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PARP1 regulates epigenetic processes through DNMT1 and UHRF1 in oxaliplatin-treated colon cancer cells

Oxaliplatin uygulanan kolon kanseri hücrelerinde PARP1, DNMT1 ve UHRF1 üzerinden epigenetik olayları düzenler

Venhar Gürbüz Can[1] Tansu Kusat[2]

[1]Karabuk University, Faculty of Medicine, Department of Medical Biology Karabuk-Türkiye
[2] Karabuk University Faculty of Medicine, Department of Histology and Embryology Karabuk-Türkiye

ABSTRACT

Aim: Colon cancer is the second most commonly diagnosed cancer among females and the third most frequently diagnosed cancer among males worldwide. Epigenetics is described as alterations in gene expression without changes in nucleotide sequence. Epigenetic mechanisms can modulate the activation or inactivation of cancer-associated genes. The aim of our study was to demonstrate the epigenetic effect of *PARP1, DNMT1, and UHRF1* genes in oxaliplatin-treatment colon cancer cell line.

Materials and Methods: HT-29 cells were cultured in suitable medium. Then, when the cells were grown up to a certain number, oxaliplatin was applied for 24, 48, and 72 hours at doses of 2.5, 5, 10, 25, 50, 100, and 200 µM to the HT-29 cells, and Cell viability was detected by XTT test. Following the completion of the XTT test, *PARP1, DNMT1, and UHRF1* gene expression levels were analyzed by the real-time PCR method.

Results: Our results revealed that Oxaliplatin significantly suppressed the expression of *UHRF1 and DNMT1* in colon cancer cells, whereas it significantly stimulated the expression of *PARP1*.

Conclusion: In conclusion, the data obtained indicates that the UHRF1, PARP1 and DNMT1 genes may function as modulators of the epigenome and that DNMT1 and UHRF1 interact negatively with PARP1. This study has demonstrated the potential of the UHRF1, PARP1 and DNMT1 genes as targets for colon cancer treatment and as candidate biomarkers.

Keywords: PARP1, DNMT1, UHRF1, Epigenetic, Colon Cancer, HT-29

ÖZ

Amaç: *Kolon kanseri dünya genelinde kadınlarda en sık görülen ikinci, erkeklerde ise en sık görülen üçüncü kanser türüdür. Epigenetik, nükleotid diziliminde değişiklik olmaksızın gen ifadesinde meydana gelen değişiklikler olarak tanımlanmaktadır. Kanserle ilişkili genlerin aktivasyonu veya inaktivasyonu epigenetik mekanizmalarla modüle edilebilmektedir. Çalışmamızın amacı, oksaliplatin ile tedavi edilen kolon kanseri hücre hattında PARP1, DNMT1 ve UHRF1 genlerinin epigenetik etkisini gösterebilmektir.*

Gereç ve Yöntem: *HT-29 hücreleri uygun besiyeri ortamında kültüre edilmiş, daha sonra, belirli bir sayıya kadar büyütüldüğünde, hücrelere 2.5, 5, 10, 25, 50, 100, 200 µM dozlarında ve 24, 48 ve 72 saat boyunca oksaliplatin uygulanmıştır. Uygulama sonrasında, hücre canlılığı XTT yöntemi ile tespit edilmiştir. XTT yönteminin tamamlanmasını takiben, PARP1, DNMT1 ve UHRF1 genlerinin ekspresyon seviyeleri gerçek zamanlı PCR yöntemi ile analiz edilmiştir.*

Corresponding author: Venhar Gürbüz Can
Karabuk University, Faculty of Medicine, Department of Medical Biology Karabuk-Türkiye
E-mail: *venhargurbuz@karabuk.edu.tr*

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Bulgular: *Oxaliplatinin kolon kanseri hücrelerinde UHRF1 ve DNMT1 ekspresyonunu önemli ölçüde baskıladığını, PARP1 ekspresyonunu ise önemli ölçüde uyardığını ortaya koymuştur.*

Sonuç: *Elde ettiğimiz veriler ışığında UHRF1, PARP1ve DNMT1 genlerinin epigenomun bir modülatörü olarak işlev görebileceğini ve DNMT1 ve UHRF1 genlerinin PARP1geni ile negatif korelasyon gösterdiğini tespit ettik. Bu çalışma, UHRF1, PARP1 ve DNMT1'in kolon kanseri tedavileri için potansiyel hedef ve aday biyobelirteçler olarak belirlenebileceğini göstermiştir.*

Anahtar Sözcükler: *PARP1, DNMT1, UHRF1, Epigenetik, Kolon kanseri, HT-29*

INTRODUCTION

Oxaliplatin is a third-generation platinum drug that is utilized as a first-line chemotherapy agent for the treatment of colorectal cancer. Colorectal cancer is a serious disease that is caused by malignant changes in the colorectal mucosa as a result of various environmental and genetic factors. The incidence of colorectal cancer is increasing annually and is observed in younger patients [1]. Epigenetics is a field of scientific study that focuses on the reversible alterations in gene expression that occur without any change in the DNA sequence [2]. It is evident that epigenetic mechanisms play a pivotal role in the maintenance of normal development and tissue-specific gene expression patterns in mammals. Alterations in epigenetic processes have been demonstrated to result in the differentiation of gene function and malignant cellular transformation, which is a hallmark of cancer. It is now widely acknowledged that, in contrast to the traditional perspective that viewed cancer as purely a genetic disease, the initiation and progression of cancer are also influenced by epigenetic changes in addition to genetic alterations. Recent advancements in the field of cancer epigenetics have demonstrated that all components of the epigenetic machinery in cancer are comprehensively reprogrammed. This includes DNA methylation, histone modifications, nucleosome position, and non-coding RNA, especially microRNA expression [3].

It is evident from the extant literature that the *UHRF1* (ubiquitin-like with plant homeodomain and RING finger domains 1) gene is an epigenetic modification factor. The results of several studies demonstrate that *UHRF1* recognizes hemi-methylated DNA at DNA replication forks and assists DNA methylation of *DNMT1* [4]. In the context of mammalian cells, the role of *UHRF1* is to facilitate the formation and maintenance of DNA methylation patterns [5]. It has been established that *UHRF1* and *DNMT1* act in a coordinated manner to induce promoter hypermethylation of tumor suppressor genes. This process results in a reduction in gene expression and the subsequent inhibition of cellular apoptosis [6]. The *UHRF1* gene is known to be overexpressed in a variety of cancers, and it has been demonstrated to play an oncogenic role [7].

DNA methylation is catalyzed by the DNA methyltransferase family (*DNMT*s) and involves the transfer of a methyl group from S-adenyl methionine (SAM) to the fifth carbon of a cytosine residue, forming 5mC. *DNMT3a and DNMT3b* are known as de novo DNMTs. Conversely, *DNMT1* exerts its function during DNA replication, ensuring the transmission of the DNA methylation pattern from the parental DNA strand to the newly synthesized daughter strand [8]. Dysregulation of DNA methylation has been demonstrated to result in the silencing of tumor suppressors or the expression of oncogenes, thus contributing to the development of numerous diseases, including cancer. In contrast to genetic alterations, however, DNA methylation changes are capable of being reversed through the use of methylation inhibitors. Consequently, this can result in the reactivation of tumor suppressor genes and the downregulation of overexpressed oncogenes. Furthermore, this process can elicit therapeutic effects by stimulating the immune response against cancer cells [9].

Poly (ADP-ribose) polymerase-1 (PARP-1) is a nuclear enzyme that belongs to the DNA damage surveillance system and is a key member of the PARP superfamily. PARP-1 plays a key role in maintaining genome stability and regulating chromatin structure, and it is also involved in some DNA repair mechanisms. Alterations in PARP-1 levels play an important role in colorectal cancer [10].

The genes selected for our study are a group of genes that have been identified as being located within the epigenome. It has been demonstrated that dysregulation of these genes can result in disruption of epigenetic pathways within the cell.

This disruption has the potential to trigger carcinogenesis. The chemo-neuropathic drug (oxaliplatin) employed in the treatment of colon cancer was utilized to observe the functionality of these genes in the epigenome and the manner in which they affect each other. The objective of this study was to ascertain the impact of the treatment on the expression levels of these genes implicated in the epigenetic mechanism, to elucidate the potential interactions between these genes, and to demonstrate the efficacy of this epigenetic pathway following treatment.

MATERIALS AND METHODS

Cell culture: The HT-29 (ATCC: HTB-38) colon cancer cell line was transferred to cell culture dishes measuring 25 cm². The cells were cultivated in DMEM medium containing 20% fetal bovine serum (FBS), 1% penicillin-streptomycin and 1% L-glutamine. The culture environment was maintained at 37°C in a 5% CO_2 incubator until a sufficient cell concentration was reached. If necessary, the medium was replaced with one containing 10% FBS, 1% Pen-Strep, 1% L-Glutamine. During the process of cell initiation, 20% FBS was utilized, while 10% FBS was employed during the viability testing phase.

Cell Proliferation (XTT) assay: The cells under investigation were divided into two groups: one group was subjected to treatment with oxaliplatin, while the other group was not treated (i.e. the control group). Following treatment of HT-29 cells with oxaliplatin (purchased from Yunbang Bio., with a solubility of 5mg/mL in water), cell viability was evaluated by XTT assay. Cells were seeded in 96-well culture plates at a cell density of $1x10^4$ cells per well. Oxaliplatin concentrations of 2.5, 5, 10, 25, 50, 100 and 200 µM were applied for 24, 48 and 72 hours. At the end of the treatment period, 25 µL of XTT solution (XTT Cell Viability Kit, Biotium, Inc.) was added to each well. The signal absorbance value was obtained by reading at a wavelength of 570 nm in a Heales MB-580 device. The 630 nm wavelength was utilized for the purpose of background absorption measurement. The normalized absorbance value was obtained by subtracting the background absorbance value from the signal absorbance value. The wells containing only medium (no cells) were determined as blank and the OD value was subtracted from the OD value of all other wells. The cell viability rate of the wells designated as negative control was evaluated as 100%, the rate of the wells designated as positive control (Group containing only cells and medium) was evaluated as 0%, and the viability rates and IC50 doses of the cells in the other wells were calculated. The IC50 value is the concentration of a compound at which 50% of cell viability is inhibited. Because of this, the lower the IC50 value, the smaller the amount required to achieve the desired effect, and the probability of off-target effects is reduced. For this reason, the IC50 dose was established at 50 µM.

RNA extraction: The cells were cultivated until a defined cell number was attained, after which they were seeded in 6-well plates, with each plate containing three replicates. The plates were then removed from the incubator after 24 hours of incubation, according to the determined IC50 dose and time (IC50 50 µM and 24 hours). Following the incubation period, the cells were removed from the plate surface using a cell scraper, collected with the medium, and subjected to centrifugation at 4000 rpm for 10 min at 4°C. Subsequent to centrifugation, the upper layer was meticulously separated without contacting the cell pellet. 1.5 mL Eppendorf tubes were then employed for RNA isolation. The process of RNA isolation was conducted in accordance with the manufacturer's instructions using the TRIzol reagent (RiboEx Kit; GeneAll Biotechnology, Seoul, Korea). The Trizol stage was utilized as the inaugural step, i.e. the lysis stage, to enhance the efficiency of the isolation process. Subsequently, we continued with the spin column method. The isolation of total RNA was accomplished through the utilization of an RNA isolation kit that employed the spin column technique (GeneAll Biotechnology, Hybrid-R, Seoul, Korea). Subsequently, the concentration and purity of the isolated RNA were measured using the device Quibit (Invitrogen, Qubit4 Fluorometer). The synthesis of cDNA from the isolated total RNAs for use in RT-PCR was initiated.

cDNA synthesis: The analysis was performed using a cDNA synthesis kit (ABT, cDNA Synthesis Kit with Rnase Inh. High Capacity, Turkey). The master mix was prepared as 2 µl of 10X Reaction Buffer, 1 µl of 20X dNTP mix, 2 µl of Random hexamer, 1 µl of RTase, 0.5 µl of RNase Inhibitor, 3.5 µl of RNase-free Water, and 10 µl of Sample were added, resulting in a total volume of 20 µl. Subsequent to this, reverse transcription was analyzed using a ProFlex thermal cycler at 25 °C for 10 min, 37 °C for 120 min and 85 °C for 5 min

(1 cycle). The synthesized cDNA samples were then stored at -80 °C.

Quantitative real time PCR: For the Real-Time PCR analysis, the master mix was prepared in accordance with the manufacturer's instructions (ABT, 2X SYBR Mastermix, Turkey), comprising 10 µl of 2X MasterMix (with SYBR-Green), 1 µl of ROX D ye, 1 µl of Forward Primer (10 µM), 1 µl of Reverse Primer (10 µM), 4 µl of cDNA Template, 3 µl of RNase-Free distilled water, totalling 20 µl.The reaction was performed on an Applied Biosystems QuantStudio-5 Real-Time PCR device. The reaction was initiated with an initial denaturation step at 95 °C for 300 seconds, followed by 40 cycles of denaturation at 95 °C for 15 seconds and an annealing step at 60 °C for 60 seconds. The samples were run in triplicate, and the primers utilized are outlined in Table-1. GAPDH was used as a reference gene in qPCR. The normalization of mRNA expressions was conducted in accordance with the control group. The '∆∆Ct Method' was utilized for the calculation of relative quantities.

Table-1. Primer sequences used for RT-PCR

Name	Primer sequences 5'-3'
HS-*UHRF1*-F	GTTCTACAGGGGCAAACAGA
HS-*UHRF1*-R	ATTCCGTCTCATCCCACA
HS-*DNMT1*-F	TTGGTGGATGAATGTGAGGA
HS-*DNMT1*-R	CTCTGTTGGCTGGGTTTTTG
HS-*PARP-1*-F	CACCAAAAAGGAGGTGGAAA
HS-*PARP-1*-R	CAACTCCTGAAGGCTCTTGG
HS-*GAPDH*-F	AGGGCTGCTTTTAACTCTGGT
HS-*GAPDH*-R	CCCCACTTGATTTTGGAGGGA

Statistical analysis

Statistical analysis of the data was conducted utilizing IBM SPSS 25.0 (Chicago, IL, USA) and GraphPad Prism 8.02 (San Diego, CA, USA). Data were acquired from at least three different experiments and are expressed as mean ± standard deviation (SD). The normality of the data distribution was evaluated using the Shapiro–Wilk test ($P > 0.05$). A one-way analysis of variance (ANOVA) followed by Tukey's post hoc test was employed to assess statistically significant differences in gene expression of DNMT1, PARP1, and UHRF1 among the experimental groups. Furthermore, Student's t-test was utilized to compare the two groups (control vs. oxaliplatin), notably to improve the clarity and visual distinction of graphical representations of different genes. A two-way analysis of variance (ANOVA) accompanied by Tukey's post hoc test was employed to assess cell viability (XTT assay) in HT-29 cells. P-value below 0.05 was deemed statistically significant.

RESULTS

Colon cancer cell lines (HT-29) were exposed to various doses of oxaliplatin, and the XTT method was employed to ascertain time- and dose-dependent cell viability. As illustrated in Figure-1, the graphs demonstrate the relationship between the applied dose and the corresponding cell viability rates. The IC50 value was subsequently calculated using these graphs. The effects of the determined IC50 dose on the gene expressions of *PARP1*, *UHRF1,* and *DNMT1* were investigated. In the experiment of the HT-29 cell line, an experimental design was employed, whereby the control and oxaliplatin dose groups were subjected to meticulous analysis in three replicates for each plate. The findings, obtained at the 24-hour time point following the administration of 200, 100, and 50 µM oxaliplatin doses, revealed a significant decline in cell viability within the HT-29 cell line when compared to the control group. This decline was found to be statistically significant ($P < 0.05$). Moreover, the findings of XTT analysis demonstrated that 200 and 100 µM oxaliplatin doses administered at 48 and 72 hours, respectively, exerted a negative effect on cell viability in the HT-29 cell line in comparison to the control group, and a statistically significant difference was observed between the two groups ($P<0.05$). These results indicated that oxaliplatin treatment impeded cell growth in colon cancer in a dose- and time-dependent. The HT-29 cell line was selected for the evaluation of the role of *PARP1*, *UHRF1,* and *DNMT1* in colon cancer cells. Alterations in gene expression levels were determined by applying an appropriate dose of oxaliplatin. *DNMT1*, *PARP1,* and *UHRF1* expression levels were found to be statistically significantly different between the HT-29/oxi (oxaliplatin treatment group) and HT-29/control groups ($P<0.05$) (Table-2). The data presented herein are expressed as the mean ± standard deviation, with these values obtained from three independent replicates.

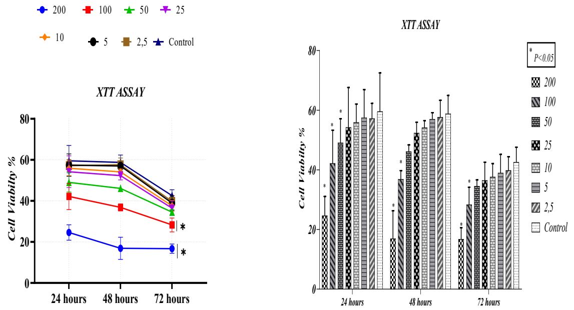

Figure-1. The dose- and time-dependent rates of cell viability.

Table-2. Results of One-Way analysis of variance of *DNMT1*, *PARP1, and UHRF1* genes in oxaliplatin-treated HT-29 cells (Abbreviation: Sig: Significant, Df: Degree of Freedom, F: F value)

ANOVA						
		Sum of Squares	df	Mean Square	F	Sig.
DNMT1	Between Groups	4.788	1	4.788	10.788	0.030
	Within Groups	1.775	4	0.444		
	Total	6.564	5			
PARP1	Between Groups	0.714	1	0.714	111.586	0.000
	Within Groups	0.026	4	0.006		
	Total	0.740	5			
UHRF1	Between Groups	4.133	1	4.133	94.514	0.001
	Within Groups	0.175	4	0.044		
	Total	4.308	5			

A statistically significant alteration in the expression levels of *DNMT1*, *PARP1,* and *UHRF1* genes was observed between the HT-29/oxi and HT-29/control groups (P< 0.05). Moreover, the investigation revealed that the UHRF1 gene expression level in HT-29/control cells was found to be higher than the gene expression level in HT-29/oxi cells. This difference was found to be statistically significant (P < 0.05). It was established that oxaliplatin was able to inhibit the expression of *UHRF1* in colon cancer cells (HT-29). A statistically significant increase in the *DNMT1* gene expression level was observed in HT-29/control cells in comparison to HT-29/oxi cells (P<0.05), as was the case with the *UHRF1* gene. In this study, we demonstrated that oxaliplatin inhibited the expression of *DNMT1* in colon cancer cells (HT-29). A significant decrease in the *PARP1* gene expression level was observed in HT-29/control cells compared to HT-29/oxi cells (P<0.05). Our findings suggest that oxaliplatin stimulates *PARP1* expression in colon cancer cells (HT-29) (Figure-2). An opposite relationship was identified between the expression of the PARP1 gene and the expression levels of DNMT1 and UHRF1.

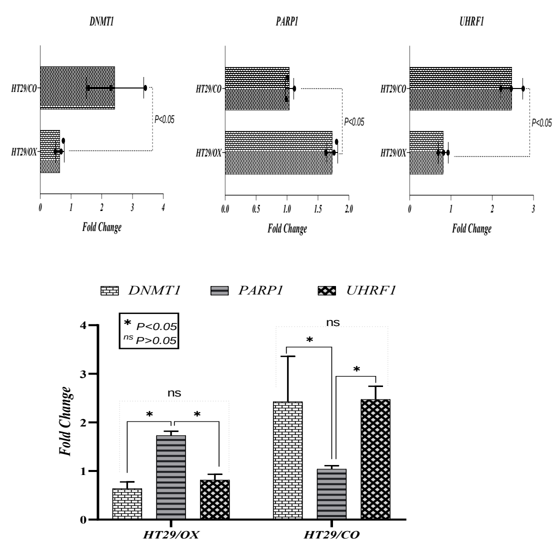

Figure-2. Altered *DNMT1*, *UHRF1* and *PARP1* expression level in HT-29 cells. Abbreviation: ns, not significant (P > 0.05).

Figure-2, provides the alterations observed between to studied genes of the HT-29/control and HT-29/oxi cell lines. The results of this study indicate a statistically significant relationship between *DNMT1*/*PARP1 and UHRF1*/*PARP1 genes* in HT-29/control cells (P<0.05). However, no statistically significant difference was observed between *DNMT1* and *UHRF1* (P>0.05). In a similar manner, statistical significance was identified in HT-29/oxi cells between the *DNMT1*/*PARP1 and UHRF1*/*PARP1 genes* (P<0.05), while no statistically significant difference was observed between *DNMT1* and *UHRF1* (P>0.05). *DNMT1* and *UHRF1* gene expression levels were found to be significantly elevated in HT-29/control cells. Conversely, *PARP1 gene* expression level was found to be significantly reduced (P<0.05). On the other hand, in HT-29/oxi cells, *DNMT1* and *UHRF1* gene expression levels were found to be significantly reduced, while *PARP1 gene* expression level was significantly increased (P<0.05).

UHRF1 is an epigenetic factor that exerts its regulatory function over transcription processes by modulating DNA methylation and histone modification [11]. *UHRF1* has been identified as a pivotal regulator of the epigenome, with the capacity to orchestrate processes involving methylation and histone modifications [12]. The SRA domain of *UHRF1* has been demonstrated to bind *DNMT1*, *HDAC1*, *PARP1,* and hemi methylated DNA [13]. Recent studies have indicated a correlation between elevated *UHRF1* levels and increased cellular proliferation, which has been detected in various cancer types, including colorectal cancer. Moreover, *UHRF1* has been observed to bind to methylated promoters of numerous tumor suppressor genes, forming complexes with *DNMT1* and *HDAC1*, a process that is believed to play a pivotal role in the development of cancer [14]. A multitude of studies have demonstrated that the *UHRF1* gene exhibits elevated levels of expression in cancerous cells, a phenomenon that is analogous to our own observations [14-18]. The majority of tumor cells exhibit elevated levels of *UHRF1*, and the over-expression of this gene is oncogenic. *UHRF1* is a critical regulator of the epigenome, playing a pivotal role in the maintenance of DNA methylation patterns in colon cancer cells and ensuring their survival. Therefore, *UHRF1* is an important regulator of the cancer epigenome, and it is highly important to elucidate its role for both basic research and medical purposes [16]. As demonstrated in the study by Wang et al., an increase in the expression levels of the *UHRF1* and GLI1 genes has been observed in hepatocellular carcinoma tissues. This upregulation has been shown to be an indicator of a poor prognosis [15]. Seo et al. (2017) found that *DNMT1* mRNA was highly expressed in colon cancer cells, especially in HCT-116 cells. Furthermore, they discovered that protein expression of *DNMT1*, as well as *UHRF1*, decreased in HCT-116 cells after treatment with hinocitol [14]. Similarly, another study found that *UHRF1* expression was significantly higher in colorectal cancers than in normal colon tissue [19]. The *DNMT1-UHRF1* expression axis has been observed to be dysregulated in the context of malignant transformation and progression across various cancer types. A study conducted in 2020 highlighted a positive correlation between increased *UHRF1* levels and those of *DNMT1* in colorectal cancer cases [5]. The study by Foran et al. demonstrated over-expression of *DNMT1* in colon cancers [20]. A further study highlighted the significance of *DNMT1* in the perpetuation of human colon cancer, asserting that its temporary suppression is adequate for the eradication of this condition. Additionally, it was posited that such suppression would render the disease more amenable to treatment with chemotherapy or radiotherapy [21]. In our study, we similarly demonstrated that Oxaliplatin significantly suppressed the expression of *UHRF1* and *DNMT1* in colon cancer cells (HT-29). Furthermore, the gene expression level of *UHRF1* and *DNMT1* in HT-29/control cells was statistically significantly higher than the gene expression level in HT-29/oxi cells. These results indicated that *UHRF1* and *DNMT1* could be identified as potential target for colon cancer therapies.

PARP-1 is a nuclear enzyme that is characterized by its high degree of conservation. It has been demonstrated to bind tightly to DNA, and to play a role in a number of processes, including DNA repair, recombination, proliferation and genomic stability [22]. Upregulated expression of the DNA repair enzyme, *PARP1*, has been observed in various carcinomas, including breast cancer, ovarian cancer, and lung cancer. Furthermore, the expression levels of *PARP1* vary significantly among these cancers [23]. Evidence has emerged demonstrating an increase in the expression of the gene in cases of colon cancer [24]. The observation of *PARP1* upregulation in various cancers and their subtypes is of significance for the potential increase in the utilization of PARP inhibitors to target a broad spectrum of human cancers [25]. A study identified that both *PARP1* and *UHRF1* act in common chromatin-associated pathways and share *DNMT1* as a protein partner, as well as modulator and regulator of *UHRF1* and *DNMT1*. It was emphasized that *PARP1* helps *UHRF1* to maintain its association with *DNMT1* and that *UHRF1* is a negative regulator of ubiquitin ligase activity on *DNMT1*. Furthermore, it has been demonstrated that the loss of *PARP1* proteins results in the disruption of the interaction between *UHRF1* and *DNMT1*, consequently leading to the repression of transcription in heterochromatic domains [26]. As posited by Hahm et al., the methylation status of *UHRF1* exerts a regulatory influence on its interaction with *PARP1* [27]. Furthermore, *PARP1* has been demonstrated to regulate DNA methylation patterns through a dual mechanism involving the modulation of *DNMT1* expression and activity [28]. Ciccarone et al. posit that *UHRF1* is a *DNMT1*-interacting protein, and that it is involved in the maintenance of heterochromatin CG methylation. Furthermore, *PARP1* facilitates the interaction between *DNMT1* and *UHRF1*, and promotes its stabilization by counteracting *UHRF1*-mediated ubiquitination of *DNMT1* [29]. Dörsam et al. emphasised the multifaceted role of *PARP1 in* colorectal cancer, highlighting its potential to both benefit and harm. Their findings revealed that *PARP1 exerts* a dual effect on colorectal carcinogenesis, counteracting tumour initiation while concurrently promoting tumour growth [10]. A study was conducted that yielded findings that indicated that *PARP1* increases oxaliplatin resistance in cases of gastric cancer [30]. A considerable body of research has demonstrated that the combination of a *PARP1* inhibitor and oxaliplatin enhances sensitivity to oxaliplatin [31, 32]. In a study by Li et al. in 2021, oxaliplatin was found to inhibit the growth of oral squamous cell carcinoma cells, and this was accompanied by increased expression of *PARP1* [33].

In our study, it was similarly demonstrated that oxaliplatin stimulated *PARP1* expression in colon cancer cells (HT-29). Furthermore, a statistically significant decrease in *PARP1* gene expression was observed in HT-29/control cells in comparison to HT-29/oxi cells. These findings suggest that *PARP1* could be identified as a potential target for colon cancer treatments.

CONCLUSION

In conclusion, the present study has demonstrated that oxaliplatin inhibited the cell viability of colon cancer cells and induced cell death in vitro. Furthermore, oxaliplatin also inhibited the expression of *UHRF1* and *DNMT1* in colon cancer cells (HT-29), whereas it stimulated the expression of *PARP1*. The results of our investigation revealed a negative association between the aforementioned genes, which suggests a potential therapeutic approach for colon cancer treatment. Specifically, our findings indicate that *UHRF1*, *PARP1*, and *DNMT1* could serve as viable targets for colon cancer therapies, with the potential to enhance patient prognosis and survival rates. This observation underscores the importance of these genes as promising biomarkers for diagnostic, prognostic, and survival assessment in clinical settings. The present study is limited in scope due to its experimental design, which was performed in a single cell line and may not be representative of all colorectal cancer types. Furthermore, the study is an in vitro experiment; therefore, further in vitro and in vivo experiments are needed to provide more comprehensive evidence. It is important to note that due to limitations in the budget, it was not performed verification at the protein level.

Conflict of interest: The author declared no conflict of interest.

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