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THE ROLE OF PROTEIN REGULATING CYTOKINESIS 1 IN THE MANAGEMENT OF GASTROINTESTINAL TUMORS

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Abstract: Objective: To investigate the expression patterns, biological functions, and prognostic significance of protein regulating cytokinesis 1 (PRC1) in gastrointestinal tumors using bioinformatics approaches, thereby providing potential guidance for clinical management. Methods: Publicly available databases were used to analyze PRC1 expression levels in gastrointestinal tumors. Co-expressed genes, underlying biological mechanisms, immune regulatory characteristics, mutation sites, and mutation types of PRC1 were systematically evaluated. In addition, the prognostic value of PRC1 expression and gene mutations was assessed across multiple tumor types, with a specific focus on gastrointestinal malignancies. Results: PRC1 was highly expressed in cholangiocarcinoma, colorectal cancer, hepatocellular carcinoma, pancreatic cancer, rectal cancer, and gastric cancer. PRC1 and its co-expressed genes jointly influenced key biological processes in gastrointestinal tumors. Gene Ontology (GO) enrichment analysis revealed that PRC1-related gene sets were predominantly enriched in mitosis-related pathways. Immunological analyses indicated that PRC1 was involved in the regulation of B cells, $CD4^+$ T cells, $CD8^+$ T cells, and other immune cells in gastric and pancreatic cancers. PRC1 alterations, including deep deletion, shallow deletion, diploid mutation, and amplification, affected tumor biological processes. Missense mutations and truncations were the predominant mutation types, influencing PRC1 translation and expression. High PRC1 expression was associated with poor prognosis in gastric and pancreatic cancers, and patients with PRC1 mutations exhibited worse clinical outcomes. Conclusion: Aberrant expression and mutation of PRC1 are associated with malignant progression and unfavorable prognosis in gastrointestinal tumors, highlighting PRC1 as a potential prognostic biomarker and therapeutic target for guiding clinical treatment strategies.
Keywords: Protein regulating cytokinesis 1; Gastrointestinal tumors; Bioinformatics analysis; Prognosis; Immunoregulation; Therapeutic target

1 INTRODUCTION

Digestive system tumors, such as gastric cancer, colon cancer, bile duct cancer, pancreatic cancer, and liver cancer, account for more than 50% of cancers worldwide, with a low 5-year overall survival rate. The high mortality rate of cancer is significantly related to the easy metastasis, rapid growth, and late detection of most digestive system tumors. Although treatments such as surgery, radiotherapy, chemotherapy, and targeted biological therapy have continuously improved the prognosis of tumors, the overall survival of patients still needs to be further extended[1]. Therefore, continuously exploring the molecular and biological mechanisms of digestive system tumors and studying the biological processes of tumor genes is of positive significance for improving the survival rate and quality of life of patients with digestive system tumors[2].

The protein regulating cytokinesis1 (PRC1) gene is located at 15q26.1 and encodes a protein composed of 620 amino acids with a relative molecular mass of 710004. It regulates parallel microtubule polarization and contractile loop assembly, and regulates cytoplasmic division and cell division. Its dysregulation may lead to tumor drug resistance and poor prognosis[3]. Previous studies have found that PRC1 plays an important role in tumorigenesis. PRC1 dysregulation increases chromosomal instability. This study aims to explore the correlation between PRC1 mutations, functional enrichment, and the abundance of immune cell (T lymphocytes, B cells, dendritic cells, macrophages, and neutrophils) infiltration in digestive system tumors by analyzing the Cancer Genome Atlas (TCGA) database and the Tumor Immune Estimation Resource (TIMER) database, and to study the impact of PRC1 gene expression and mutations on the prognosis of digestive system tumors, so as to provide a reference for the diagnosis and treatment of digestive system tumors[4].

2 MATERIALS AND METHODS

2.1 Gene Expression Profiling Interactive Analysis (GEPIA)

Database (http://gepia.cancer-pku.cn/indexhtml) GEPIA was used to analyze data from the TCGA database and genotype-tissue expression database. RNA sequencing expression data from 9736 tumor and 587 normal samples in the ExPression (GTEX) database were processed using standard pipelines. GEPIA generated jittered box plots for comparing expression in several cancer types[5].

2.2 Integrative Multi-Species Prediction (IMP)

IMP analyzes experimental results within the functional context of gene-gene networks across multiple organisms. IMP uses data-driven methods to mine networks of function-related genes and enables gene ontology (GO) analysis for further functional experiments.

2.3 Enrichr-KG Analysis

Gene and protein enrichment analysis is a crucial step in analyzing data from omics experiments. Enrichr is a gene set enrichment analysis tool containing hundreds of thousands of annotated gene sets; it provides a comprehensive resource for annotating gene sets based on existing biological knowledge. Enrichr-KG is a knowledge graph and web server application that combines selected gene set libraries from Enrichr and presents these libraries to users for integrated analysis and visualization. In Enrichr-KG, each node is either a gene or a function item, closely linking genes to their enriched items, further revealing the intrinsic relationship between genes and tumor development.

2.4 TIMER Database Analysis

The TIMER web server was used to systematically analyze immune infiltration in different types of cancer. The abundance of six types of diffuse immune cells (B cells, CD4+ T cells, CD8+ T cells, neutrophils, macrophages, and dendritic cells) was estimated using the TIMER algorithm. Based on gene expression profiles, the relative abundance of tumor-infiltrating lymphocytes (TILs) was inferred through genomic variation analysis .

2.5 cBioPortal Database Analysis

The cBioPortal database (http://www.cbioportal.org/) is an open web resource for querying, analyzing, and visualizing multidimensional genomic data from various databases. A digestive system tumor-related dataset was selected, and the Mutations module was used to analyze PRC1 gene variations. The Comparison/Suvival module was used to analyze the impact of mutations on the prognosis of digestive system tumors.

2.6 Kaplan-Meier Plotter Prognostic Analysis

The Kaplan-Meier survival plot can analyze the correlation between the expression of all genes (mRNA, miRNA, protein) and survival rate in 30,000 samples from 21 types of tumors (including cholangiocarcinoma, gastric cancer, pancreatic cancer, and colorectal cancer). The statistical methods used included Cox proportional hazards regression and calculation of false discovery rate. The primary purpose of this tool is to discover and validate prognostic biomarkers.

2.7 Statistical Methods

In the GEPIA database analysis, a custom threshold for line variation was set using the Iog2FC cutoff point. A custom p-value threshold was set. Matching normal data was performed: "TCGA normal + GTEX normal" or "TCGA normal only" were selected for differential analysis and plotting. The differential analysis method was one-way ANOVA, calculating differential expression levels with disease state (tumor or normal) as the variable. Co-expression analysis was performed using this database, and Pearson correlation analysis was used to perform pairwise gene expression correlation analysis on the given TCGA and/or GTEX expression datasets. Pearson correlation analysis was used to analyze the correlation between PRC1 mRNA and immune cell infiltration. (Bio Porta and Kaplan-Meier Plotter divided patient samples into two groups, compared the two patient cohorts using Kaplan-Meier survival plots, and calculated the hazard ratio of 95% confidence intervals and logrank P values. $P < 0.05$ was considered statistically significant.)

3 RESULTS

3.1 PRC1 Gene Expression in Digestive System Tumor Tissues

GEPIA database analysis showed that the expression level of PRC1 gene in digestive system tumor tissues was higher than that in normal digestive tract tissues, suggesting that the PRC1 gene may play an important role in the occurrence and development of digestive system tumors. Enrichr-KG analysis showed that the expression level of PRC1 gene was high in digestive system tumor cell lines.

3.2 PRC1-Associated Genes and Functional Enrichment

IMP analysis showed that PRC1 has a related gene network in digestive system tumors, and the associated gene set is of great significance in the biological processes of tumors. Further GO enrichment analysis showed that PRC1 plays an important role in tumor cell mitosis, and various associated genes and PRC1 are highly co-expressed.

3.3 Correlation of PRC1 and Associated Gene Sets in Disease Systems

Enrichr-KG analysis showed that PRC1 and its highly associated genes are involved in the development of both diabetes and tumors, influencing tumor biological processes, or indirectly affecting tumor development through non-coding RNAs.

3.4 High PRC1 mRNA Expression and the Digestive System

Analysis of the TIMER database showed the correlation between PRC1 mRNA expression levels and the abundance of six TILs. Results indicated that in gastric and pancreatic cancers, PRC1 mRNA levels were closely correlated with TIL expression.

3.5 PRC1 Mutation Mechanisms in Gastrointestinal Tumors

Analysis of the BioPortal database showed that high expression of PRC1 in digestive system tumors was caused by missense mutations, truncation mutations, in-frame deletions, splicing mutations, and fusion mutations, with missense mutations playing a major role. From the perspective of copy number changes, deep deletion, shallow deletion, and amplification were important mechanisms by which PRC1 affected the biological processes of digestive system tumors.

3.6 Impact of PRC1 on the Prognosis of Gastrointestinal Tumors

Analysis of the Kaplan-Meier Plotter database showed that high PRC1 expression predicted poor prognosis for gastric and pancreatic cancer. Further analysis revealed that PRC1 mutations affected the prognosis of digestive system tumors.

4 CONCLUSION AND DISCUSSION

Digestive system tumors are deadly malignant tumors, and surgical resection combined with radiotherapy and chemotherapy remains the main treatment method. However, the 5-year overall survival rate of digestive system tumors is low, and complications are common. With the development of molecular biology and bioinformatics, targeted therapy has brought more survival opportunities to cancer patients, providing more treatment options for patients. Previously, studies have confirmed that many targeted drugs are involved in the molecular regulatory pathways of gastrointestinal tumor development[6]. Trastuzumab targets HER-2 positive tumors, and targeted inhibitors such as sorafenib and lenvatinib have been applied to hepatocellular carcinoma, all of which have achieved good clinical efficacy. Sunitinib and everolimus have been approved for the treatment of gastrointestinal neuroendocrine tumors, and personalized treatment methods are increasingly being applied to digestive system tumors[7]. It has been confirmed that PRC1 is essential for cytokinesis and normal cell division, and PRC1 dysregulation leads to cell division defects, promotes chromosomal instability, and thus promotes tumor heterogeneity and progression. The results of this study show that the expression level of PRC1 in digestive system tumor tissues and cells is significantly higher than that in normal tissues and cells. High PRC1 expression predicts poor prognosis of gastric cancer and pancreatic cancer, which is consistent with the close relationship between PRC1 and tumor evolution as explained by Li et al. The results of this study also show that the biological role of PRC1 in tumors is mainly to regulate the stability of chromatin during cell mitosis, which suggests that PRC1 is closely related to the proliferation, migration, and invasion of digestive system tumors. Previous studies have confirmed that PRC1 participates in mouse oocyte mitosis under the regulation of KIF4A21[8]. This study performed high-precision analysis of highly associated genes of PRC1, revealing that in addition to KIF4A, genes such as BUB1B, CCNB1, CDK1, and CENPE interact to jointly regulate tumor biological behavior, consistent with multiple research findings. In this study, the disease regulatory network showed that PRC1 and its highly associated genes simultaneously participate in the development of diabetes and tumors. Schertbl24 studies have shown a close relationship between diabetes and digestive system tumors, with metabolic changes in diabetes such as hyperglycemia, insulin resistance, and hyperinsulinemia potentially promoting tumor development and progression. The results of this study reveal that PRC1 and its highly associated genes, while regulating tumor development and progression, also influence the course of diabetes, suggesting a possible link between diabetes and tumor development. The tumor microenvironment is a key environment affecting tumor survival and development, including cancer-associated fibroblasts, vascular endothelial cells, and TILs25. Immune cell infiltration is the most significant change in the tumor cell microenvironment and also affects[9]. This study found that PRC1 is positively correlated with the infiltration of immune cells (B cells, macrophages, CD4+ T lymphocytes, etc.) during the development of gastric and pancreatic cancer, providing new insights for future research on immunotherapy methods. Simultaneously, the results confirmed that PRC1 mutations are significant in the development of digestive system tumors, with missense mutations being the main mutational pattern[10]. Furthermore, the study found that PRC1 mutations predict poor prognosis in gastrointestinal tumors. This holds promise for developing targeted drugs against PRC1 mutation sites, providing a reference for the clinical treatment of cancer patients.

In summary, PRC1 is associated with the occurrence, development, and immune infiltration of digestive system tumors. Moreover, PRC1 mutations affect the prognosis of digestive system tumors, providing a theoretical basis for the future development of corresponding targeted drugs. This study could not further investigate the mechanism by which PRC1 affects digestive system tumors, which will be a direction for future research[11]. This study also found that PRC1 and its highly associated genes are involved in the development of both diabetes and cancer. The mechanisms between diabetes and cancer require further investigation to guide drug development and treatment decisions.

COMPETING INTERESTS

The authors have no relevant financial or non-financial interests to disclose.

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