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Gene-Level Modulation of Apoptosis in the Colon under Intermittent Fasting Conditions

Aralıklı Oruç Koşullarında Kolon Dokusunda Apoptozisin Gen Düzeyinde Modülasyonu

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Gene-Level Modulation of Apoptosis in the Colon under Intermittent Fasting Conditions

ABSTRACT

Intermittent fasting (IF) has gained recognition as a metabolic strategy with significant impacts on cellular stress pathways, including apoptosis. This study examined the transcriptional regulation of key apoptotic genes in colon tissue following an intermittent fasting regimen. Twelve-month-old male Wistar rats were subjected to an 18-hour daily fasting protocol for 35 consecutive days. The control group had *ad libitum* access to food and water. Quantitative real-time PCR analysis was employed to evaluate mRNA expression levels of anti-apoptotic genes B-cell lymphoma 2 (BCL-2) and B-cell lymphoma-extra-large (BCL-XL) and pro-apoptotic mediators BCL-2 homologous antagonist/killer (BAK), BCL-2-associated X protein (BAX), and Cysteine-aspartic acid protease 3 (Caspase-3). IF significantly increased BCL-2 and BCL-XL expression while concurrently downregulating BAK, BAX, and Caspase-3. These findings indicate that intermittent fasting induces a transcriptional shift that reduces apoptotic susceptibility in colon, thereby promoting a cytoprotective phenotype. The results underscore IF as a potential non-pharmacological intervention to enhance colonic resilience during aging, supporting its application in mitigating age-related apoptotic and metabolic dysregulation at the molecular level.

Keywords: Intermittent fasting, Apoptosis, Bcl-2 family genes, Colon gene expression, Wistar rat

Highlights

- Intermittent fasting reduces apoptotic susceptibility in aged rat colon tissue.
- IF increased anti-apoptotic BCL-2 and BCL-XL mRNA expression.
- IF decreased pro-apoptotic BAK, BAX, and Caspase-3 expression
- These changes indicate suppression of the intrinsic apoptotic pathway.
- IF may support colonic cellular resilience during aging.

Aralıklı Oruç Koşullarında Kolon Dokusunda Apoptozisin Gen Düzeyinde Modülasyonu

ÖZ

Aralıklı açlık (IF), apoptoz dâhil olmak üzere hücrel stres yolları üzerinde belirgin etkiler gösteren bir metabolik strateji olarak giderek daha fazla kabul görmektedir. Bu çalışma, aralıklı açlık protokolü sonrasında kolon dokusunda temel apoptoz genlerinin transkripsiyonel düzenlenmesini incelemiştir. On iki aylık erkek Wistar sıçanları, 35 gün boyunca günlük 18 saatlik açlık rejimine tabi tutulmuştur. Kontrol grubu yem ve suya *ad libitum* erişime sahipti. Anti-apoptotik genler olan B-cell lymphoma 2 (BCL-2) ve B-cell lymphoma-extra-large (BCL-XL) ile pro-apoptotik düzenleyiciler olan BCL-2 homologous antagonist/killer (BAK), BCL-2-associated X protein (BAX) ve Cysteine-aspartic acid protease 3 (Caspase-3) genlerinin mRNA ekspresyon düzeyleri, kantitatif gerçek zamanlı PCR ile analiz edilmiştir. Aralıklı açlık, BCL-2 ve BCL-XL genlerinin ekspresyonunu anlamlı düzeyde artırırken, BAK, BAX ve Caspase-3 ekspresyonlarını ise belirgin şekilde azaltmıştır. Bu bulgular, aralıklı açlığın kolon dokusunda apoptotik duyarlılığı azaltan bir transkripsiyonel değişimi tetiklediğini ve böylece hücrel koruyucu bir fenotip oluşturduğunu göstermektedir. Sonuçlar, aralıklı açlığın yaşlanma sürecinde kolon dokusunun dayanıklılığını artırmaya yönelik farmakolojik olmayan bir müdahale olarak potansiyelini vurgulamakta ve moleküler düzeyde yaşa bağlı apoptoz ve metabolik düzensizliklerin hafifletilmesinde uygulanabilirliğini desteklemektedir.

Anahtar Kelimeler: Aralıklı açlık, Apoptoz, Bcl-2 ailesi genleri, Kolon gen ekspresyonu, Wistar sıçanı

Öne Çıkanlar

- Aralıklı açlık, yaşlı rat kolon dokusunda apoptotik duyarlılığı azaltmıştır.
- Aralıklı açlık, anti-apoptotik BCL-2 ve BCL-XL mRNA ekspresyonunu artırmıştır.
- Aralıklı açlık, pro-apoptotik BAK, BAX ve Caspase-3 ekspresyonunu azaltmıştır.
- Bu değişiklikler, intrinsik apoptotik yolun baskılandığını göstermektedir.
- Aralıklı açlık, yaşlanma sürecinde kolonik hücrel dayanıklılığı destekleyebilir.

I. INTRODUCTION

Intermittent fasting (IF) has emerged as a nutritional strategy that has garnered increasing research interest in recent years due to its regulatory effects on metabolic health [1]. IF protocols have been demonstrated to influence a wide array of physiological processes, including energy metabolism, modulation of oxidative stress, mitochondrial biogenesis, and regulation of gene expression [2, 3]. Recent evidence indicates that fasting-mimicking and intermittent fasting regimens exert broad effects on metabolic regulation and cellular protection pathways, thereby promoting longevity and reducing the incidence of age-related diseases [4]. Notably, fasting periods exceeding 16 hours have been shown to enhance homeostatic balance by inducing autophagy and decelerating age-related degenerative processes [5, 6]. In 35-day experimental protocols employing an 18-hour daily fasting regimen, an increase in alpha diversity of the gut microbiota, a balanced Firmicutes/Bacteroidetes ratio, and improved microbial dysbiosis have been observed [7]. Furthermore, infrared spectrochemical analyses have indicated that IF induces significant biomolecular changes in myocardial tissue, such as an increase in saturated lipid levels, enhancement of membrane dynamics, and a reduction in protein oxidation [8]. Similarly, markers of oxidative damage decrease in colon and ileum tissues, while protein conformation is better preserved [9]. Collectively, these findings suggest that IF exerts systemic effects on multiple organ systems and functions as a pleiotropic regulator of cellular homeostasis.

Apoptosis is a crucial mechanism for maintaining tissue integrity, particularly sensitive to metabolic and oxidative stimuli in organs with high energy demands [10]. Members of the BCL-2 protein family serve as key regulators of the intrinsic apoptosis pathway by modulating mitochondrial outer membrane permeability [11]. Research indicates that calorie restriction and fasting protocols upregulate anti-apoptotic genes, such as BCL-2 and BCL-XL, while suppressing the expression of pro-apoptotic genes like BAX and BAK [12]. This transcriptional reprogramming mitigates mitochondrial destabilization and reduces the cell's susceptibility to programmed cell death. Furthermore, it has been reported that the activity of Caspase-3, the final effector molecule in apoptosis, decreases in many tissues following fasting regimens [13]. However, the literature predominantly examines the effects of intermittent fasting on apoptotic signaling pathways in young or early adult rodent models, with a notable lack of research on the regulation of apoptosis-related genes at the transcriptional level in aged organisms [14]. Recent studies have also shown that intermittent fasting enhances stress resistance and suppresses apoptotic signaling in several animal models of aging, suggesting a conserved mechanism linking fasting to improved cellular resilience and longevity [15].

This investigation focuses on elucidating the modulatory impact exerted by an intermittent fasting regimen, administered over a 35-day period in 12-month-old male Wistar rats, on the expression of key genes associated with apoptosis in colon tissue. The mRNA levels of anti-apoptotic genes, such as BCL-2 and BCL-XL, along with pro-apoptotic genes, including BAX, BAK, and Caspase-3, were quantitatively assessed using the RT-qPCR method. The primary hypothesis posits that intermittent fasting will induce a transcriptional reprogramming that promotes cellular survival by inhibiting apoptotic signalling pathways in colon tissue. The findings elucidate the colon's adaptive response to metabolic stress at the molecular level and offer significant mechanistic insights into the role of intermittent fasting in molecular plasticity during the aging process.

II. MATERIAL AND METHODS

A. Animal Studies

Twelve-month-old male Wistar rats were selected as the experimental model for this investigation. The experimental group (n=7) was subjected to an intermittent fasting regimen lasting 35 consecutive days. Throughout the protocol, animals in this group had unrestricted access to water, but their food intake was limited to a 6-hour daily window, specifically between 09:00 a.m. and 03:00 p.m., during which they were provided with a standard laboratory chow. Unlike the experimental group, control animals (n=7) had unrestricted access to standard chow and water throughout the entire 24-hour cycle. The dietary protocol followed was consistent with our previous experimental design [16]. Although seven animals were included in each group, five samples were randomly selected for gene expression analysis, and each was analysed in triplicate. Upon completion of the 35-day intervention, all rats were lightly anesthetized using ether prior to euthanasia. Colon tissues were promptly

excised, flash-frozen using dry ice, and stored at -80°C for subsequent molecular analyses. All procedures were conducted under standard housing and care conditions for laboratory animals, in compliance with ethical standards and with formal approval granted by the Institutional Animal Care and Use Committee of Saki Yenilli (Protocol No: 2021/05).

B. Tissue-Derived RNA Purification and Reverse Transcription Protocol

Colon samples served as the source for total RNA extraction using a standardized purification protocol utilizing the GeneAll® Hybrid-R™ isolation kit (Catalog No: 305-101, Korea), following the standard protocol recommended by the manufacturer. The quality and quantity of the isolated RNA were evaluated using a 96-well microplate reader in conjunction with NanoDrop QC SkanIt 4.1 software. Complementary DNA (cDNA) synthesis was subsequently carried out using the SuScript First Strand cDNA Synthesis Kit (Cat. No: RT01A025, Turkey). The reverse transcription procedure included an initial denaturation phase at 70°C for 5 minutes, an enzymatic reaction at 42°C for one hour, after which enzymatic activity was halted by heating to 80°C for 5 minutes to inactivate the enzyme. These thermal incubation steps were performed on a Sensoquest Labcycler thermocycler equipped with a 96-well gold-plated silver thermoblock (Model: 012-103, Germany). The resulting cDNA products were preserved at -20°C to ensure stability for downstream gene expression analyses, consistent with our previously established methodology [9].

C. Design of Target-Specific Primers and Relative Gene Expression Assessment

All primer sequences were designed through the Primer3 platform (<http://primer3.ut.ee/>), ensuring specificity for the target genes. Quantitative real-time PCR (qPCR) reactions were conducted using the SuScript 1-Step SYBR qPCR Kit (Catalog No: RT01A046, 200 reactions, Ankara, Turkey) on the Rotor-Gene Q instrument (QIAGEN, Hilden, Germany), with a total reaction volume of $10\ \mu\text{L}$ dispensed into $0.1\ \text{mL}$ strip tubes. The thermal amplification protocol began with an initial incubation at 50°C for 2 minutes, followed by enzyme activation at 95°C for 1 minute. The subsequent amplification phase included 40 cycles consisting of denaturation at 95°C for 10 seconds and annealing/extension at 60°C for 30 seconds. Glyceraldehyde-3-phosphate dehydrogenase (GAPDH) served as the internal reference gene to normalize expression levels. Although the classical $2^{-\Delta\Delta\text{CT}}$ method [17] provided the conceptual foundation for the analysis, an adapted normalization strategy was implemented to enhance the statistical interpretability of individual biological samples. Within each sample, gene expression was first assessed by calculating the difference in cycle threshold values between the gene of interest and the internal calibrator. This ΔCT value was then adjusted using the average value observed in the control group to enable direct cross-sample evaluation. This refined normalization approach allowed for direct statistical comparison of biological replicates, preserving intra-group variability and enabling the visualization of individual data points—a strategy particularly advantageous in experiments with limited sample sizes. By avoiding excessive reliance on group means, this method facilitates a more nuanced interpretation of biologically relevant variance [18]. The data analysis relied on ΔCT values normalized relative to control means, with final results derived and expressed from these calibrated inputs [16, 17]. The nucleotide sequences of the primers are shown in **Table 1**.

Table 1. Oligonucleotide sequences designed for each target gene.

Gene name	Elongation Position	Sequence (5'-3')	Reference
BCL2	Forward	GAGGATTGTGGCCTTCTTTG	[21]
	Reverse	AGGTACTCAGTCATCCACA	
BCL-XL	Forward	AGGATACAGCTGGAGTCAG	[22]
	Reverse	TCTCCTTGCTACGCCTTCC	
BAK	Forward	CCCAGGACACAGAGGAGGTTT	[23]
	Reverse	GCCTCCTGTTCCTGCTGATG	
BAX	Forward	ATGGAGCTGCAGAGGATGA	[21]
	Reverse	CCAGTTTGCTAGCAAAGTAG	
CASPASE-3	Forward	TGGTGATGAAGGGTCATTTAT	[24]
	Reverse	TTCGGCTTCCAGTCAGACTC	
GAPDH	Forward	TGGACCTCATGGCCTACATG	[25]
	Reverse	AGGGAGATGCTCAGTGTGG	

Note: GAPDH was used as a housekeeping reference.

D. Statistic

All statistical computations in this study were executed using GraphPad Prism version 10.0.1. All numerical outcomes are reported as arithmetic means with associated standardized deviation from the mean value (SEM), reflecting within-group variability. Differences in gene expression were statistically analyzed by applying a two-sided, unpaired Student's t-test, which assumes independent sampling. Findings with p-values

under 0.05 were regarded as statistically meaningful. Statistical outcomes were annotated according to the following threshold system: non-significant (ns) for p-values above 0.05; * for values below 0.05; ** for $p < 0.01$; *** for $p < 0.001$; and **** for results with p-values under 0.0001. Group labels were abbreviated as Cnt for the control group and IF for the intermittent fasting group.

III. RESULTS

A. The Effect of Intermittent Fasting on BCL2 Gene Expression

In the cohort subjected to intermittent fasting, there was a significant elevation in BCL-2 mRNA expression levels within colon tissue ($p = 0.001$) (**Figure 1**). This transcriptional upregulation of BCL-2, an anti-apoptotic gene, implies that intermittent fasting induces a molecular adaptation in colon that enhances protection against apoptosis. The marked difference observed in comparison to the control group suggests that cellular survival mechanisms under metabolic stress may be activated through BCL-2. This finding indicates that intermittent fasting could serve as a potential biological strategy for mitigating age-related sensitivity to apoptosis.

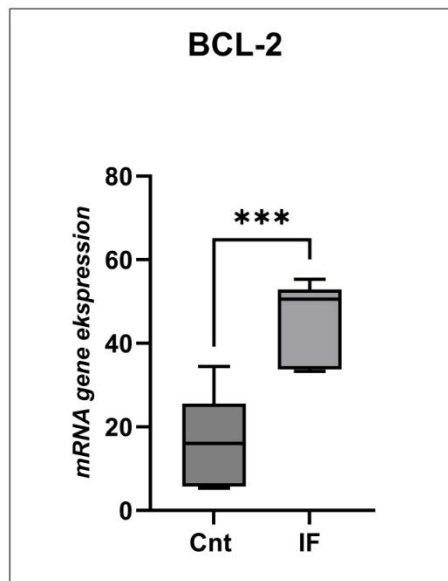


Figure 1. Relative mRNA expression levels of the apoptosis-associated gene BCL-2 following intermittent fasting intervention. Each data point reflects the mean $\pm$ SEM, calculated from a total of five biologically distinct samples, each measured in triplicate ($n = 5$, 3 technical replicates). Statistical evaluation was performed using an unpaired Student's t-test. A statistically significant difference between groups is indicated by *** ($p < 0.001$), denoting a highly significant change. Abbreviations: Cnt, control group; IF, intermittent fasting group.

B. The Effect of Intermittent Fasting on BCL-XL Gene Expression

In the cohort subjected to intermittent fasting, there was a statistically significant elevation in BCL-XL mRNA expression levels relative to those observed in the control group ($p = 0.0086$) (**Figure 2**). BCL-XL serves as a pivotal anti-apoptotic regulator, instrumental in inhibiting mitochondrial apoptosis and crucial for sustaining intracellular survival signals. This observation suggests that intermittent fasting enhances cellular integrity under metabolic stress by augmenting anti-apoptotic gene expression in colon tissue. The significance of this increase ($p < 0.01$) implies that intermittent fasting may mitigate age-related apoptotic sensitivity through BCL-XL. Consequently, intermittent fasting could be considered a viable molecular intervention strategy for reprogramming cellular stress responses.

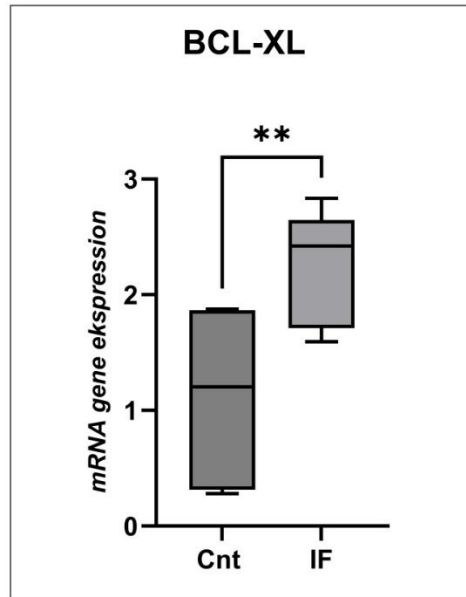


Figure 2. Relative mRNA expression levels of the apoptosis-associated gene BCL-XL following intermittent fasting intervention. Each data point reflects the mean $\pm$ SEM, calculated from a total of five biologically distinct samples, each measured in triplicate ($n = 5$, 3 technical replicates). Statistical evaluation was performed using an unpaired Student's t-test. A statistically significant difference between groups is indicated by *** ($p < 0.001$), denoting a highly significant change. Abbreviations: Cnt, control group; IF, intermittent fasting group.

C. The Effect of Intermittent Fasting on BAK Gene Expression

BAK mRNA expression levels were significantly reduced in the group subjected to intermittent fasting compared to the control group ($p = 0.0153$) (**Figure 3**). BAK, an apoptosis-inducing factor categorized under the BCL-2 protein family, plays a critical role in initiating the intracellular apoptosis process by increasing mitochondrial outer membrane permeability. This suppression observed in our study indicates that intermittent fasting inhibits the initiation mechanisms of apoptosis at the transcriptional level in colon tissue. This finding demonstrates that intracellular metabolic stress responses are reprogrammed by intermittent fasting, and that the sensitivity to apoptosis is reduced, thereby preserving colon integrity. The decrease in BAK gene expression can be considered a molecular reflection of the cytoprotective effects of intermittent fasting via the mitochondrial pathway.

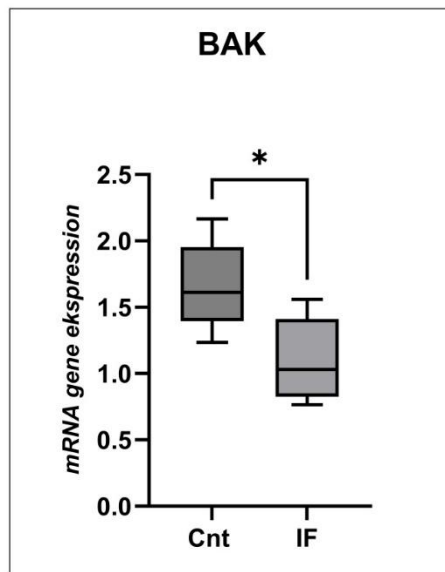


Figure 3. Relative mRNA expression levels of the apoptosis-associated gene BAK following intermittent fasting intervention. Each data point reflects the mean $\pm$ SEM, calculated from a total of five biologically distinct samples, each measured in triplicate ($n = 5$, 3 technical replicates). Statistical evaluation was performed using an unpaired Student's t-test. A statistically significant difference between groups is indicated by *** ($p < 0.001$), denoting a highly significant change. Abbreviations: Cnt, control group; IF, intermittent fasting group.

D. The Effect of Intermittent Fasting on BAX Gene Expression

The expression of BAX mRNA was significantly reduced in the group subjected to intermittent fasting (IF) compared to the control group ($p = 0.0253$) (**Figure 4**). BAX, an apoptosis-inducing factor categorized under the BCL-2 protein family, initiates apoptosis by inducing pore formation in the mitochondrial outer membrane, which leads to cytochrome c release and subsequent caspase activation. The observed decrease in BAX gene expression in this study suggests that intermittent fasting induces transcriptional reprogramming that reduces the propensity for apoptosis in colon. The suppression of BAX can be considered a crucial molecular indicator for the preservation of mitochondrial integrity and the acquisition of resistance to programmed cell death. When considered alongside the concurrent increase in anti-apoptotic genes such as BCL-2 and BCL-XL, the reduction in BAX expression supports the hypothesis that intermittent fasting establishes an anti-apoptotic genetic signature in colon tissue.

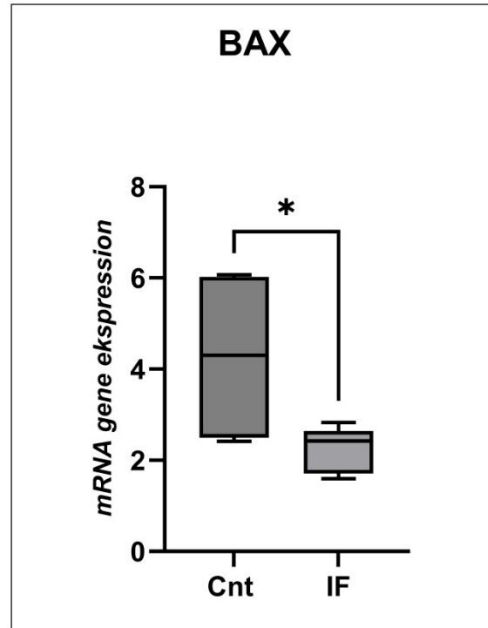


Figure 4. Relative mRNA expression levels of the apoptosis-associated gene BAX following intermittent fasting intervention. Each data point reflects the mean $\pm$ SEM, calculated from a total of five biologically distinct samples, each measured in triplicate ($n = 5$, 3 technical replicates). Statistical evaluation was performed using an unpaired Student's t-test. A statistically significant difference between groups is indicated by *** ($p < 0.001$), denoting a highly significant change. Abbreviations: Cnt, control group; IF, intermittent fasting group.

E. The Effect of Intermittent Fasting on Caspase-3 Gene Expression

Caspase-3, a principal effector caspase involved in the final phase of apoptosis, demonstrated significantly reduced expression levels in the group subjected to intermittent fasting compared to the control group ($p = 0.0102$; unpaired t-test). Although this reduction was not as substantial as that observed in the Bak and Bax genes, the significant decrease in Caspase-3 transcription indicates a suppression of apoptotic signal transduction. This phenomenon can be attributed to a reduction in upstream pro-apoptotic stimuli and suggests that intermittent fasting exerts a comprehensive genetic suppressive effect on both the initiator and effector phases of apoptosis. This transcriptional modulation of the Caspase-3 gene represents a critical adaptive response that contributes to the maintenance of cellular integrity in aged colon tissue.

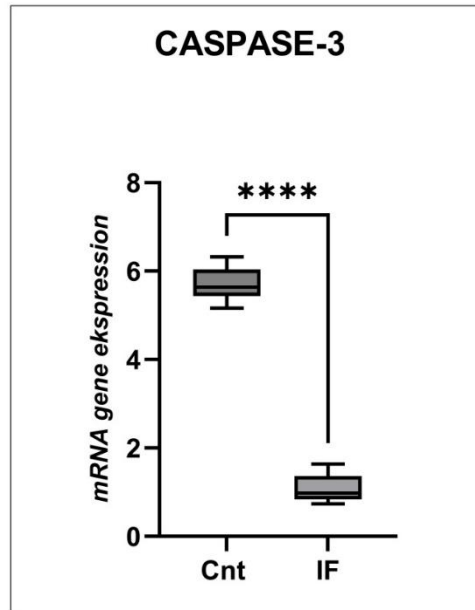


Figure 5. Relative mRNA expression levels of the apoptosis-associated gene Caspase-3 following intermittent fasting intervention. Each data point reflects the mean $\pm$ SEM, calculated from a total of five biologically distinct samples, each measured in triplicate ($n = 5$, 3 technical replicates). Statistical evaluation was performed using an unpaired Student's t-test. A statistically significant difference between groups is indicated by *** ($p < 0.001$), denoting a highly significant change. Abbreviations: Cnt, control group; IF, intermittent fasting group.

IV. DISCUSSION

Intermittent fasting (IF) is garnering increasing attention as a non-pharmacological intervention that modulates cellular homeostasis through its influence on metabolic reprogramming, autophagy induction, and redox balance. Beyond its systemic advantages, recent literature increasingly underscores the impact of IF on cellular fate decisions, particularly in the regulation of apoptotic mechanisms across various tissue types. Our study assessed the transcriptional alterations in key anti- and pro-apoptotic genes within colon tissue following a 35-day IF regimen in 12-month-old Wistar rats. Our findings, discussed below on a gene-by-gene basis, enhance the understanding of the protective molecular response elicited by IF in the colon.

The notable increase in BCL-2 gene expression suggests that intermittent fasting induces an anti-apoptotic transcriptional reprogramming at the colon tissue level. The BCL-2 protein, which inhibits mitochondrial outer membrane permeability to prevent cytochrome c release and subsequent caspase activation, is among the well-characterized regulators of intrinsic apoptosis. This finding is consistent with previous studies demonstrating the suppression of apoptotic signals in various tissues following fasting [13]. Similarly, it has been reported that decreased apoptotic sensitivity by showing increased membrane integrity and reduced protein oxidation in myocardial tissue under the same IF protocol [8]. Moreover, it has been observed that a reduction in oxidative stress markers and preservation of protein structures in liver and colon tissues [9]. In light of this comprehensive data, the increase in BCL-2 expression can be considered not only a marker of apoptotic suppression but also an active component of the cytoprotective network activated by IF. Furthermore, the increase in BCL-2 is predominantly a response induced in parallel with autophagy and serves as an important indicator of the interaction between IF-mediated metabolic restructuring and its effects supporting cellular viability [2].

The marked upregulation of the BCL-XL gene expression further corroborates the anti-apoptotic characteristics observed in colon tissue in conjunction with IF. Functionally analogous to BCL-2, BCL-XL contributes to the stabilization of mitochondrial membrane potential by inhibiting the oligomerization of pro-apoptotic proteins such as BAX and BAK [12]. The simultaneous elevation of BCL-2 and BCL-XL indicates the activation of mechanisms that support cellular survival under metabolic stress in a coordinated fashion. Enhanced mitochondrial function alongside increased BCL-XL levels was documented in a model where intermittent fasting and high-intensity interval training were concurrently applied [13]. Prior research has also demonstrated increased membrane dynamics and reduced oxidative load, suggesting an environment conducive to survival rather than cell death [9]. In this context, the upregulation of BCL-XL can be regarded as a critical molecular checkpoint in the resilience mechanisms induced by IF.

The observed suppression of BAK gene expression indicates a significant reduction in pro-apoptotic signals at the mitochondrial level. The BAK protein, in conjunction with BAX, initiates apoptosis by facilitating MOMP (mitochondrial outer membrane permeabilization), but was transcriptionally inhibited following fasting. This observation aligns with studies indicating that caloric restriction and IF protocols enhance cell survival by suppressing BAK expression in tissues such as the liver and pancreas [12]. Furthermore, our previous FTIR analyses revealed decreased carbonylation and improved protein preservation, with the reduction in BAK expression potentially being part of this molecular protection strategy [9]. In conclusion, it can be asserted that IF directly suppresses the initiation of apoptosis and fosters cellular survival.

The observed reduction in BAX gene expression suggests that intermittent fasting (IF) systematically suppresses apoptosis at the transcriptional level within colon tissue. BAX oligomerizes within the mitochondrial membrane, facilitating the release of cytochrome c and initiating the caspase cascade. Previous research has demonstrated a decrease in BAX expression in rats subjected to IF, correlating with a general reduction in apoptotic markers [13]. In our study, the concurrent decrease in both BAX and BAK expression, alongside an increase in anti-apoptotic members of the BCL-2 family, indicates that IF effectively suppresses the mitochondrial apoptotic propensity. This molecular pattern aligns with previously reported cytoprotective findings, such as enhanced membrane dynamics and diminished oxidative stress [8, 9].

Caspase-3, a terminal effector of apoptosis, degrades structural and regulatory proteins, culminating in irreversible cellular destruction. In this study, a significant reduction in Caspase-3 gene expression was observed in the IF group. Although this reduction is less pronounced compared to the suppression observed in upstream genes (BAX, BAK), it nonetheless indicates that downstream apoptotic mechanisms are also inhibited. It has been reported that a systematic decrease in Caspase-3 expression following IF, observed across multiple organ systems [13]. Our findings corroborate these results at the transcriptional level in colon and liver tissue and support, in agreement with previous spectrochemical analyses, the reduction of protein degradation markers [9]. Consequently, the suppression of Caspase-3 levels demonstrates that IF establishes a multi-layered cellular protection mechanism, inhibiting the apoptotic process at both the initiation and effector stages.

V. CONCLUSION

The present study elucidates the regulatory function of a 35-day intermittent fasting (IF) protocol on the apoptotic response by examining its transcriptional impact on apoptosis-related gene expression in colon tissue in aged male Wistar rats. The results demonstrate significant upregulation of the anti-apoptotic genes BCL-2 and BCL-XL, alongside notable downregulation of the pro-apoptotic markers BAX, BAK, and Caspase-3. This transcriptional reorganization implies that IF fosters a molecular environment at the colon tissue level that inhibits cell death and promotes cellular survival. When integrated with prior biochemical and spectroscopic data, these findings substantiate the hypothesis that IF may serve as a protective strategy against aging-related cellular deterioration in colon tissue by mitigating oxidative stress, preserving mitochondrial stability, and preventing apoptosis. In this context, intermittent fasting emerges as a promising therapeutic tool for the prevention of age-related metabolic and degenerative diseases.

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