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# *GINS1* as a Novel Biomarker of Survival in Colon Adenocarcinoma Patients

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**Abstract:** The study focused on elaborating the role of *GINS1* expression and its regulatory mechanisms in colon adenocarcinoma (COAD). Using the UALCAN informational index, *GINS1* expression assessment unveiled a critical up-regulation in malignant cells that stood out from normal controls, suggesting its contribution to COAD expansion. Further dismantling *GINS1* expression across various boundaries revealed unsurprising up-regulation in different malignant development stages, racial groups, genders, and age classes in COAD patients, characteristics for its imperative role in cancer progression. Moreover, this study investigated the promoter methylation status of *GINS1*, uncovering a critical uniqueness between COAD samples and normal controls. Analyzing promoter methylation across various clinical boundaries uncovered powerful variations, with particular methylation patterns seen across cancer stages, race groups, genders, and age groups. Survival analysis using the Kaplan-Meier (KM) plotter tool showed a colossal connection between *GINS1* expression levels and overall survival (OS) in COAD patients, with low *GINS1* expression interfacing with higher OS. Additionally, mutational examination using the cBioPortal stage revealed that no critical change was found in COAD. Overall, these findings revealed the complex contribution of *GINS1* in COAD pathogenesis, underlining its actual limit as a prognostic biomarker and supportive therapeutic agent in COAD management.

**Keywords:** Colon adenocarcinoma; Diagnosis; Treatment

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## 1. Introduction

Cancer is the most common cause of morbidity worldwide [1]. Cancer-developing leading factors include obesity, alcohol intake, smoking, hormonal imbalance, the lack of physical exercise etc. [2]. *GINS1* is an essential part of the GINS complex and plays a vital role in the DNA replication process. Up-regulation of *GINS1* is reported in different human cancers like lung and breast cancer.

Colon adenocarcinoma (COAD) is a commonly found malignant tumor. COAD is considered about 10% of all cancer diagnoses and cancer-related deaths worldwide [3]. COAD is the second most common cancer

in females and the third most commonly found cancer in males [4]. The treatment of COAD cancer including surgery at early stages plays a significant role in better results [5]. However, COAD treatment results in more challenging situations at later stages which ultimately allows COAD metastasis to be the main factor resulting in cancer-related deaths [6]. The prognostication for COAD disease remains quite alarming, with a five-year survival rate for stages 3 and 4 of about 65.4% and 12.8% respectively [7]. The poor treatment results depicted that the current study mechanisms should be better for tumor genesis and progression [8].

In this research, different bioinformatics methods are used to explore the mechanism of *GINS1* in the prognosis of COAD. The role of the *GINS1* gene which relates to COAD is elucidated by examining its clinical and molecular mechanism. We used the available database at Cancer Genome Atlas (TCGA), UALCAN database, Kaplan-Meier (KM) plotter, and cBioportal to investigate *GINS1* expression for the benefit of COAD patients.

## 2. Materials and methods

### 2.1. Expression analysis of *GINS1* gene in COAD view

TIMER (Tumor Immune Estimation Resource) 2.0 stands as an essential database by providing invaluable awareness of the complicated interaction between normal and malignant cells [9]. TIMER, this comprehensive platform offers the best tools and resources for research. In the present study, the GEPIA2 platform was utilized for expression analysis of the *GINS1* gene in COAD view.

### 2.2. Expression analysis of *GINS1* across different stages of COAD

The UALCAN database is a comprehensive, user-friendly, and attractive web resource for analyzing cancer genomics data [10]. The UALCAN database enables researchers to access Level 3 RNA-seq data from The Cancer Genome Atlas (TCGA) and perform gene expression and survival analysis on about 20,500 protein-coding genes, 15,000 lncRNAs, and 2,000 miRNAs across 33 cancer types. It allows users to identify biomarkers or perform *in silico* validation of potential genes of interest, evaluate epigenetic regulation of gene expression by promoter methylation, and perform pan-cancer gene expression analysis. In the present study, this database was used for the expression analysis of *GINS1* across different stages of the specified cancer, in which this gene shows significant dysregulation as well as a significant correlation with worse overall survival (OS).

### 2.3. Promoter methylation analysis of *GINS1*

The data related to RNA expression, DNA methylation, viral infection, and clinical features of cancer patients are present UALCAN database. For the analysis of the promotor methylation level of *GINS1* in COAD, we used the UCALAN database. Moreover, we also analyzed promoter methylation data of *GINS1* in different clinical parameters, such as patients' age, gender, and race.

### 2.4. Survival analysis of *GINS1*

The KM plotter is a sophisticated online survival analysis tool that allows researchers to assess the association between gene expression and survival in various cancer types. Researchers can utilize the KM plotter to investigate the relationship between gene expression levels and patient survival in different cancer types, including breast cancer, lung cancer, ovarian cancer, and gastric cancer. By using this tool, researchers can gain insights into potential biomarkers, identify genes associated with prognosis, and explore the impact of gene expression on patient outcomes across various cancers. The tool performs real-time calculations and provides interactive Kaplan-Meier plots for survival analysis. In this study, the KM plotter tool was used to analyze the effect of *GINS1* dysregulation on the OS of cancer patients.

## 2.5. Mutational analysis of *GINS1*

cBioPortal for cancer genomics is a platform that allows researchers to access, visualize, and analyze large datasets of cancer genomics information [11]. It provides a user-friendly interface for exploring tumor mutations, gene expression, and other genomic data across different cancer types. The portal aims to bridge the gap between complex genomic data and cancer researchers by providing intuitive access to molecular profiles and clinical attributes. Users can interact with the cBioPortal through a simple and flexible interface, intuitive visualization options, and a programmatic web interface. In this study, this data was used to perform a mutational analysis of *GINS1* across COAD cancer.

# 3. Results

## 3.1. Expression analysis of *GINS1* in COAD and normal controlled samples

Utilizing the UALCAN database, our initial study focused on *GINS1* expression in cancerous and normal controlled samples. Our findings revealed considerable variations in the *GINS1* expression pattern, as depicted in **Figure 1**. In particular, colon adenocarcinoma (COAD) exhibited significantly higher *GINS1* expression as compared to normal tissues.

## 3.2. Expression analysis of *GINS1* in COAD samples based on different stages

Eventually, after analyzing *GINS1* expression in COAD and normal samples, we did an expression analysis of *GINS1* in the COAD samples based on different individual stages (**Figure 2**). We found significant overexpression of *GINS1* in COAD patients at different stages.

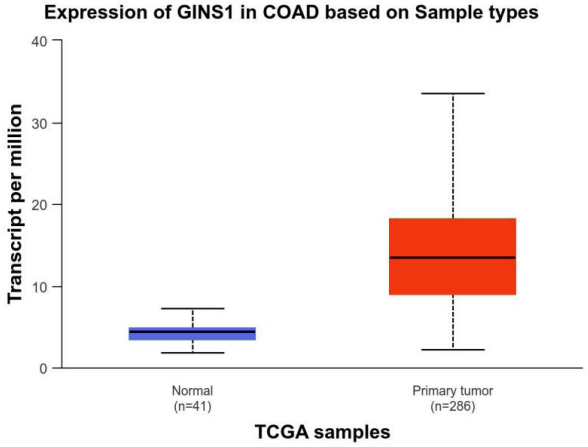


**Figure 1.** The expression profiling of *GINS1* in COAD and normal tissue samples

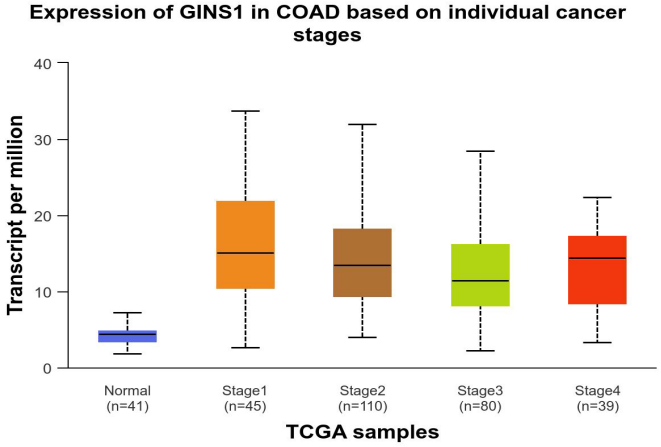


**Figure 2.** The expression profiling of *GINS1* in different stages COAD and normal tissue samples

## 3.3. Expression analysis of *GINS1* in COAD samples of different parameters of patients

After that, we set patient gender as our parameter for expression analysis and ascertained information that samples of different genders with COAD showed considerable variations in expression and were found significantly over-expressed in males and females with COAD (**Figure 3A**). Then we set patient race as our parameter to analyze the *GINS1* expression. We came to notice that samples of different races with COAD showed variations in expression and were found significantly over-expressed as compared to normal samples (**Figure 3B**). Eventually, we set patient age as our parameter to analyze *GINS1* expression in COAD and normal

samples and found that there was significant overexpression in patients with COAD at different ages (**Figure 3C**). Overall, this analysis highlighted the considerable role of the *GINS1* in COAD development.

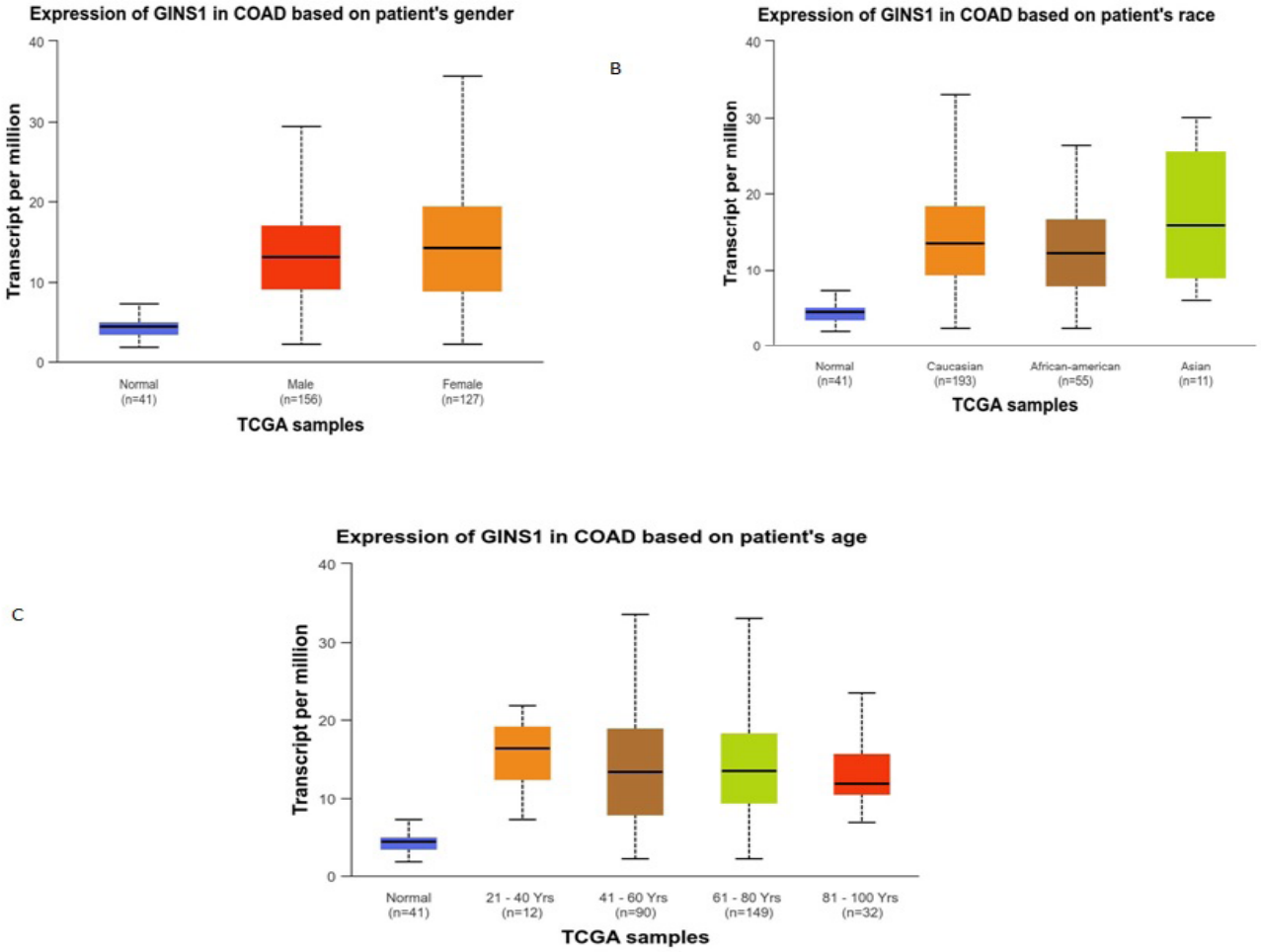


**Figure 3.** The expression profiling of *GINS1* in COAD based on patients' gender, race, and age respectively

## 3.4. Promoter methylation of *GINS1* in COAD

Moreover, we analyzed the difference in promoter methylation of *GINS1* in COAD samples and normal control samples utilizing the UALCAN data set (**Figure 4**). Our analysis uncovered a huge variety, explicitly hypermethylation, in the promoter methylation value of *GINS1* in COAD compared with normal control samples. This perception recommends potential epigenetic dysregulation of *GINS1*, featuring its association with COAD pathogenesis. Such findings add to how we might interpret the molecular mechanism underlying COAD improvement and proposition experiences into the role of *GINS1* as a potential biomarker or therapeutic target in COAD management.

## 3.5. Promoter methylation of *GINS1* in COAD samples divided based on different parameters

We explored different clinical boundaries to dissect the promoter methylation of *GINS1* in COAD (**Figure 5**). Primarily, we investigated *GINS1* promoter methylation across various COAD stages compared with normal samples. Our findings revealed variations among stages, with stage three displaying hypermethylation; however, stages one, two, and four displayed hypomethylation (**Figure 5A**). Subsequently, examination of *GINS1* promoter methylation as per patient age divulged explicit variations across the different age groups (**Figure 5B**). Moreover, we examined *GINS1* promoter methylation in view of the race in COAD patients.

Curiously, we noticed hypermethylation in *GINS1* promoter regions across races besides in African Americans, which observed notable hypomethylation (**Figure 5C**). Finally, analysis of *GINS1* promoter methylation according to patient gender unveiled gender-specific variations, with females exhibiting hypermethylation and males showing hypomethylation (**Figure 5D**). These broad assessments feature the complicated association between *GINS1* promoter methylation and different clinical boundaries in COAD, uncovering understanding of the multifaceted systems fundamental *GINS1* expression guideline in COAD pathogenesis.

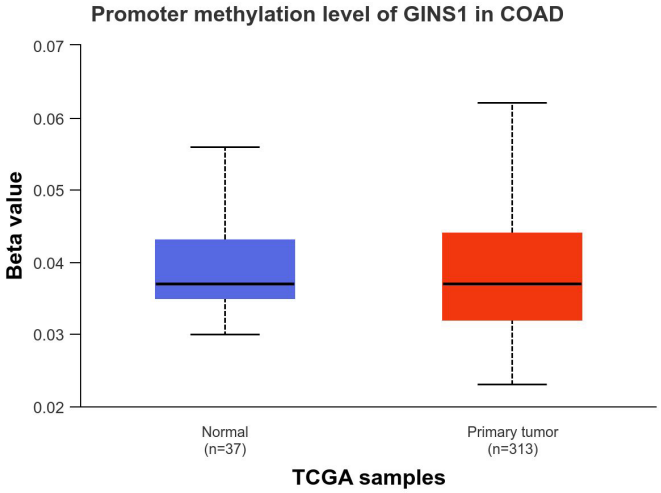


**Figure 4.** Promoter methylation pattern of *GINS1* in COAD and normal control samples

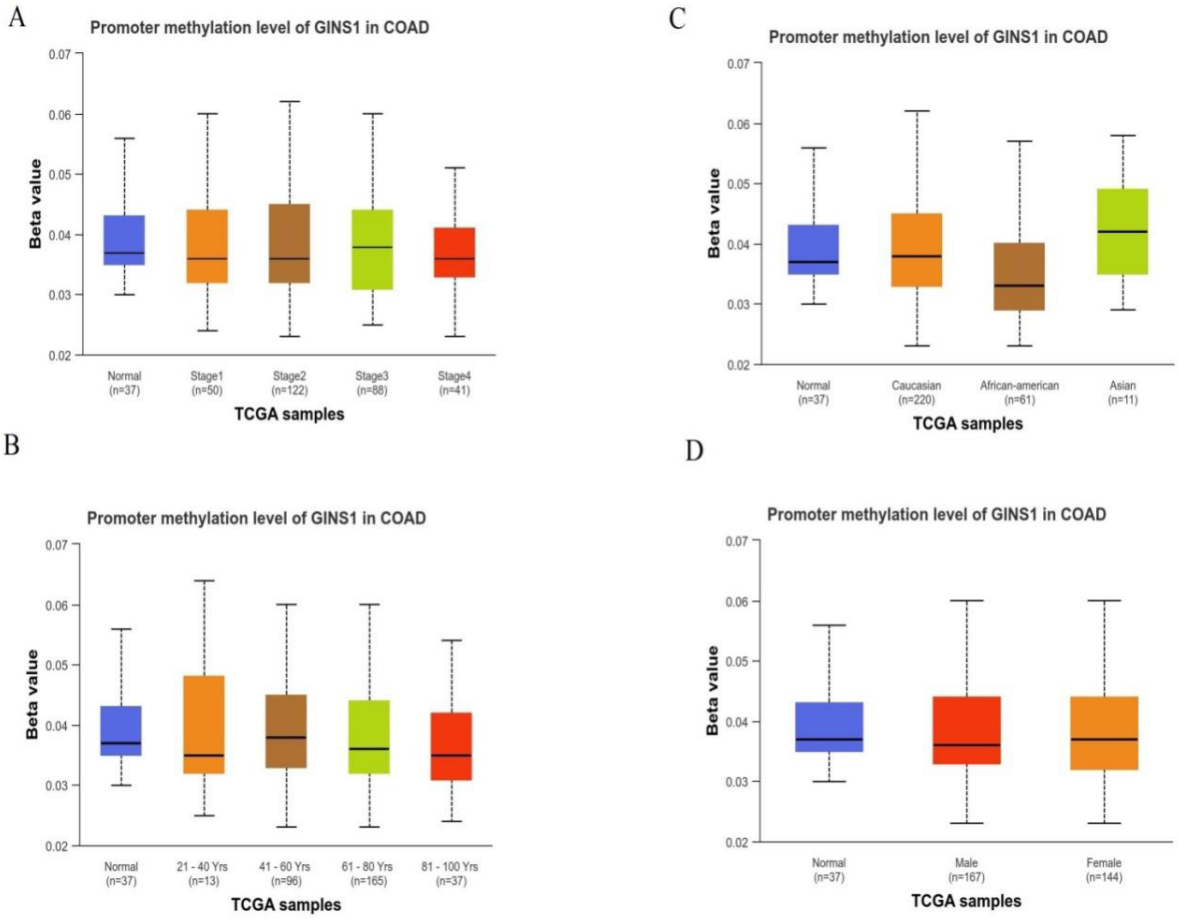


**Figure 5.** *GINS1* promoter methylation pattern across different clinical boundaries

## 3.6. Survival analysis of *GINS1*

Eventually, for a more extensive exploration of the clinical significance associated with the *GINS1* gene, we took onboard the KM plotter tool to assess patients' OS. As depicted in **Figure 6**, our analysis revealed that in COAD individuals exhibiting high *GINS1* expression experienced significantly worse OS compared to individuals with low *GINS1* expression. These findings emphasize the crucial role of *GINS1* in patient survival within the context of COAD.

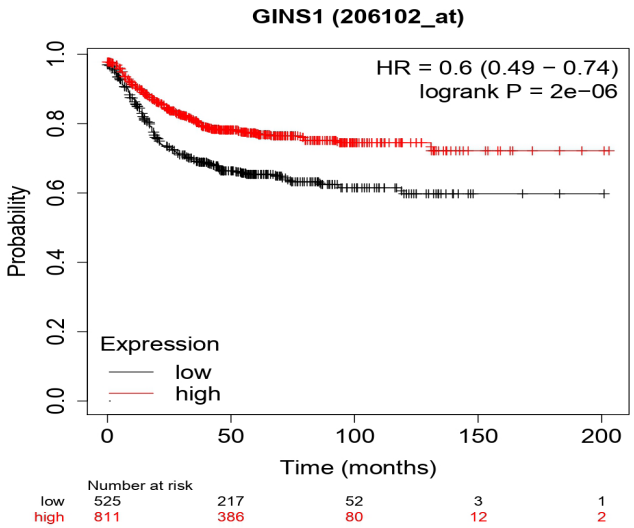


**Figure 6.** The survival analysis of *GINS1* in COAD and normal tissue samples

## 3.7. Mutational analysis of *GINS1*

To explore the genomic alterations of *GINS1* in COAD, we employed the cBioPortal platform to assess TCGA datasets for mutation detection. Our analysis revealed that less mutation of *GINS1* was found in COAD, about 3%, which is insignificant as shown in **Figure 7**.

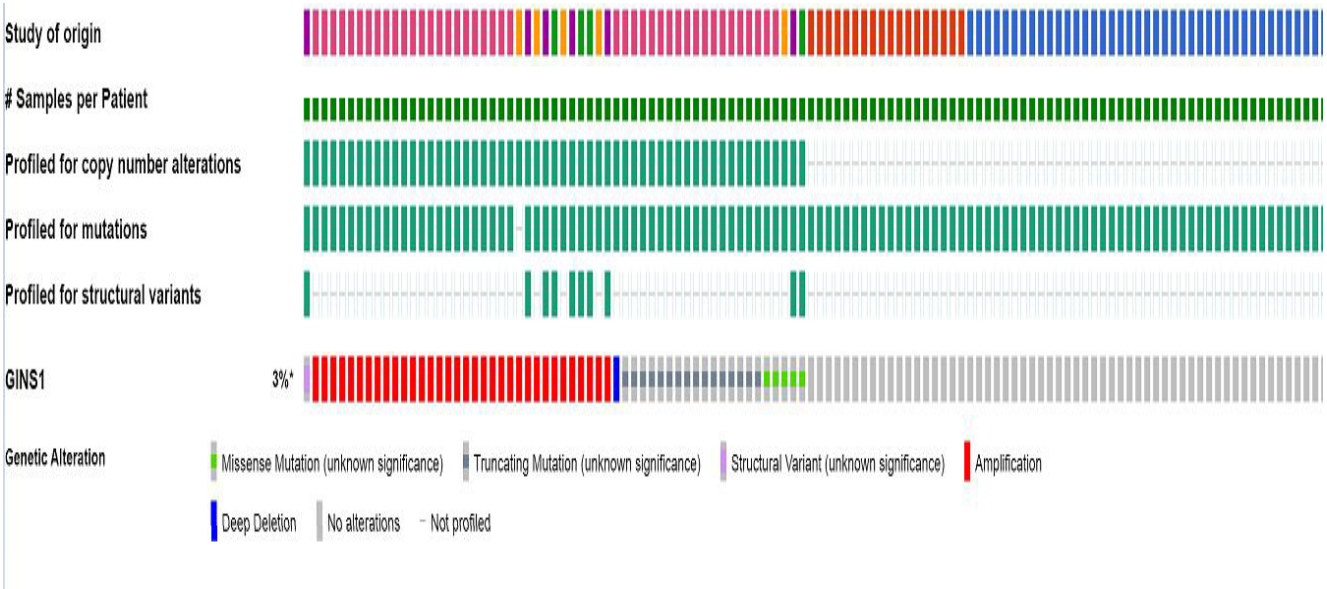


**Figure 7.** The mutational analysis of *GINS1* in COAD and normal tissue samples

## 4. Discussion

In our current study, *GINS1* expression patterns in COAD and normal control uncovered a critical up-regulation of *GINS1* in malignant cells contrasted with normal control. These findings infer a likely relationship between *GINS1* expression and COAD multiplication, recommending *GINS1* as a putative controller in COAD pathogenesis.

In general, dysregulation of any member from the GINS complex has been demonstrated to be related to the progression of malignant growths and impacted the forecast of patients with fluctuated cancers [12,13]. The fundamental domain of *GINS1* contains an alpha-helical structure which is fundamental for DNA replication [14]. Previously research revealed that *GINS1* was overexpressed in lung cancer and *GINS1* consumption impacted proliferation and cell cycle arrest in cellular breakdown in lung cells. Nakahara has shown that *GINS1* is highly expressed in breast cancer cells, which is an element of enhanced activity of *GINS1* promoter. Interim, the down-regulation of *GINS1* restrains anchor-independent development of breast cancer cells [15].

Additionally, expression of *GINS1* has been accounted for to relate with the improvement of liver malignant growth adrenal cortex adenocarcinoma, non-small cell lung cancer, and colorectal cancer [16,17]. The *GINS1* has also been correlated with poor OS in prostate cancer patients [18]. In the current review, UALCAN data sets were used to decide the statement of *GINS1* in COAD. In the UALCAN analysis, the current review showed that upregulated *GINS1* expression was seen in various stages, individual types, age, gender, and racial groups. As to malignant growth, the result of the present study demonstrated that *GINS1* expression was notably higher in COAD tissues compared to normal tissues. Moreover, in the KM plotter tool, our analysis revealed that COAD individuals exhibiting high *GINS1* expression experienced significantly worse OS compared to individuals with low *GINS1* expression. Our study revealed that neither epigenetic nor genetic alterations significantly contribute to the dysregulation of *GINS1* in COAD samples.

Overall, the current study exhibited that enhanced *GINS1* expression might be a valuable and predictive biomarker for poor prognosis in patients with colon cancer. The result of the current study gives knowledge into the ongoing comprehension of *GINS1* in colon malignant growth. Nevertheless, further experiments are required to prove whether the role of *GINS1* in the pathogenesis of COAD involves other members of the CMG (Cdc45-MCM-GINS) complex.

## 5. Conclusion

Fundamentally, our study demonstrates that *GINS1* overexpression in COAD is firmly connected with poor overall survival, promoter methylation levels, and genetic mutations. Through a deliberate usage of different public data sets including UALCAN, cBioPortal, and KM plotter, we have revealed insight into the symptomatic, prognostic, and possibly helpful role of *GINS1* in COAD. Notwithstanding, further exploration is justified to approve and affirm these findings, as well as to explain the hidden components driving *GINS1* dysregulation in COAD. These experiences may at last contribute to the development of improved diagnostic tools and therapeutic procedures for COAD patients.

## Disclosure statement

The authors declare no conflict of interest.

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