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# THE IMPACT OF MICRORNAS ON IRRITABLE BOWEL SYNDROME: A SYSTEMATIC REVIEW

***Laura Garcia***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0009-2328-5049

***Gustavo Leone Caroni***
Centro Universitário Barão de Mauá
Ribeirão Preto – SP
https://orcid.org/0009-0003-0302-4454

***Lucas Maitan Francisco Alves***
Fundação Educacional do Município de Assis
Assis - SP
https://orcid.org/0009-0008-7122-7858

***Nara Manella***
Fundação Educacional do Município de Assis
Assis - SP
https://orcid.org/0009-0005-2874-8920

***Maria Eduarda Scaramal Scolari***
Fundação Educacional do Município de Assis
Assis - SP
https://orcid.org/0009-0003-8898-5413

***Mylla Ortega Brandão***
Fundação Educacional do Município de Assis
Assis - SP
https://orcid.org/0009-0006-7164-4606

***Gustavo Oldani Batista Cozza***
Fundação Educacional do Município de Assis
Assis - SP
https://orcid.org/0009-0008-1479-2439

***Yaskara Harumi Kato***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0002-9425-7618

***Júlia Maschio da Silva***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0008-3213-9062

***Anna Julia Prata de Campos***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0006-8249-3663

***Luís Henrique Lima Negro Júnior***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0008-2164-8515

***Alcielle Alves de Oliveira***
Fundação Educacional do Município de Assis
Assis – SP
https://orcid.org/0009-0000-5979-9409

**Abstract:** Irritable Bowel Syndrome (IBS) is characterized by changes in bowel habits such as changes in consistency and increased fecal frequency, flatulence, tenesmus and abdominal pain. The condition progresses with periods of remission, in which symptoms reduce or disappear for weeks, months or even years. In another spectrum, relapses may occur with an increase in the frequency and intensity of signs and symptoms. Despite affecting individuals at any stage of life, approximately 5% to 10% of the world's healthy population, the underlying causes and exact mechanisms that lead to the development of IBS are not yet fully understood. Recently, advances have revealed that several non-protein-coding and highly evolutionarily conserved miRNAs (20–24 nucleotides) are intimately involved in the pathogenesis of Irritable Bowel Syndrome (IBS). MiRNAs play a fundamental role in the post-transcriptional regulation of gene expression through mechanisms that depend on specific sequences, binding to messenger RNAs (mRNAs) and modulating translation and consequent protein synthesis. In the context of Irritable Bowel Syndrome (IBS), miRNA-29a, miRNA-125b, miRNA-16 and miRNA-144 increase the permeability of the intestinal barrier, allowing the entry of unwanted substances into the bloodstream, which contributes to the symptoms of IBS. IBS. Other miRNAs, such as miRNA-15/107, miRNA-24, miRNA-29, miRNA-199, miRNA-200 and miRNA-495, play a crucial role in regulating hyperalgesia responses. Inflammatory responses, in turn, are mainly controlled by miRNA-181 and miRNA-510, which record patients' signs and symptoms. Currently, available medications are mainly aimed at relieving symptoms, without addressing the etiology of the disease. Therefore, understanding epigenetics is essential to develop therapeutic approaches that can act not only during periods of

remission and relapses, but also with the curative objective of the syndrome.

## INTRODUCTION

Irritable Bowel Syndrome (IBS) is a condition characterized not only by functional gastrointestinal disorders but as a pathology of complex interaction between intestine and brain [3]. Gut-brain disorders (DGBI) recognizes that signs and symptoms such as flatulence, tenesmus, intense abdominal pain are not only due to factors such as injuries, inflammation, lack of control of the intestinal microbiota, but are also influenced by psychic and neural factors (stress, anxiety, depression, sleep disorders). As a result, even inadequate transmission of nerve impulses can generate intense pain perception accompanied by changes in intestinal motility [1,2].

Understanding IBS as a DGBI helps in the therapeutic management of the patient as the approach must include traditional medications, psychological therapies such as cognitive-behavioral and stimulation of the CNS with the use of probiotics. Intestinal bacteria produce various metabolites, such as short-chain fatty acids (SCFAs), neurotransmitters (such as serotonin), and other bioactive compounds that can have direct and indirect effects on the brain. [1,22]

At the same time, to diagnose IBS, the Rome IV criteria, developed by the ROMA Foundation, are used, a set of guidelines aimed at diagnosing functional gastrointestinal disorders, including Irritable Bowel Syndrome (IBS) [23]. To be diagnosed with IBS according to the Rome IV criteria, a patient must present with recurrent abdominal pain that occurs at least one day per week for the past three months and that began at least six months before diagnosis [24]. The pain must be related to defecation, may improve or worsen after a bowel movement, and must be associated with changes in the frequency of bowel movements or the shape of the stool, such as more frequent or less frequent bowel movements than normal, and harder stools or softer than normal [25].

The Rome IV criteria classify IBS into subtypes based on predominant stool characteristics. Constipation-Predominant IBS (IBS-C) is characterized by hard or lumpy stools in more than 25% of bowel movements and soft or liquid stools in less than 25% of bowel movements [5,6]. Diarrhea Predominant IBS (IBS-D) presents with soft or liquid stools in more than 25% of bowel movements and hard or lumpy stools in less than 25% of bowel movements. IBS with Mixed Stool Pattern (IBS-M) involves both hard/lumpy stools and soft/liquid stools in more than 25% of bowel movements, while Unclassifiable IBS (IBS-U) refers to stool patterns that do not fall into none of the categories above [4].

Molecular advances such as biomarkers can play a crucial role in diagnosing Irritable Bowel Syndrome (IBS) by offering an objective way to identify the condition and differentiate it from other gastrointestinal diseases. Biomarkers are measurable substances in the body, such as proteins, genes or metabolites, that can indicate the presence or severity of a disease [12,11].

In the case of IBS, biomarkers can help in several ways: providing an accurate diagnosis, confirming the presence of IBS and differentiating it from conditions with similar symptoms, such as inflammatory bowel disease (IBD) or celiac disease; identifying the different subtypes of IBS (Constipation Predominant, Diarrhea Predominant, and Mixed Evacuation Pattern), allowing for a more personalized and effective treatment; monitoring response to treatment over time, helping clinicians adjust interventions as needed to improve outcomes; providing information about the severity of IBS and

helping to predict disease progression, which aids in planning long-term management; and revealing the biological mechanisms underlying IBS, contributing to the understanding of the causes of the disease and the development of new targeted treatments [9,10].

Furthermore, regarding new advances in biotechnology, microRNAs are non-coding structures, that is, a RNA molecule that is not translated into protein. Instead, miRNAs perform regulatory and structural functions within cells, being able to degrade mRNA or inhibit its translation [7]. This process occurs when miRNAs bind to complementary mRNAs, thus modulating the amount of proteins produced from messenger RNAs. Furthermore, miRNAs have shown promise as biomarkers, as their expressions can reflect pathological changes and help in the diagnosis, prognosis and monitoring of various diseases, including IBS [8].

The biogenesis of miRNAs is a process that begins within the cell nucleus and involves several steps: transcription of pri-miRNAs, processing of pri-miRNAs into pre-miRNAs, export of pre-miRNAs to the cytoplasm [4]. The process begins with the transcription of primary miRNAs (pri-miRNAs) from specific genes in DNA by the enzyme RNA polymerase II (POL II). Pri-miRNAs are long RNA molecules that contain characteristic secondary structures such as loops and double helix regions [20].

After synthesis, pri-miRNAs are processed into pre-miRNAs (miRNA precursors) through a specific protein complex composed of RNase III called DROSHA and the RNA-binding protein known as DiGeorge syndrome critical region 8 (DGCR8); [13]. DROSHA and DGCR8 work together to cut pri-miRNAs, resulting in the formation of pre-miRNAs.

Pre-miRNAs have stem-loop or hairpin structures, where the part called stem is a double helix of complementary bases and the loop is a loop of unpaired nucleotides. This stable secondary configuration results from the RNA folding back on itself, allowing specific proteins such as DROSHA and DGCR8 to recognize and process pre-miRNAs into mature miRNAs [14]. The hairpin shape is crucial for the regulatory function of miRNAs, facilitating their processing and incorporation into the RISC complex, where they perform their regulatory role [8].

Finally, pre-miRNAs are exported to the cytoplasm. After formation, pre-miRNAs are transported out of the cell nucleus by a protein called Exportin-5 (XPO5). Mature miRNAs, once in the cytoplasm, play their regulatory role by incorporating themselves into a protein complex called the RISC complex (RNA-induced silencing complex) [10]. Within the RISC, miRNAs pair with complementary sequences on target mRNAs, leading to mRNA degradation; if the complementarity between the miRNA and target mRNA is high, the mRNA is cleaved and degraded. Furthermore, it is possible that the translation of mRNA may be inhibited; if the complementarity is partial, the translation of the mRNA is inhibited, reducing the production of the corresponding protein. Thus, miRNAs play an essential role in regulating gene expression, influencing several cellular and physiological processes [11].

In recent years, research into microRNAs (miRNAs) has revealed their crucial role in several health conditions, including Irritable Bowel Syndrome (IBS), hyperalgesia and inflammation. In the context of IBS, cellular regulation of the intestinal barrier and permeability involves miR-29a, miR-125b, miR-16 and miR-144, highlighting their importance in maintaining the integrity of the intestinal epithelium. In relation to hyperalgesia, miRNAs such as miRNA-15/107, miRNA-24, miRNA-29,

miRNA-199, miRNA-200 and miRNA-495 act as molecular switches, modulating exacerbated pain responses [18,19]. Finally, inflammatory responses are significantly influenced by miRNA-181 and miRNA-510, which control complex inflammatory processes in the body. This set of studies highlights the relevance of miRNAs as multifaceted regulators in different pathologies, offering new perspectives for innovative therapeutic approaches.

## METHODOLOGY

For Irritable Bowel Syndrome (IBS), an integrative review was conducted using virtual databases such as the Virtual Health Library (VHL), PUBMED and MEDLINE. The research selected articles published between 2019 and 2024, in English and Portuguese. The keywords used included "irritable bowel syndrome", "intestinal disorders", "microRNA biogenesis", "gastrointestinal diseases" and "microRNA expression".

The article selection process occurred in three distinct stages. Initially, 357 articles were analyzed, excluding those that repeated themes, presented inconclusive data, were experimental trials, dissertations, theses and conference abstracts. After this initial screening, 59 articles were selected for full analysis. Subsequently, after a more in-depth analysis, 27 works were considered relevant for the final review.

The selected articles were reviewed in detail to identify and synthesize information on the biogenesis of miRNAs and their relationship with IBS. This integrative review sought to understand the molecular mechanisms involved in the pathogenesis of IBS, exploring how miRNAs can influence processes such as intestinal inflammation, gastrointestinal motility and immune responses, central aspects in understanding and managing this complex clinical condition.

## DISCUSSION

### BARRIER AND PERMEABILITY: THE ROLE OF miR-29a, miR-125b, miR-16 AND miR-144 IN CELLULAR REGULATION IN IRRITABLE BOWEL SYNDROME (IBS)

Intestinal permeability is carefully regulated by tight junction proteins (TJs) and aquaporins (AQPs), which maintain intestinal barrier integrity and fluid homeostasis. Among the TJs, Claudin-1 (CLDN1), Claudin-2 (CLDN2), Occludin (OCLN), Cingulin (CGN), Zonula Occludens (ZO-1, ZO-2, ZO-3) stand out. CLDN1 is related to cell adhesion, CLDN2 facilitates the passage of cations by acting on barrier selectivity, OCLN interacts with other TJ proteins and the actin cytoskeleton acting on structuring, CGN is a cytoplasmic protein that binds to other TJ proteins (such as ZO- 1, ZO-2, and ZO-3) [15,16,17]. CGN helps stabilize tight junctions and regulates the expression of other TJ proteins. Finally, ZO proteins are adapters that connect integral tight junction membrane proteins to the actin cytoskeleton. They facilitate intracellular signaling and the structural stability of tight junctions [20,21].

Aquaporins (AQPs) are transmembrane water channels that facilitate the rapid and selective transport of water across cell membranes, the main ones involved in intestinal function include: AQP1, which is involved in water transport in various parts of the body, including the intestine, helping with the absorption and secretion of water and maintaining water balance; AQP3, present in intestinal epithelial cells, contributes to water reabsorption and can also transport glycerol, playing a role in cellular hydration and lipid metabolism; and AQP8, located in the epithelial cells of the small intestine, facilitates water absorption, essential for digestion and nutrient absorption [15,20].

The dysfunction of TJs and AQPs is related to the pathophysiology of Irritable Bowel Syndrome mainly through the relationship with miR-29a, miR-125b, miR-16 and miR-144. Changes in the pattern of TJs lead to increased intestinal permeability, a condition known as "leaky gut", allowing toxins, microorganisms and antigens to enter the bloodstream and triggering inflammatory and immunological responses conducive to IBS [15]. Changes in aquaporins can result in water imbalances, contributing to conditions such as diarrhea (due to excess water secretion) or constipation (due to insufficient water reabsorption), directly affecting stool consistency and intestinal comfort.

**MiR-29a**

Clinical studies have demonstrated that miR-29 levels are altered in IBS patients compared to healthy individuals. MiRNA-29 plays a crucial role in regulating the permeability of the intestinal barrier, being relevant in Irritable Bowel Syndrome (IBS). MiRNA-29 regulates the expression of several tight junction proteins [14]. By binding to the 3'-UTR regions of mRNAs that encode these proteins, miR-29 can decrease their expression, affecting the integrity of TJs. miR-29a negatively regulates ZO-1 expression, which may compromise tight junction stability and increase paracellular permeability. Reducing ZO-1 levels weakens the intestinal barrier, allowing substances that would normally be blocked to pass through. miR-29a also negatively regulates claudin-1 expression, which results in decreased barrier integrity [27]. Furthermore, miR-29 can influence the expression of pro-inflammatory cytokines, which affect the expression and function of tight junction proteins, leading to the opening of these junctions and increased intestinal permeability.

Studies in intestinal epithelial cell cultures have shown that modulation of miR-29 levels affects the expression of tight junction proteins and cell permeability [11,12]. Overexpression of miR-29 can reduce the expression of claudins and occludin, increasing cell permeability [27]. In animal models of IBS, manipulation of miR-29 levels has demonstrated significant impacts on the integrity of the intestinal barrier, with animals presenting elevated levels of miR-29 showing increased intestinal permeability and exacerbation of inflammatory symptoms [11].

**MiR-125b and miR-16**

Like miR-29a, miR-125b and miR-16 also play roles in regulating the intestinal barrier. These miRNAs negatively regulate the expression of claudin-2 (CLDN2) and cingulin (CGN). CLDN2 allows the passage of cations, and its negative regulation can affect the ionic selectivity of the barrier. CGN is a cytoplasmic protein that stabilizes tight junctions by binding to other TJ proteins and the actin cytoskeleton. Reduced expression of CLDN2 and CGN contributes to the intestinal barrier dysfunction observed in IBS and other gastrointestinal conditions [5].

Furthermore, miRNA-16 is also implicated in the regulation of serotonin receptor 4 (HTR4), an important serotonin receptor expressed in the intestinal mucosa. Studies have identified that genetic variations in HTR4, influenced by the interaction with miRNA-16, can affect visceral sensitivity and intestinal motility in patients with IBS-D. The downregulation of miRNA-16 in the jejunum of IBS-D patients correlates with a higher expression of HTR4, which may be linked to the visceral hypersensitivity observed in these patients [4].

These findings highlight the critical role of miRNA-16 in the pathophysiology of IBS, not only through its influence on intestinal

permeability through the regulation of CLDN2, but also through its impact on modulating the visceral sensory response mediated by HTR4 [4]. Understanding these mechanisms may offer new therapeutic strategies for managing chronic gastrointestinal symptoms associated with IBS [5,4].

**MiR-144**

MiR-144 plays a crucial role in regulating intestinal permeability, especially in the context of Irritable Bowel Syndrome (IBS). Studies indicate that increased expression of miR-144 is associated with reduced expression of the proteins OCLN (occludens) and ZO-1 (zonula occludens-1), which are fundamental in the formation of tight junctions (TJs) [5]. Dysfunction of these proteins, mediated by miRNAs such as miR-144, is closely associated with the pathophysiology of several gastrointestinal diseases, including not only IBS but also other inflammatory and autoimmune conditions that affect the gastrointestinal tract. miR-144 represents a potential target for therapeutic interventions that aim to restore intestinal barrier function and reduce inflammation associated with gastrointestinal diseases [4].

## MOLECULAR KEYS TO HYPERALGESIA: MIRNA-15/107, MIRNA-24, MIRNA-29,

**MiRNA-199, miRNA-200, miRNA-495**

Patients with chronic visceral pain often seek medical help due to the significant impact of this condition on their daily activities, affecting the ability to work, sleep, eat and perform other daily tasks. Pain does not result from a single cause, but from a complex interaction of biological, psychological and environmental factors. The intensity and symptoms can vary widely between individuals [12]. In some cases, infections or inflammatory conditions of the gastrointestinal tract, such as gastroesophageal reflux and peptic ulcer disease, may trigger pain, which may persist as chronic even after the initial inflammation resolves. Hyperalgesia, a condition in which there is an increased sensitivity to pain, is often observed in patients with functional bowel disorders such as irritable bowel syndrome [13]. In this condition, the nerves innervating the gastrointestinal tract become hyper-responsive, resulting in intense pain in response to stimuli that would not normally be painful. Recently, several studies have highlighted the role of selective miRNAs in visceral hyperalgesia associated with IBS, pointing to new paths in understanding and treating this debilitating condition.

**MiRNA-16; miRNA-103**

MiRNA-16 and miRNA-103 regulate gene expression by modulating inflammatory, cell growth and stress biological processes. In the context of prodominant diarrhea-type irritable bowel syndrome (ISS-D), reduced expression of these two microRNAs in the jejunum has been observed [14]. Inflammation is the main factor in hyperalgesia, so reduced expression can result in more sensitive and reactive nerves. Another essential component is chronic stress, known to aggravate ISS-D symptoms, with miRNA-16 and miRNA-103 also being involved in regulating the stress response [12].

MiRNA-16 and miRNA-103 play crucial roles in regulating the stress response in IBS-D by influencing the expression of several genes: MiRNA-16 regulates the BCL2 gene, known for its role in apoptosis, affecting cell survival and response to stress. Furthermore, miRNA-16 controls the CCND1 gene, involved in cell cycle progression, whose dysregulation can impact cell proliferation in stress situations [12]. MiRNA-103, in turn, regulates the CAV1 gene, essential for cell signaling and membrane

integrity, and the SIRT1 gene, which plays a role in inflammation and oxidative stress, being a key regulator of the stress response and cellular longevity [14]. Both microRNAs can also influence HSP family genes such as HSP70, which are heat shock proteins important for cellular protection, and pro-inflammatory genes such as IL6, which play a significant role in the inflammatory response. Furthermore, miRNA-16 regulates the PTEN gene, a tumor suppressor and regulator of cell signaling pathways in response to stress [8].

Amplifying the effect, MiRNA-16 and miRNA-103 can influence cortisol production by regulating the expression of these key genes NR3C1, CRH, POMC, CYP11A1, CYP11B1 in the hormone biosynthesis and regulation pathway [12]. Inappropriate modulation of these microRNAs can result in imbalances in the stress response, affecting cortisol release and sensitivity, which may be relevant to understanding how disorders such as IBS-D can be exacerbated under conditions of chronic stress [7].

**MiRNA-15/107**

Other microRNAs are involved in the pathophysiology of IBS hyperalgesia, such as miRNA-15/10 can act on serotonin receptor 4 (HTR4) and regulate genes involved in modulating neural sensitivity and the inflammatory response in the gastrointestinal tract [4]. Inappropriate regulation of miRNA-15/107 may contribute to greater sensitivity to visceral pain in IBS patients. HTR4 is implicated in the modulation of visceral sensitivity and pain perception [7]. Changes in the expression or function of this receptor can affect pain sensitivity in the gastrointestinal tract, contributing to conditions such as Irritable Bowel Syndrome [4].

**MiRNA-29**

MiRNA-29 regulates genes involved in the extracellular matrix and fibrosis, playing a crucial role in tissue remodeling and modulating neural sensitivity in the intestine in chronic inflammatory conditions such as irritable bowel syndrome. Furthermore, studies have revealed that miRNA-29 shows increased expression in the colon tissues of IBS patients, where it targets the serotonin receptor 7 (HTR7) [7].

**MiRNA-24; miRNA-200a**

The miRNAs miRNA-24 and miRNA-200a play specific roles in regulating the serotonergic system in the context of irritable bowel syndrome. MiRNA-24 acts on the serotonin reuptake transporter (SERT), decreasing serotonin uptake and possibly impacting visceral pain perception [7]. In contrast, miRNA-24 is associated with the regulation of genes that control the immune response and inflammation. Its expression may affect the intensity of the inflammatory response in the intestine, which may influence hyperalgesia in IBS [20].

**MiRNA-199**

MiRNA-199 regulates genes involved in processes such as apoptosis and cellular response to stress, playing a crucial role in modulating cell survival and the sensitivity of neurons in the gastrointestinal tract in conditions such as irritable bowel syndrome IBS [7]. Regarding the TRPV1 receptor (Transient Receptor Potential Vanilloid 1), it is known that this receptor is involved in the detection and transmission of pain signals in the peripheral nervous system, including the gastrointestinal tract. Activation of TRPV1 can result in the perception of visceral pain, being an important mediator in the hyperalgesia observed in conditions such as IBS [8].

## INFLAMMATION: THE INFLUENCE OF miRNA-181, miRNA-510

Traditionally considered a functional condition of the intestine without visible inflammation or detectable structural lesions, IBS is increasingly being recognized for its association with low-grade inflammation, especially in specific subgroups of patients [9]. Studies have revealed markers of inflammation, such as increased immune cells and inflammatory mediators in intestinal tissue and peripheral blood, which may contribute to symptoms such as abdominal pain, changes in bowel pattern and discomfort [19].

Changes in the intestinal microbiota, known as dysbiosis, are frequently observed in patients with IBS and have been associated with localized inflammatory responses in the intestine. These changes in microbial composition can trigger or intensify symptoms of the condition [19]. Furthermore, patients with IBS often have an altered immune response in the gut, characterized by an increase in the production of pro-inflammatory cytokines and a decrease in the activity of immune regulatory cells, which may contribute to increased sensitivity to visceral pain (hyperalgesia); [18].

### MiRNA-181

MiRNAs from the miRNA-181 family are essential in regulating the inflammatory response in various physiological and pathological scenarios such as: cell proliferation, apoptosis, autophagy, mitochondrial function and immunological response. They exert significant influence on the immune response by controlling the expression of genes involved in several crucial inflammatory processes [17]. MiRNAs-181 are capable of modulating the differentiation, activation and function of key immune cells, such as T cells, B cells, macrophages and dendritic cells, playing a crucial role in the adaptive and innate immune system response during inflammation [18].

In addition to regulating immune cells, miRNA-181 is directly involved in modulating the secretion of inflammatory cytokines, such as TNF-α, IL-6, IL-1β and IFN-γ, as well as anti-inflammatory cytokines [19,24]. By influencing the expression of these cytokines, miRNA-181 are able to modulate not only the intensity but also the duration of the inflammatory response, playing a critical role in immunological homeostasis [19].

### MiRNA-510

MiRNA-510 has significant anti-inflammatory potential in different pathological contexts, including post-infectious Irritable Bowel Syndrome (IBS-PI) and lipopolysaccharide (LPS)-induced inflammation [25].

In IBS-PI, characterized by chronic inflammation following intestinal infections, a reduction in the expression of miRNA-510 is observed in affected intestinal tissues. This decrease is associated with TNF-α, an important inflammatory marker [25]. When miRNA-510 is overexpressed, it negatively regulates the expression of Peroxiredoxin 1 (PRDX1), an essential antioxidant protein that neutralizes reactive oxygen species (ROS) involved in the inflammatory process. The ability of miRNA-510 to modulate PRDX1 expression and influence redox balance in intestinal cells suggests that it plays a crucial role in regulating oxidative stress and persistent inflammation associated with IBS [12]. This positions it as a potential therapeutic target for interventions aimed at reducing chronic inflammation in inflammatory bowel conditions.

## CONCLUSION

Irritable Bowel Syndrome (IBS) is a complex condition involving interactions between the gut and the brain, known as gut-brain disorders (GBD). Its symptoms include flatulence, tenesmus and intense abdominal pain, influenced by injuries, inflammation, imbalances in the intestinal microbiota, as well as psychological factors such as stress, anxiety, depression and sleep disorders [1,3]. Intense pain perception and changes in intestinal motility can be aggravated by inadequate transmission of nerve impulses [9].

The integrity of the intestinal barrier, maintained by tight junction proteins (TJs) and aquaporins (AQPs), is crucial for regulating the flow of substances between the intestine and the bloodstream. Proteins such as Claudin-1, Occludin and Zonula Occludens are essential in the formation and stability of TJs, while AQPs such as AQP1, AQP3 and AQP8 facilitate selective water transport, directly influencing stool consistency and water homeostasis [20,21]. MiRNAs, such as miR-29a, miR-125b, miR-16, and miR-144, are critical in regulating these processes.

Furthermore, miRNAs such as miR-15/107, miR-24, miR-199, miR-200, and miR-495 are implicated in visceral hyperalgesia observed in IBS, influencing pain sensitivity and inflammatory response in the gastrointestinal tract [ 12,13]. These miRNAs regulate genes associated with neural and inflammatory modulation, revealing new insights into the mechanisms underlying chronic pain and the exacerbated inflammatory response in IBS.

Irritable Bowel Syndrome (IBS) is being recognized for its association with low-grade inflammation in specific subgroups of patients, evidenced by increased immune cells and inflammatory mediators in intestinal tissue and peripheral blood, contributing to symptoms such as abdominal pain and changes in intestinal pattern [17,18]. Dysbiosis in the gut microbiota is common in IBS and is linked to localized inflammatory responses in the gut. MiRNA-181 regulates the inflammatory response by influencing immune cells such as T cells, B cells, macrophages and dendritic cells [9]. It plays a crucial role in immune homeostasis by modulating the secretion of pro- and anti-inflammatory cytokines. MiRNA-510 demonstrates anti-inflammatory potential in post-infectious IBS and LPS-induced inflammation, reducing cell apoptosis and pro-inflammatory cytokines by negatively regulating PRDX1.

In summary, understanding the role of these miRNAs in the regulation of intestinal permeability, inflammatory response and pain sensitivity offers new perspectives for the development of therapeutic strategies aimed at the effective management of IBS [12,25]. The identification of these biomarkers and molecular targets could pave the way for more precise and personalized interventions aimed at mitigating symptoms and improving the quality of life of patients affected by this complex gastrointestinal condition.

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