A Pan-cancer Study of the Expression Level of Selenoprotein SELENOO in Human Malignancies and Its Impact on Their Survival Prognosis

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Abstract

The relationship between Selenium (Se) and selenoproteins and cancer has become one of the hot issues in the field of cancer prevention and treatment. In this paper, SELENOO mRNA was firstly investigated in 27 human tumours by using GTEx database, CCLE database and TCGA database to explore its expression and further analyse its effect on the survival prognosis of 33 tumours. We also explored the correlation between SELENOO mRNA and tumour immune infiltration, tumour microenvironment (TME), immune neoantigens, immune checkpoint genes, tumour mutational load (TMB) and microsatellite instability (MSI), followed by GSEA analysis of high and low expression of SELENOO mRNA in pan-cancer. The results showed that aberrant expression of SELENOO mRNA correlated with the prognosis of a variety of tumours, particularly ACC, UVM, PAAD and UCEC. SELENOO mRNA expression was negatively correlated with TME, especially in LUSC and BLCA. It is suggested that SELENOO may be an important potential prognostic biomarker in pan-carcinoma and is associated with tumor immunity and metabolism.

Keywords

Pan-cancer, SELENOO, Tumour immunity, Prognosis, Biomarkers

1. Introduction

In recent years, the relationship between Selenium (Se) and selenoproteins and tumours has become one of the hot issues in the field of tumour prevention and treatment. Selenium is an essential trace element in humans and mammals, mainly in the form of selenocysteine (Sec, U), which exerts biological functions in the form of selenoproteins [1]. At least 25 selenoproteins have been isolated from mammals, and these selenoproteins can be involved in regulating various physiological and pathological responses in the body, playing different biological functions in immune regulation, anti-aging, cancer prevention and cardiovascular disease prevention [2]. Previous studies have shown that selenium and selenoproteins play a very important role in anti-tumour [3], may also play an important role in the anti-tumour field. Previous studies have shown that selenium and selenium proteins play an important role in anti-tumor activities. Rusolo F et al. [4] showed for the first time the selenium-MRNas profile specific to human breast cells, indicating that the expression of these genes changes according to ER positive or negative breast cancer cells. Pons DG et al. [5] showed that the chemical form of selenium amino acid and its binding with selenium protein may affect the regulation of REDOX state of breast cancer cells. Hughes DJ et al. [6] demonstrated that the change of selenium protein expression could be used as a marker of functional selenium status and colorectal adenoma canceration.
In this study, we used a pan-cancer study design from the selenoprotein SELENOO to firstly explore its mRNA levels in 27 human malignant tumour tissues, and then analysed its impact on the survival prognosis of 33 tumours to explore the correlation between SELENOO expression and tumour immune infiltration, tumour microenvironment (TME), immune neoantigens, immune checkpoint genes, tumour mutation load (TMB) and microsatellite instability (MSI), DNA mismatch repair genes (MMR) and DNA methylation, followed by GSEA analysis of the high and low expression of SELENOO mRNA in 33 tumours. These analyses aimed to reveal the impact of SELENOO on the development of human malignancies and to provide new targets for immunotherapy and prognosis prediction of tumours.

2. Materials and methods

2.1 Data sources

The mRNA sequencing data of 31 normal human tissues were obtained from the GTEx database (https://gtexportal.org/home/), the mRNA expression data of 21 tumour cell lines were obtained from the CCLE database (https://portals.broadinstitute.org/ccle/), and The mRNA sequencing data and clinical information data of 20 tumour tissues and normal tissues adjacent to cancer were obtained from the TCGA database (http://www.gsea-msigdb.org/gsea/index.jsp). Considering the small number of normal samples in the TCGA database, data from normal tissues in the GTEx database and tumour tissues in the TCGA database were integrated to assess the differential expression of SELENOO mRNA in 27 tumours, and the analysis was preceded by R language software to normalise the data and remove batch effects for subsequent analysis.

3. Results and Discussion

3.1 Expression levels of SELENOO in normal and tumor tissues

SELENOO mRNA was expressed at higher levels in tissues such as liver and prostate, but at lower levels in tissues such as heart and pancreas (Figure 1A). SELENOO mRNA was expressed in bladder uroepithelial carcinoma (BLCA), breast invasive carcinoma (BRCA), colon carcinoma (COAD), esophageal carcinoma (ESCA), head and neck squamous cell carcinoma (HNSC), renal clear cell carcinoma (KIRC), lung squamous cell carcinoma (LUSC), prostate adenocarcinoma (PRAD), rectal adenocarcinoma (READ), gastric carcinoma (STAD), and endometrial carcinoma (UCE), while the expression levels in bile duct carcinoma (CHOL), renal smallpox cell carcinoma (KICH), renal papillary cell carcinoma (KIRP), and thyroid carcinoma (THCA) were higher than normal tissues, and lower than normal tissues (Figure 1C). Integrating the data from TCGA database and GTEx database, the results showed that the expression levels of SELENOO mRNA were higher than normal tissues in 22 tumours including adrenocortical carcinoma (ACC) and BLCA, except for CHOL, KIRP, lung adenocarcinoma (LUAD), ovarian plasmacytoid cystic adenocarcinoma (OV) and THCA (Figure 1D).

3.2 Correlation between SELENOO and survival prognosis of human malignancies

Single-factor survival analysis was used to analyze the relationship between SELENOO mRNA expression and prognostic OS, DSS, PFI and DFI in 33 TCGA tumors. As shown in Figure 4A-D, low expression of SELENOO mRNA is beneficial to DSS of KIRP and unfavorable to DSS of THCA. High expression of SELENOO mRNA is associated with better prognosis for BLCA, cervical squamous and adenocarcinoma (CESC), pancreatic cancer (PAAD), pheochromocytoma and paraganglioma (PCPG), thymic cancer (THYM), and endometrial cancer (UCEC). Especially beneficial to PAAD (OS, HR=0.96, P=1.3×10⁻²; DSS, HR=0.98, P=1.8×10⁻³) and UCEC (OS, HR=0.99, P=2.9×10⁻²; DSS, HR=0.98, P=2.1×10⁻²; PFI, HR=0.99, P=3.3×10⁻²). High expression of SELENOO mRNA was associated with poor prognosis of ACC, COAD, PRAD, SARC and UVM, especially ACC (OS, HR=1.02, P=5.2×10⁻⁴; DSS, HR=1.02, P=6.0×10⁻³; PFI, HR=1.02, P=1.0×10⁻⁴; DFI, HR=1.03, P=4.9×10⁻⁴) and UVM (OS, HR=1.06, P=1.2×10⁻²; DSS, HR=1.06, P=1.6×10⁻²; PFI, HR=1.08, P=4.2×10⁻⁴). To further investigate the correlation between SELENOO mRNA expression levels and the prognosis of patients with various tumours, patients were divided into high and low expression groups according to their SELENOO mRNA expression levels and Kaplan-Meier survival curves were plotted (see Figure 2 for details). These results confirm the prognostic value of SELENOO in certain specific types of tumours.

3.3 Correlation of SELENOO with tumor immune infiltration and tumor microenvironment

Immune infiltration analysis confirmed that SELENOO mRNA expression correlated with the level of immune
infiltration in different tumour types, especially in BRCA, COAD, and brain low-grade glioma (LGG) (Figure 3A). In BRCA, SELENOO mRNA expression correlated with the infiltration of B cells (R=-0.075, P=1.27 × 10^{-02}), CD8+ T lymphocytes (R=0.239, P=1.21 × 10^{-03}), macrophages (R=-0.178, P=2.95×10^{-03}), neutrophils (R=-0.105, P=5.13×10^{-04}), and positively correlated with infiltration of CD4+ T lymphocytes (R=0.072, P=1.7×10^{-02}). In COAD, the expression of SELENOO mRNA was associated with B cells (R=0.171, P=2.44×10^{-04}), CD8+T lymphocytes (R= -0.342, P=5.34×10^{-14}), dendritic cells (R= -0.14, P=2.64×10^{-3}), macrophages (R= -0.211, P=5.52×10^{-6}) and neutrophils (R= -0.151, P=1.19×10^{-3}) were negatively correlated. In LGG, SELENOO mRNA expression was correlated with B cells (R=-0.219, P=4.07×10^{-7}), CD8+T lymphocytes (R=-0.473, P=0), dendritic cells (R=-0.156, P=3.41×10^{-5}), macrophages (R= -0.119, P=6.2×10^{-3}), neutrophils (R=-0.2, P=3.95×10^{-6}).

Figure 1. (A) GTEx database showing the expression levels of SELENOO mRNA in different normal tissues. (B) CCLE database showing the expression levels of SELENOO mRNA in different tumor tissues. (C) TCGA database showing the difference of SELENOO mRNA expression in normal and tumor tissues next to cancer. (D) Integrated data from TCGA database and GTEx database showing the difference of SELENOO mRNA expression in normal and tumor tissues adjacent to cancer. * indicates significant correlation P < 0.05, ** indicates significant correlation P < 0.01 and *** indicates significant correlation P < 0.001.

Figure 2. Forest plot of the relationship between SELENOO mRNA expression and OS (A), DSS (B), PFI (C) and DFI (D) in 33 tumours.
3.4 Correlation of SELENOO with immune checkpoint genes and immune neoantigens

Correlation analysis between SELENOO mRNA expression and 47 common immune checkpoint genes in 33 tumour tissues showed that TNFRSF14 and TNFRSF25 correlated most strongly and positively with SELENOO mRNA expression in a variety of tumours. SELENOO mRNA expression correlated with 22 immune checkpoint genes in COAD, 20 immune checkpoint genes in testicular cancer (TGCT), 20 immune checkpoint genes in TGCT and 19 immune checkpoint genes in PRAD (Figure 4A). Correlation analysis between SELENOO mRNA expression and neoantigen quantity in 19 tumor samples showed that: There was a weak positive correlation between SELENOO mRNA expression and the number of antigens in KIRP (R=0.162, P=3.81×10^-2), HNSC (R=0.146, P=1.48×10^-2) and LGG (R=0.146, P=4.04×10^-2). There was a weak negative correlation between the expression of SELENOO mRNA and the number of antigens in LUSC (R= -0.157, P=3.84×10^-2) and KIRC (R= -0.106, P=3.45×10^-2) (Figure 4B).

4. Conclusion

Aberrant expression of SELENOO mRNA correlated with the prognosis of a variety of tumours. Among them, it was significantly associated with poor prognosis in ACC and UVM, and significantly associated with better prog-
nosis in PAAD and UCEC. SELENOO mRNA expression correlated with the level of immune infiltration in different tumor types, especially in BRCA, COAD, LGG, and it was positively correlated with infiltration of CD4+ T lymphocytes except in BRCA, while it was negatively correlated with infiltration of B cells, CD8+ T lymphocytes, neutrophils, macrophages and dendritic cells in BRCA, COAD and SELENOO mRNA expression was negatively correlated with the immune and stromal components of TME, especially in LUSC and BLCA. The above findings suggest that SELENOO can be an important potential prognostic biomarker in pan-cancer and is associated with tumour immunity and tumour metabolism.

References


