World Journal of Surgery and Surgical Research

Research Article
Published: 27 May, 2019

# Role of SPC24 Expression in Glioblastoma based on Oncomine and GEO Database

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## Abstract

**Background:** Glioblastoma (GBM) is one of the malignant tumors causing death worldwide. Most of the patients were found in the middle and late stages with poor prognosis. The purpose of this study was to investigate the expression and significance of SPC24 in GBM.

**Methods:** The information about SPC24 in Oncomine database was collected, and the data in current database were calculated by secondary analysis. The role of SPC24 in GBM was meta-analyzed. The expression of SPC24 in glioma cell lines was retrieved by CCLE database, and the survival of patients was analyzed *via* GEO database.

**Results:** A total of 792 different types of SPC24 were collected in Oncomine database. Among them, 38 studies showed statistical differences in the expression of SPC24, 24 studies showed increased expression of SPC24 and 14 studies showed decreased expression. Four studies involving the expression of SPC24 in GBM cancer and normal tissues included 1,189 samples. Compared with the control group, SPC24 was highly expressed in GBM ($P<0.05$). Moreover, SPC24 was highly expressed in glioma cell lines. There was a correlation between the expression of SPC24 and the overall survival rate of GBM. The overall survival rate of patients with high expression of SPC24 was worse, while the prognosis of patients with low expression of SPC24 was better ($P<0.05$).

**Conclusion:** Through in-depth mining of oncomine gene chip database and GEO, we demonstrate that SPC24 is highly expressed in GBM tissues and is related to the prognosis of GBM, which may provide an important theoretical basis for the treatment of GBM.

**Keywords: SPC24; Glioblastoma; Oncomine; Geo**

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**Received Date**: *15 Apr 2019*
**Accepted Date:** *22 May 2019*
**Published Date:** *27 May 2019*

***Citation:***
*Ning X, Luo J, Ling G, Zhong X, Xu B. Role of SPC24 Expression in Glioblastoma based on Oncomine and GEO Database. World J Surg Surgical Res. 2019; 2: 1131.*



## Introduction

Glioblastoma (GBM) is a serious threat to human health and one of the most lethal malignant tumors, which has caused tremendous economic burden to society [1]. Although many new therapies have been found in recent years, most of them are in the middle and late stages, and the prognosis has not been significantly improved. Studying the mechanism of SPC24 occurrence and development at molecular level is conducive to discovering new molecular targets and developing new therapeutic methods. It is very important to reduce patients' pain and prolong survival time of patients.

Oncomine database is the largest oncogene chip database and integrated data mining platform in the world, aiming at mining cancer gene information [2]. So far, 715 gene expression datasets and 86,733 samples of cancer and normal tissues have been collected in the database. Using Oncomine database, we can compare common cancer types and their normal tissues for differentially expressed sorting. We can also explore various cancer subtypes and analyze them based on clinic and pathology, carry out differentially expressed sorting and co-expression analysis, find differentially expressed genes in a certain cancer, identify target genes, and then determine research directions, which can not only save the cost of scientific research, but also reduce the cost of scientific research. And its information is more comprehensive.

Cell proliferation is an important life activity of organisms. Cells proliferate by division. Chromosome instability is a common feature of cancer cells and may be an important mechanism of tumorigenesis [3]. The molecular mechanism of its occurrence is a hot topic in cancer pathology. The correct alignment and separation of chromosomes during cell mitosis is coordinated by the dynamic interaction between spindle microtubules and kinetochores. The Ndc80 complex is

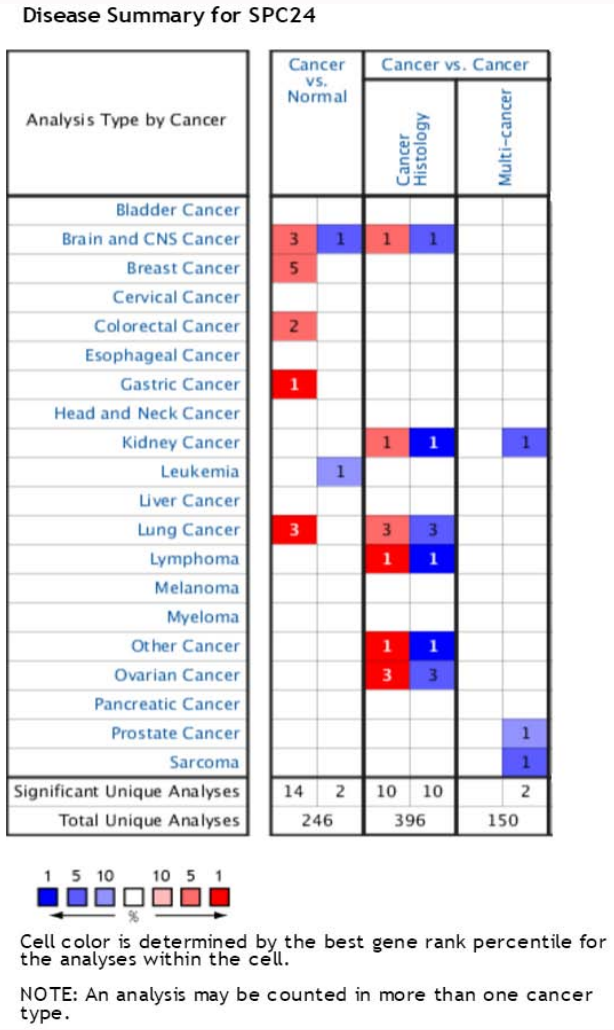


**Figure 1:** Expression data for SPC24 in a variety of normal and human cancer tissues in database Oncomine.

located in the outer layer of the kinetochore and consists of Hec1, Nuf2, Spc24 and SPc25. It plays an important regulatory role in the above process [4]. Spc24, as a component of the Ndc80 complex, is a part of the kinetochore-microtubule formation mechanism, which involves the important links of mitosis and tumorigenesis. Although previous studies have shown that SPC24 is highly expressed in a variety of tumor tissues and cells, few studies have been carried out in glioblastoma tissues [5,6].

In this study, Oncomine database and GEO database were used to analyze the expression and prognosis of SPC24 in GBM, and the possible relationship between SPC24 and GBM was meta-analyzed by secondary analysis, which provided clues and basis for further study of the mechanism of SPC24 in the occurrence and development of GBM.

## Methods

### Data extraction from oncomine database

Oncomine database is a gene chip-based database and integrated data mining platform, in which data can be screened and mined according to their own needs. In this study, we set the screening conditions as follows: (1) Cancer Type: Brain and CNS Cancer; (2) Gene: SPC24; (3) Data Type: RNA and DNA copy number; (4)

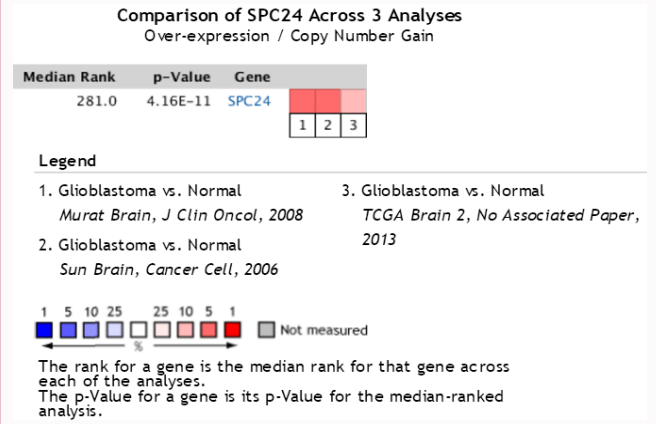


**Figure 2:** Expression of SPC24 in GBM in the studies identified in the Oncomine database. 1-3 represent the 3 studies on the expressions of SPC24 in GBM. Darker red indicates higher GBM expression in the chips.

Analysis Type: Cancer *vs.* Normal Analysis; (5) Critical value setting conditions (P<1E-4, fold change >2, gene rank=top 10%). Select the bar chart to show the results.

### Retrieval of SPC24 expression in glioma cell lines by CCLE database

The expression of SPC24 in various cancer cell lines was analyzed by CCLE website (https://portals.broadinstitute.org/ccle) [7]. In this study, we set the screening conditions as follows: (1) Gene: SPC24. Select the bar chart to show the results.

### GEO database for patient life cycle analysis

The GBM dataset of GEO database was analyzed online by using proggene V2 website (http://watson.compbio.iupui.edu/chirayu/proggene/database/?Url=proggene). The PROGgene database (http://www.compbio.iupui.edu/proggene) is a web application that can be used for studying prognostic implications of mRNA biomarkers in a variety of cancers [8]. We have compiled data from public repositories such as GEO, EBI array express and The Cancer Genome Atlas for creating this tool. With 64 patient series from 18 cancer types in our database, this tool provides the most comprehensive resource available for survival analysis to date. The screening conditions are as follows: (1) Cancer: Brain Cancer; (2) Gene: SPC24; (3) Survival: OS.

### Statistical methods

The difference of SPC24 expression between normal tissues and GBM patients was analyzed by t-test. The relationship between SPC24 expression and GBM prognosis was analyzed by Kaplan-Meier model. All the data were analyzed by SPSS 20.0, and the difference was statistically significant with bilateral P<0.05.

## Result

The results of expression of SPC24 in common tumour types were collected in Oncomine database. A total of 792 different types of research results were collected (Figure 1). Among them 38 were statistically different in expression of SPC24, and SPC24 was expressed in Oncomine database. There were 24 studies of increased expression and 14 studies of decreased expression.

### SPC24 overexpressed in GBM tissue

The results of SPC24 expression in GBM were found in Oncomine database. Since 2006, there have been three studies involving the expression of SPC24 in GBM and normal tissues (Figure 2), with a

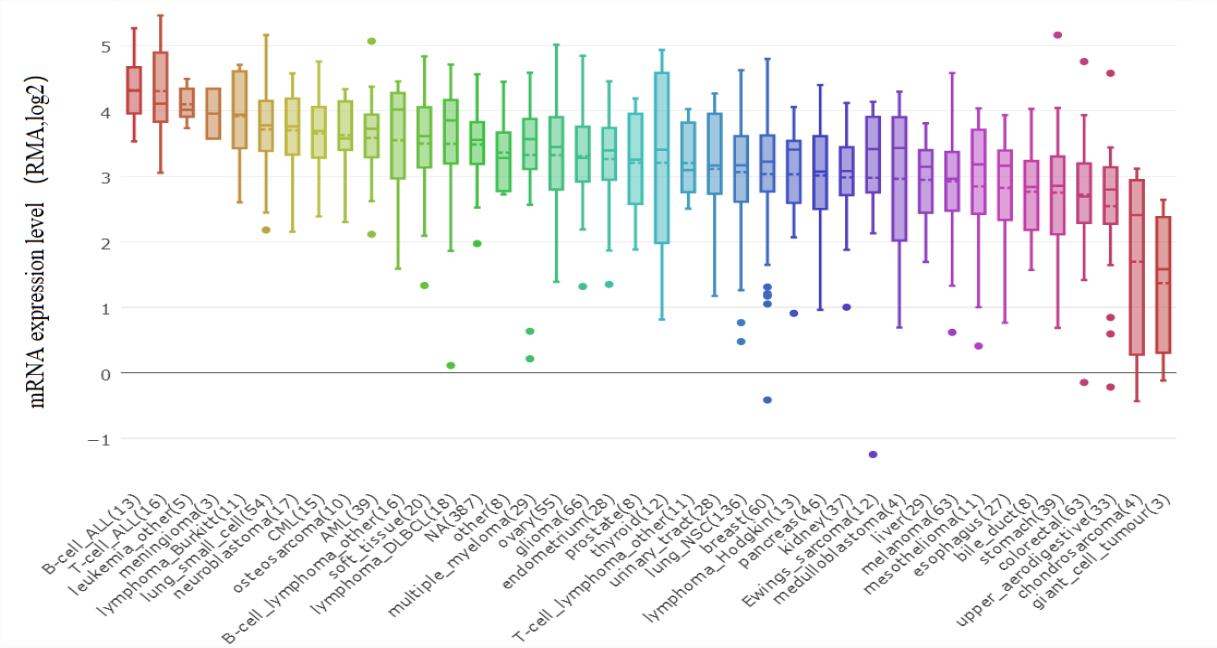


**Figure 3:** The expression of SPC24 in different cancer cell lines.

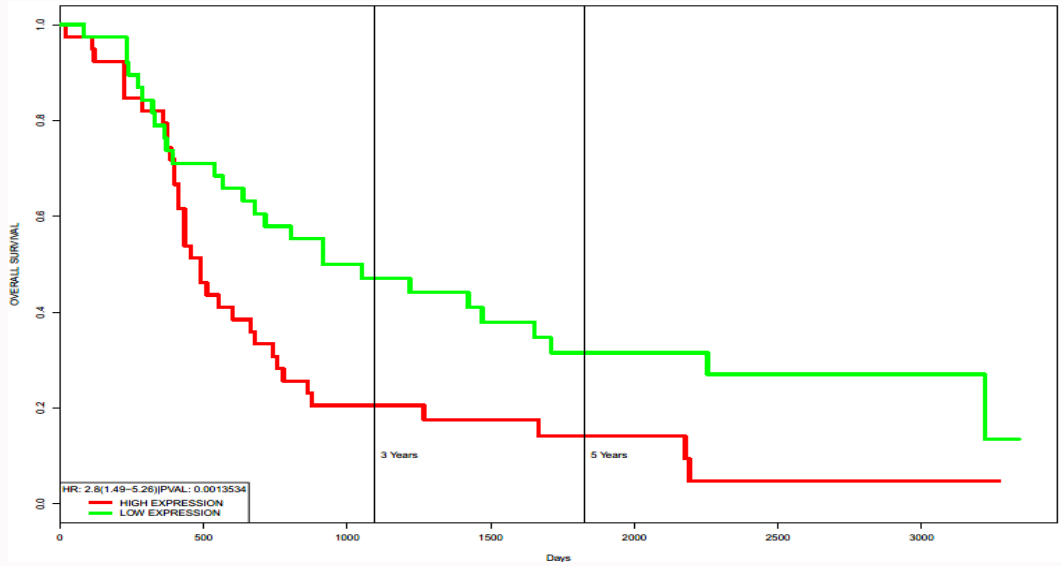


**Figure 4:** Relationship between the expression of SPC24 and the prognosis of GBM.

total of 1,795 samples. The results were published in Cancer Cell, 2006, J Clin Oncol, 2008, TCGA Brain 2, No Associated Paper, 2013 [9,10]. Meta-analysis of three studies in Oncomine database showed that the median value of SPC24 gene ranked 689.5, P=0.007 among all differentially expressed genes, suggesting that SPC24 was highly expressed in GBM.

### SPC24 overexpressed in glioma cell line

The expression of SPC24 in different cancer cell lines is shown in Figure 3. The expression of SPC24 in different cancer cell lines is shown in CCLE database. SPC24 is highly expressed in glioma cell lines.

### SPC24 worsens the prognosis of GBM

The relationship between SPC24 and prognosis of GBM patients showed that the expression of SPC24 had a significant impact on the overall survival time of patient's *via* Kaplan-Meier Plotter data. Compared with the low expression group, the total survival time of GBM patients in the SPC24 high expression group was significantly reduced (Figure 4). HR=2.8(1.49-5.28), p=0.001, Data are based on GSE4271-U133B.

## Discussion

Glioblastoma is one of the most lethal malignant tumors in the world. Epidemiological statistics show that the incidence of glioblastoma in gliomas is increasing. For a long time, the prognosis of GBM has been poor. With the development of molecular biology technology, a number of glioma-related genes such as PTEN, PDCD4, IDH1/2 have been discovered, and some targeted drugs

have been developed, which greatly improve the prognosis of glioma patients [11-13]. However, mutations in these genes only exist in some patients with glioma. Therefore, searching for key molecules or targets for the occurrence and development of glioblastoma has important theoretical and clinical significance for the development of new targeted drugs for the treatment of GBM, and has always been a research hotspot.

### Biological function of SPC24 gene

For higher eukaryotic animals, accurate mitotic regulation network can ensure the accurate and stable inheritance of genetic material. The core event is the correct alignment and separation of chromosomes, which directly determines the fidelity of mitosis [14]. Kinetochore is a complex of multi-component and multi-structure proteins assembled on the centromere of sister chromatids. It directly regulates the junction between chromosomes and spindle microtubules, ensures that the microtubules capture sister chromatids correctly and evenly distribute them equally to progeny cells [15]. Kinetochore protein Ndc80 is located in the outer layer of the moving point. It consists of four subunits: Ndc80 (Hec1 or KNTC2), Nuf2 (CDCA1), SPC24 and SPC25. The four subunits maintain high affinity, forming two stable dimers of Ndc80/Nuf2 and SPC24/SPC25, and assembled into dumbbell-like structure [16].

The four subunits of Ndc80 complex are highly conserved in evolution. Any mutation of any subunit may affect the biological function of Ndc80 complex and the normal process of cell filament separation. The results showed that mutation of SPC24 or SPC25 would lead to abnormal function of spindle checkpoint and seriously affect normal mitotic process [17]. The dysfunction of the Ndc80 complex will prolong the spindle indefinitely, exert a non-polar pull on sister chromatids, lead to abnormal chromosome distribution, resulting in aneuploid cells, leading to the occurrence and development of cancer [18].

The spherical end of SPC24/SPC25 subunit contains RWD domain, which can form a solid three-dimensional structure with the N-terminal of histone CENP-T and provide a platform for centromere and spindle assembly, thus effectively maintaining the dynamic connection of the inner and outer kinetin complexes [19]. Histone Cnn1 is tightly linked to SPC24/SPC25 dimer by a helix structure. Studies have shown that once SPC24 or SPC25 gene mutation occurs, the stabilizing force between them is destroyed, which then affects the dynamic interaction between centromere motility point and spindle microtubule, which is a fatal error event for cell mitosis [20]. Motion point protein Ndc80 complex regulates many key events in cell mitotic cycle. Abnormal expression of any of its subunits is likely to contribute to the occurrence and progression of cancer.

Preliminary studies have shown that the expression level of SPC24 gene in colon cancer and rectal cancer tissues is significantly higher than that in adjacent normal tissues, and the abnormal expression of SPC24 gene will directly affect the expression levels of SPC25, Ndc80 and Nuf2. More importantly, the interaction of these genes is closely related to the invasion and metastasis of malignant tumors, leading to poor prognosis of patients [21].

### SPC24 worsens the prognosis of GBM

Although most studies have found that SPC24 is highly expressed in many tumors, including GBM, there is a lack of high reliability due to the small sample size in independent studies, which easily leads to sampling errors [9]. Oncomine database is the largest gene chip database and integrated data mining platform in the world. First, we used Oncomine database to mine the expression information of GBM gene in colorectal cancer, breast cancer, gastric cancer and other common tumors. The results showed that in 38 studies with statistical differences, 24 studies showed that KIF23 was highly expressed in common tumors. The results of GBM chip detection were analyzed by Oncomine database. It was also proved that SPC24 was highly expressed in GBM tissues in more than 1,000 samples. At the same time, we used CCLE cell database to confirm the high expression of SPC24 in glioma cell lines. The prognostic value of SPC24 in GBM was found for the first time through PROGgene database. The results showed that the expression of SPC24 was clearly correlated with the overall survival rate of GBM, and the overall survival time of patients with high expression of SPC24 was significantly reduced. The high expression of SPC24 may affect the occurrence of tumors. Perhaps the abnormal expression of SPC24 gene will directly affect the biological function of Ndc80 complex, affect the normal process of cell filament separation, and produce aneuploidy cells, eventually leading to tumorigenesis [22]. All of our data are from gene chips, and the research methods are consistent, including the largest sample size so far, eliminating errors caused by sample size problems, and increasing the credibility of the conclusions.

## Conclusion

Through in-depth mining of SPC24 related information in GBM tissues, we demonstrate that SPC24 is overexpressed in GBM tissues and is related to the prognosis of GBM. Using the database for large sample analysis can avoid the error caused by the small sample size of a single study and provide an important theoretical basis for clinical treatment. The specific mechanism of SPC24 in the development of GBM disease needs further experiments in the future.

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