned above were performed in cBioPortal (http://www.cbioportal.org).

Results and discussion

Genetic alterations of *ST7* in 6 cancer types from TCGA datasets

To investigate if functional activation or inactivation of *ST7* might be an important event in most cancer types, we surveyed the frequency of gene copy number alteration, mutations, and other alteration-related *ST7* function in TCGA datasets. Six cancer types with "Mutation and DNA copy-number alterations" data were selected for characterizing *ST7* genetic alterations (**Table 1**). Analyzed data was indicated in a bar graph (**Figure 1A**). Vertical bars represent alterations for single cancer. Alterations of *ST7* were highest in OSC and lowest in GMB. Copy number variations (CNV) in *ST7* were frequent in all selected cancers. *ST7* amplification was found to be a frequent alteration event in OSC (5.7 %), SC (3.83 %), LHC (3.82 %) and GMB (1.1 %), respectively. Deep deletion was most frequent in prostate adenocarcinoma (1.22 %) while missense mutation could be highly detected in bladder urothelial carcinoma(1.7 %) (**Figure 1A**). Most mutations were missense throughout the entire *ST7* protein and no specific hot spots mutation was detected (**Figure 2B**). Our finding consistent with a previous report

indicating that direct mutation was not the main mechanism affecting *ST7* function [4-8]. The level of *ST7* mRNA expression was then investigated and analyzed using the cBioPortal in 6 types of cancer as indicated in **Table 1**. LHC and OSC, compared to other cancers, had a higher level of *ST7* mRNA expression (**Figure 2C**). The expression was found lowest in BUA which percentage of mutation and deep deletion were most frequent in this cancer. Thus, the function of *ST7* is distinct in different cancers and its expression was correlated with the present of alteration patterns found in each cancer.

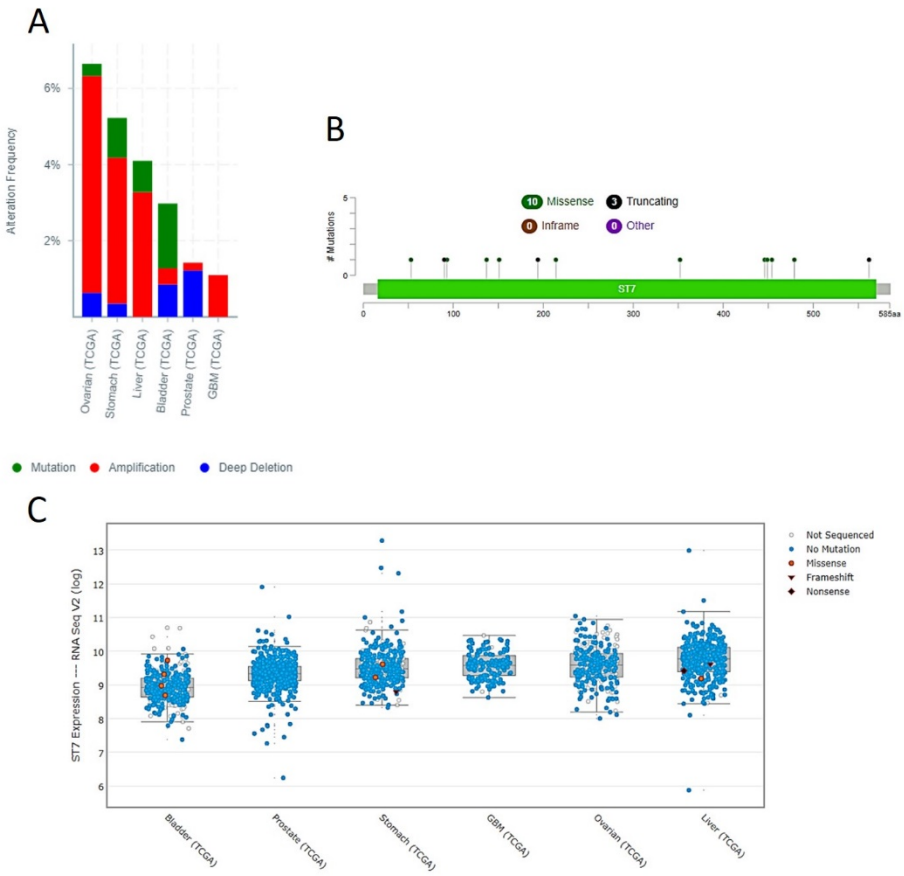

Figure 1 Summary graph of *ST7* alterations and analysis of *ST7* mRNA expression level data in individual cancers. The data were obtained and analyzed using cBioPortal. (A) The amplification, mutation, and deletion were represented as red, green and blue bars, respectively. The percentage of *ST7* alteration frequency is indicated. (B) *ST7* mutation detected in TCGA cancer group are shown. (C) Level of *ST7* mRNA expression in 6 types of cancer. The median and interquartile range are presented. Every spot represents a single study. White spots represent those analyzed without gene sequencing, blue spots represent normal results of gene sequencing and red spots represent missense mutations.

Table 1 Cancer types and number of TCGA samples selected for *ST7* genetic alteration characterization.

Cancer type	TCGA cancer abbreviation	Cancer sample (n)
Ovarian Serous Cyst adenocarcinoma	OSC	316
Stomach Adenocarcinoma	SC	287
Liver Hepatocellular Carcinoma	LHC	366
Prostate Adenocarcinoma	PRAD	492
Glioblastoma Multiforme	GBM	273
Bladder Urothelial Carcinoma	BUC	235

Genetic alterations of *ST7* and 2 groups *of ST7*-related genes in 6 cancer types from TCGA datasets

We examined the relationship between *ST7* and other *ST7*-related genes alterations including angiogenesis -related genes (*SERPINE 1, MMP13* and *VEGFA*) and *ST7*-associated genes (*PRMT5* and *SMARCA4*) in 6 cancers from TCGA dataset. To generate an OncoPrint profile, cancer samples with CNA (Copy Number Alteration), mutation, mRNA, and protein data were downloaded for this study as follow: ovarian serous cystadenocarcinoma (OSC; TCGA provision), liver hepatocellular carcinoma (LHC; TCGA provision), bladder urothelial adenocarcinoma (BUA; TCGA provision), stomach adenocarcinoma (SC; TCGA provision), prostate adenocarcinoma (PRAD; TCGA provision) and glioblastoma multiforme (GBM; TCGA provision). As shown in **Figure 2** OncoPrint, by downloading 3 more data types, mRNA up-regulation and down-regulation were also be included in alteration frequency calculation. The results indicated that *ST7* alteration frequencies were highest detected in SC (19 %) consisting mainly of *ST7* mRNA up-regulation and were lowest detected in PRAD (5 %). The similar alteration frequency was observed between *ST7* and angiogenesis-related gene, *SERPINE 1* in OSC, and GBM cases (**Figures 2A** and **2F**) while the similar alteration frequency between *ST7* and *VEGFA* was observed in PRAD, SC and LHC cases (**Figures 2B, 2C, 2E**). Moreover, *ST7* and *MMP13* alterations were identified at a similar frequency in 4 - 5 % and 9 - 10 % of PRAD and OSC cases, respectively. The relationship of *ST7* genetic alterations and alteration evens in *SERPINE1*, *VEGFA*, and *MMP13* across 6 TCGA cancer samples was analyzed and summarized in **Table 2**. The result indicated that *ST7* alterations in BUA, OSC and SC, studies have shown a tendency towards co-occurrence with *SERPINE1* alteration events with a significance of P-0.018, $p < 0.001$ and $p < 0.001$, respectively. *ST7* and *VEGFA* tend to be mutual exclusivity (non-significance) in LHC, SC and PRAD cases. Co-occurrence between *ST7* and *MMP13* alteration was not statistically significant in all cancer studies. Regarding *ST7*-related genes (*PRMT5* and *SMARCA4*), alteration frequency of these 3 queried genes was highest detected in OSC (66 %) and lowest detected in PRAD (15 %) (**Figure 3**). *ST7* and *PRMT5* alterations were identified at a similar frequency in 5 - 6 % and 16 - 18 % of PRAD and GBM studied, respectively (**Figures 3A - 3B**) while the similar alteration frequency between *ST7* and *SMARCA4* was observed in GBM, PRAD and LHC cases (**Figures 3A, 3B, 3E**). *ST7* alterations have a tendency towards co-occurrence with *PRMT5* alteration event in SC studied with significant of P -0.027. Gene pair between *ST7* and *SMARCA4* indicated the co-occurrent alteration in GBM cancer group ($p < 0.001$) while co-occurrence between *PRMT5* and *SMARCA1* alteration was also observed with a significance of P -0.005 (**Table 3**). The mechanism of this co-occurrence between the alteration of *ST7* and *SERPINE1* and their pathway events remains unknown even though the previous study reported that *SERPINE1* was up-regulated in *ST7*-transfected prostate cancer cell line [3]. Therefore, this finding suggests that *ST7* and *SERPINE*1 alterations mostly coexist in some cancer, but alterations in these genes are on independent pathways to drive carcinogenesis. However, *PRMT5* and *SMARCA4* were reported to suppress *ST7* transcription in cancers [15] which co-existing between *ST7* and these 2 genes alteration could be detected in SC and GBM, respectively (**Table 3**).

Table 2 Summary table of P-values and log odd ratio showing tendency for co-occurrence and mutual exclusivity between *ST7* alterations and angiogenesis-related genes (*SERPINE1*, *VEGFA*, and *MMP13*) in 6 TCGA cancer groups.

Type of cancer	Gene A	Gene B	Neither	A Not B	B Not A	Both	Log Odds Ratio	p-Value	Adjusted p-Value	Tendency
Bladder Urothelial Carcinoma	*ST7*	SERPINE1	353	31	21	8	1.467	0.003	0.018	Co-occurrence*
	ST7	VEGFA	348	34	26	5	0.677	0.156	0.936	Co-occurrence
	ST7	MMP13	355	36	19	3	0.443	0.345	1	Co-occurrence
Ovarian Serous Cystadenocarcinoma	*ST7*	SERPINE1	514	41	37	14	1.557	<0.001	<0.001	Co-occurrence*
	ST7	VEGFA	519	48	32	7	0.861	0.053	0.318	Co-occurrence
	ST7	MMP13	498	47	53	8	0.47	0.175	1	Co-occurrence
Liver Hepatocellular Carcinoma	*ST7*	MMP13	385	46	7	4	1.565	0.026	0.158	Co-occurrence
	ST7	SERPINE1	375	45	17	5	0.896	0.09	0.538	Co-occurrence
	ST7	VEGFA	348	46	44	4	-0.374	0.342	1	Mutual exclusivity
Stomach Adenocarcinoma	*ST7*	SERPINE1	428	12	30	8	2.252	<0.001	<0.001	Co-occurrence*
	ST7	VEGFA	423	19	35	1	-0.452	0.546	1	Mutual exclusivity
	ST7	MMP13	450	19	8	1	1.085	0.322	1	Co-occurrence
Prostate Adenocarcinoma	*ST7*	SERPINE1	436	17	39	6	1.373	0.012	0.073	Co-occurrence
	ST7	VEGFA	449	23	26	0	<-3	0.283	1	Mutual exclusivity
	ST7	MMP13	457	22	18	1	0.143	0.6	1	Co-occurrence
Glioblastoma Multiforme	*ST7*	SERPINE1	528	32	40	4	0.501	0.262	1	Co-occurrence
	ST7	VEGFA	550	34	18	2	0.586	0.337	1	Co-occurrence
	ST7	MMP13	538	34	30	2	0.053	0.583	1	Co-occurrence

Asterisk (*) indicates statistically significant co-occurrence between 2 gene pairs

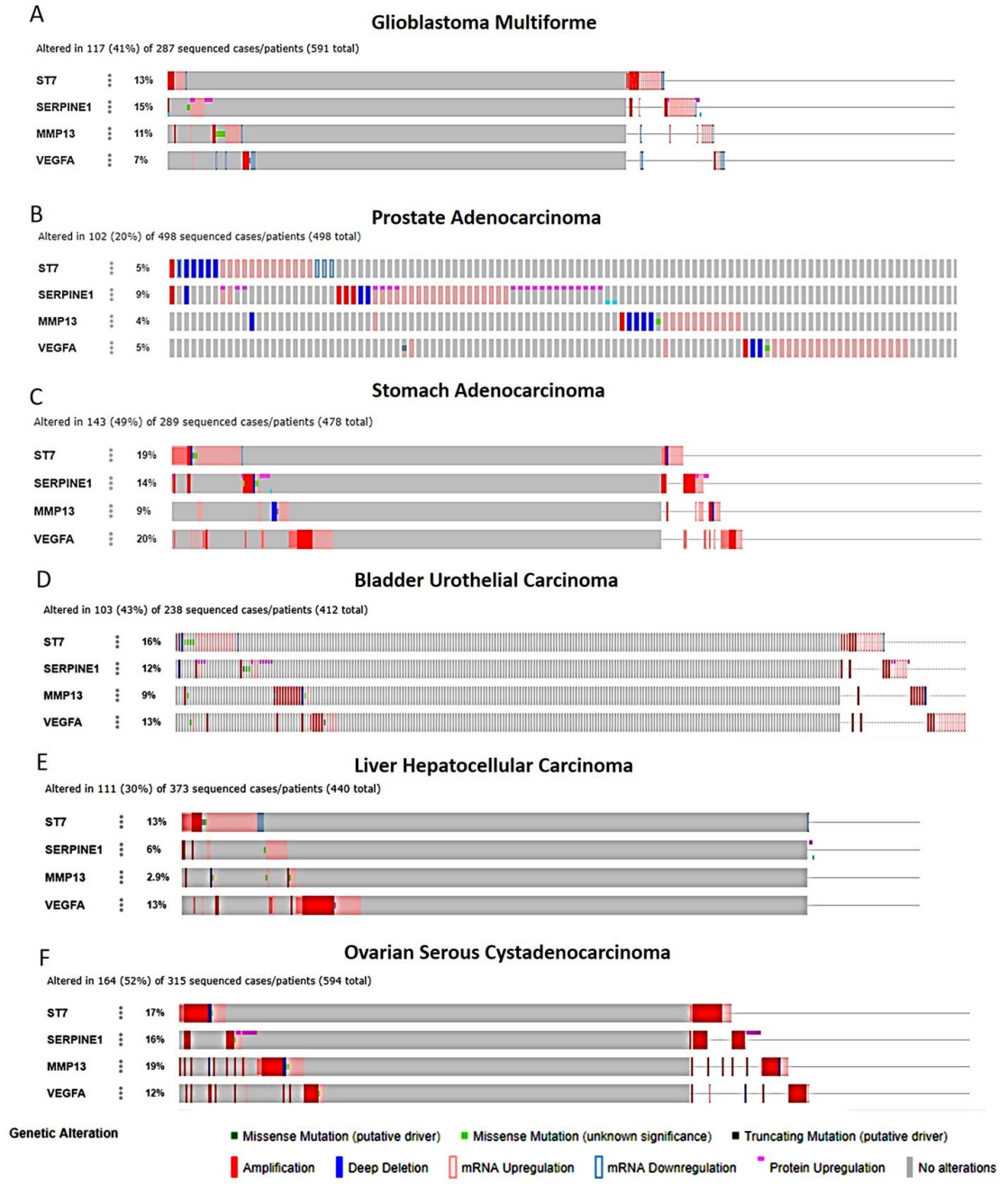

Figure 2 The OncoPrint tab summarizes genomic alterations in 4 queried genes including *ST7*, *SERPINE1, MMP 13* and *VEGFA* across 6 TCGA cancer samples. Each row represents a gene, and each column represents cancer sample. Mutations, copy number alterations, mRNA and protein alterations of 6 genes are shown for each cancer of the TCGA dataset. Percentage of each gene alteration was shown in each TCGA cancer sample including glioblastoma multiforme (A), prostate adenocarcinoma (B), stomach adenocarcinoma (C), bladder urothelial carcinoma (D), liver hepatocellular carcinoma (E), and ovarian serous cystadenocarcinoma (F).

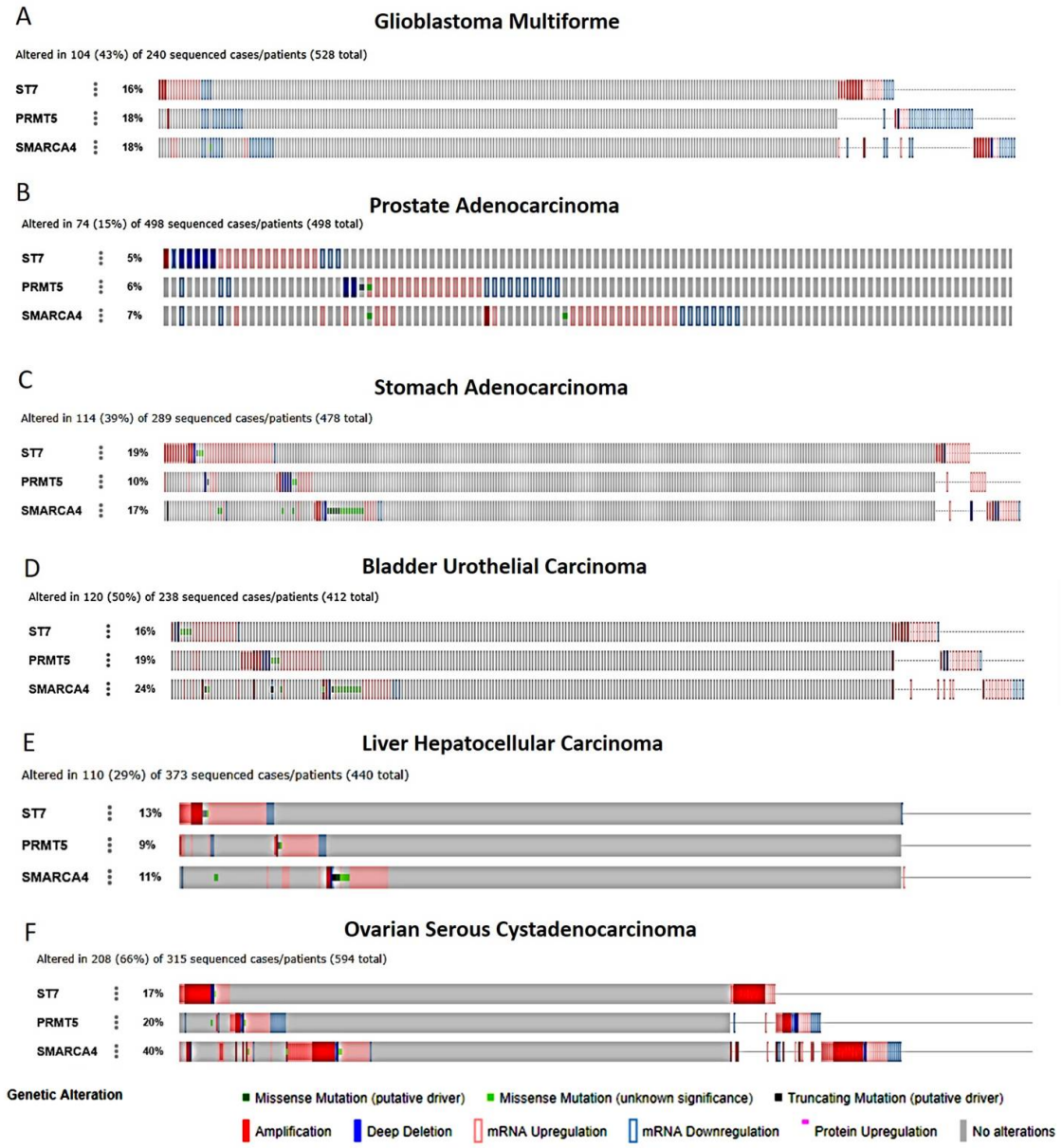

Figure 3 The OncoPrint tab summarizes genomic alterations in three queried genes including *ST7*, *PRMT5* and *SMARCA4* across 6 TCGA cancer samples. Each row represents a gene, and each column represents cancer sample. Mutations, copy number alterations, mRNA and protein alterations of three genes are shown for each tumor of the TCGA dataset. Percentage of each gene alteration was shown in each TCGA cancer sample including glioblastoma multiforme (A), prostate adenocarcinoma (B), stomach adenocarcinoma (C), bladder urothelial carcinoma (D), liver hepatocellular carcinoma (E), and ovarian serous cystadenocarcinoma (F).

Table 3 Summary table of P-values and log odd ratio showing tendency for co-occurrence and mutual exclusivity among *ST7*, *PRMT5,* and *SMARCA4* alterations and in 6 TCGA cancer groups.

Type of cancer	Gene A	Gene B	Neither	A Not B	B Not A	Both	Log Odds Ratio	p-Value	Adjusted p-Value	Tendency
Bladder Urothelial Carcinoma	*ST7*	SMARCA4	327	30	47	9	0.736	0.064	0.191	Co-occurrence
	ST7	PRMT5	333	34	41	5	0.178	0.444	1	Co-occurrence
Ovarian Serous Cystadenocarcinoma	*ST7*	SMARCA4	438	42	113	13	0.182	0.347	1	Co-occurrence
	ST7	PRMT5	492	49	59	6	0.021	0.553	1	Co-occurrence
Liver Hepatocellular Carcinoma	*ST7*	PRMT5	365	43	27	7	0.789	0.074	0.223	Co-occurrence
	ST7	SMARCA4	354	46	38	4	-0.211	0.471	1	Mutual exclusivity
Stomach Adenocarcinoma	*ST7*	PRMT5	403	47	20	8	1.232	0.009	0.027	Co-occurrence *
	ST7	SMARCA4	380	48	43	7	0.254	0.348	1.000	Co-occurrence
Prostate Adenocarcinoma	*ST7*	PRMT5	448	20	28	3	0.875	0.165	0.495	Co-occurrence
	ST7	SMARCA4	446	19	30	4	1.141	0.063	0.189	Co-occurrence
	PRMT5	SMARCA4	443	22	25	9	1.981	<0.001	<0.001	Co-occurrence *
Glioblastoma Multiforme	*ST7*	PRMT5	450	34	39	5	0.529	0.216	0.648	Co-occurrence
	ST7	SMARCA4	456	28	33	11	1.692	<0.001	<0.001	Co-occurrence *
	PRMT5	SMARCA4	450	34	34	10	1.359	0.002	0.005	Co-occurrence *

Asterisk (*) indicates statistically significant co-occurrence between 2 gene pairs

Survival analysis of altered *ST7* and 4 queried genes in 6 types of TCGA cancer cases

We examined the impact of *ST7* alteration clinical outcome in the TCGA data sets from 6 types of cancer. The differences of overall survival are computed between tumor samples that have at least one alteration in *ST7* gene and tumor samples that do not contain any alteration. The results were displayed kaplan-meier plots with P- values from a log rank test. A query for *ST7* alterations in each type of cancer is used to illustrate these results. The analysis showed that all cancer groups with altered *ST7* did not show significant shorter overall survival rate. However, alteration of *ST7* tends to be associated with decreased survival of patients. Median month's survival of OSC, GBM and BUC cases was reduced from 45.47 to 45.11 months (0.8 %), 14.19 to 11.66 months (18 %) and 35.38 to 27.04 (76.42 %), respectively, when compared with cases without *ST7* alteration (**Figures 4A - 4C**). When we considered about the *ST7* expression level among these 3 cancers, we found that *ST7* mRNA expression was lowest in BUC correlating with mutation and deep deletion which are the majority of *ST7* alteration types in this cancer. These types of alteration would affect *ST7* function in maintaining cellular structure and regulating the proliferation rate since *ST7* has been proposed as a tumor suppressor gene and its function is involved in the oncogenic pathway [1,2]. We also examined the impact of alterations *ST7* together with other 3 genes including *SERPINE, VEGFA,* and *MMP13*. We found that all cancer studies did not show a significant shorter overall survival rate. However, month survival was reduced in GMB patients (no significance) and the shorter disease-free survival rate was significant observed (*p -0.0258*) when used those 3 queried gene alteration analysis (**Figures 5A** and **5B**). We then examined the impact of alterations of *ST7* together with other 2 genes including *PRMT5* and *SMARCA4* which was reported to be directly involved in the repression of *ST7* transcription [15]. Alteration of these 3 queried genes was significantly associated with decreased survival and shorter disease-free survival rate in bladder urothelial carcinoma with P-0.00103 and P-0.00101, respectively, (**Figures 6A** and **6B**) while alteration of *ST7* alone did not show significantly reduced of survival event in BUC samples. This finding suggests that repressing *ST7*

transcription by *PRMT5* and *SMARCA4* through regulating chromatin accessibility was the important mechanism for suppressing *ST7* expression which related to the reduction cancer patient's survival rate.

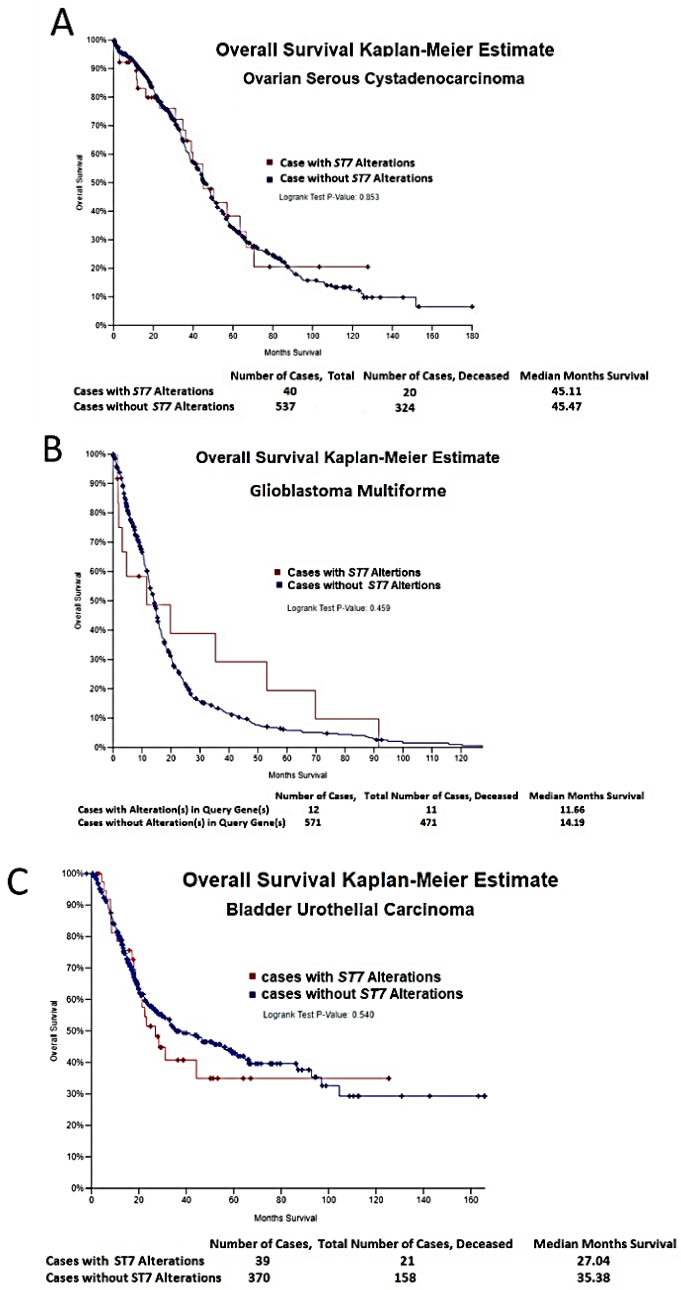

Figure 4 Kaplan-Meier survival curve for overall survival of 3 cancer patients with and without altered *ST7*. The red color plot indicates overall survival for patients with changes in *ST7* while blue color indicates cases without *ST7* alterations. The patients with the altered *ST*7 in 6 studied cancers (TCGA provisional) did not show significant differences in their overall survival. However, the reduced median month's survival was observed in ovarian serous cystadenocarcinoma (A), glioblastoma multiforme (B) and bladder urothelial carcinoma (C) compared with patients without *ST7* alterations.

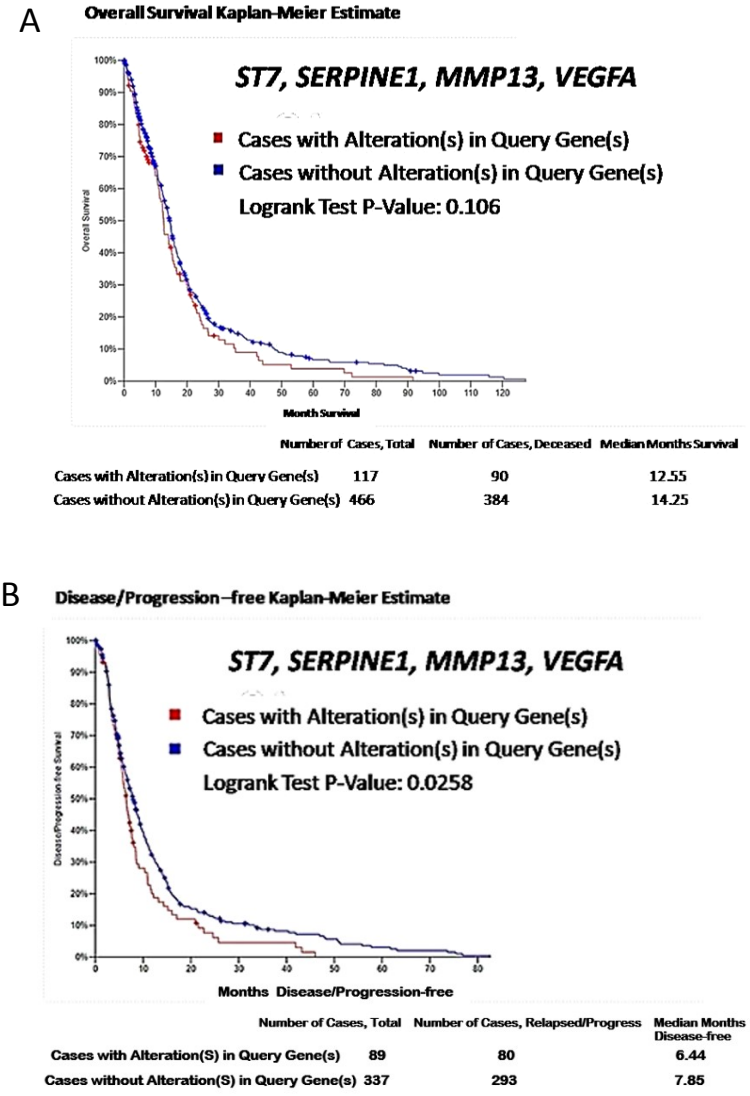

Figure 5 Kaplan-Meier survival curve for glioblastoma multiforme patients with and without *ST7 SERPINE1*, *MMP13*, *VEGFA* alteration. GBM patients with 4 queried genes alteration did not show significant shorter overall survival rate but revealed significant shorter disease-free survival rate (A) but revealed significant shorter disease-free survival rate, (B) compared to GBM patients without those 4 queried genes alteration.

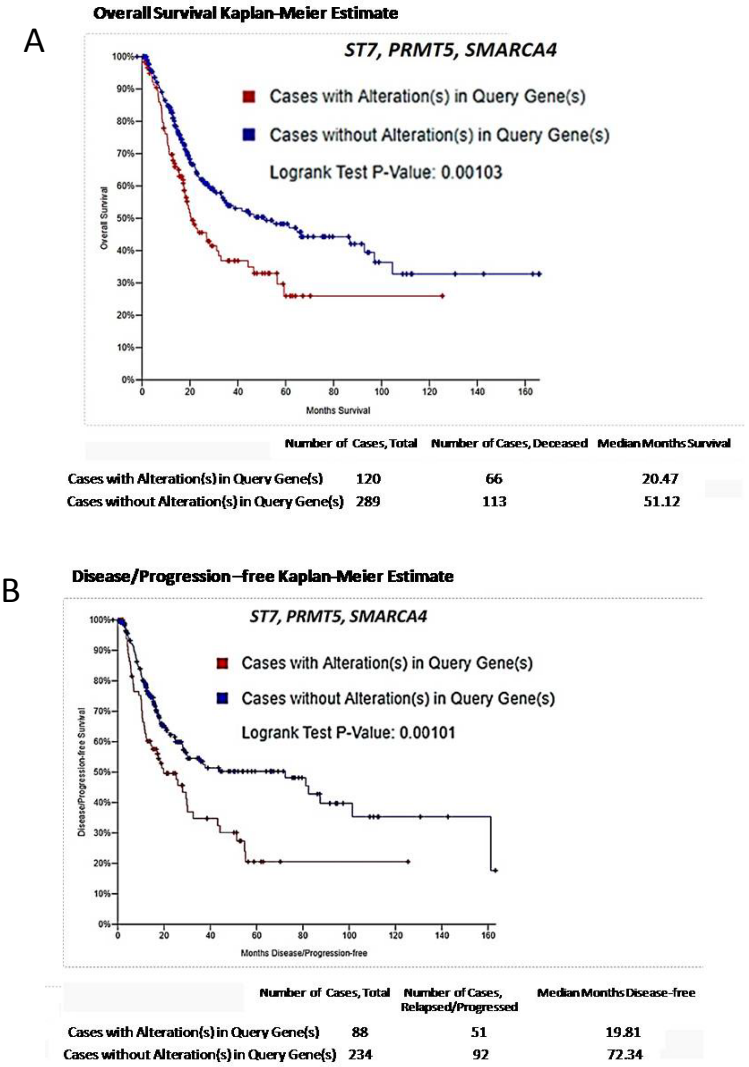

Figure 6 Kaplan-Meier survival curve for bladder urothelial carcinoma patients with and without *ST7*, *PRMT5* and *SMARCA4* alteration. Overall survival (A) and disease/progression free survival rate (B) in BUC patients was influenced by *ST7*, *PRMT5* and *SMARCA4* status.

Conclusions

ST7 is a not very well studied protein in cancer patients. Previous reports indicated that *ST7* is higher expressed in normal tissues than cancer samples [1]. However, very little is known regarding the pattern of *ST7* alteration, the association between *ST7* and angiogenesis-related genes as well as *ST7*-regulated genes in human cancer even though the significant correlation among these genes were reported in some cancer cell lines [3]. In the current study, we used The cBioPortal for Cancer Genomics as a tool for exploring, visualizing, and analyzing the biological and clinical features of *ST7* alterations in 6 cancer types from TCGA databases. Our study is the first data mining study to explore the relationship between alterations of *ST7* and 5 *ST7*-related genes and patient prognosis in TCGA dataset. Our findings reveal that *ST7* is altered with different patterns in many types of human cancer cells and even types of *ST7*

genetic alterations in cancer were dependent on cell type-specificity and *ST7*-mediated cell signaling pathways. Therefore, this gene might have different roles depending on cellular context and can play an important role in cancer. Interestingly, our study found that *ST7* and *SERPINE1* alterations mostly coexist in BUC, OSC, and SC while *MMP13* and *VEGFA* do not show significant relations. However, neither *ST7* nor *SERPINE1* were associated with both survival events (overall survival and disease free survival) in our study but alterations in these 3 genes indicated a significant shorter disease-free survival rate in GMB patients. Therefore, alterations in these genes are on independent pathways to GMB. Moreover, the association among 3 genes which are *ST7*, *PRMT5* and *SMARCA4* revealed significant shorter overall survival rate and shorter disease-free survival rate in BUC sample while single *ST7* alteration did not show significant results. Taken together, this analysis demonstrates that *ST7* alterations were not suggested as a proper indicator for observing the cancer patient survival. However, combined analysis between *ST7* with other *ST7*-related genes (*PRMT5* and *SMARCA4*) could be used as indicators for analyzing the patient survival in some cancer cases. Moreover, this study indicated that cBioportal and TCGA database provides a new perspective to simultaneously perform the analysis of genetic alterations and clinical outcomes for searching impact biomarkers for cancer prognosis and treatment in the future.

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