Rebamipide alleviates radiation-induced colitis through improvement of goblet cell differentiation in mice

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Introduction

Radiotherapy and accidental exposure to ionizing radiation cause severe damage to healthy tissue. The gastrointestinal tract is a radiation-sensitive organ, and gastrointestinal complications of radiation are collectively referred to as gastrointestinal acute radiation syndrome (GI-ARS).1 GI-ARS can cause a clinical problem, called acute radiation enteritis, which involves inflammation, edema, epithelial barrier impairment, ulceration, a decrease in mitotic activity, and crypt defects in the gastrointestinal tract.2–4 Bacterial translocation is defined as the passage of viable endogenous bacteria and endotoxins from the gastrointestinal tract to extraintestinal sites such as the mesenteric lymph node (mLN) complex, liver, spleen, kidney, and bloodstream.5–6 Endotoxemia and bacteremia are critical events in the pathogenesis of GI-ARS, and the colon is the primary source of endotoxins, which thus highlights the importance of this tissue’s injury during radiation exposure.4

Goblet cells are columnar epithelial cells specializing in the secretion of high-molecular-weight glycoproteins, called mucins, which consist of a protein core, rich in threonine, proline, or serine residues, supplemented with an O-linked oligosaccharide.7 These cells play a pivotal role in epithelial defense against luminal stimulants and pathogens.8–10 Mucin 2 (MUC2), synthesized by goblet cells, is the predominant structural component of the intestinal mucus layer that functions as a barrier to protect the epithelium.11,12 Furthermore, it is well known that goblet cells decrease in number or are depleted in the inflamed mucosa of animal models of colitis and in patients with inflammatory bowel disease.13–16 However, the pathophysiological changes occurring in goblet cells in irradiated colonic tissue are still unknown.

Rebamipide is a quinolone derivative with anti-inflammatory activity and is widely used as an antigastric ulcer drug.17 It is known that the application of topical rebamipide increases both the number of goblet cells and the level of mucin-like substances in the bulbar conjunctiva of rabbits.18,19 It promotes the proliferation.

Abstract

Background and Aim: Radiation-induced colitis is a common clinical problem associated with radiotherapy and accidental exposure to ionizing radiation. Goblet cells play a pivotal role in the intestinal barrier against pathogenic bacteria. Rebamipide, an anti-gastric ulcer drug, has the effects to promote goblet cell proliferation. The aim of this study was to investigate whether radiation-induced colonic injury could be alleviated by rebamipide.

Methods: This study orally administered rebamipide for 6 days to mice, which were subjected to 13 Gy abdominal irradiation, to evaluate the therapeutic effects of rebamipide against radiation-induced colitis. To confirm the effects of rebamipide on irradiated colonic epithelial cells, this study used the HT29 cell line.

Results: Rebamipide clearly alleviated the acute radiation-induced colitis, as reflected by the histopathological data, and significantly increased the number of goblet cells. The drug also inhibited intestinal inflammation and protected from bacterial translocation during acute radiation-induced colitis. Furthermore, rebamipide significantly increased mucin 2 expression in both the irradiated mouse colon and human colonic epithelial cells. Additionally, rebamipide accelerated not only the recovery of defective tight junctions but also the differentiation of impaired goblet cells in an irradiated colonic epithelium, which indicates that rebamipide has beneficial effects on the colon.

Conclusions: Rebamipide is a therapeutic candidate for radiation-induced colitis, owing to its ability to inhibit inflammation and protect the colonic epithelial barrier.
of cultured rat conjunctival goblet cells, and induces the mucin secretion from cultured conjunctival goblet cells of rats. Application of rebamipide alleviates the inflammation in the small intestine through its anti-inflammatory effects and activation of the Wnt/β-catenin pathway. In this study, because goblet cells play important roles in intestinal barrier damage, we investigated whether rebamipide could attenuate the radiation-induced colitis by inducing differentiation of goblet cells in mice model and human colonic epithelial cell line.

**Methods**

**Mice.** Specific pathogen-free male C57BL/6 mice (7 weeks old) were obtained from Harlan Laboratories (Indianapolis, IN, USA) and maintained under specific pathogen-free conditions at the animal facility of the Korea Institute of Radiological and Medical Sciences. All mice were housed in a temperature-controlled room with a 12-h light/dark cycle, and food and water were provided ad libitum. The mice were acclimated for 1 week before experiments and assigned to the following groups: (i) control (n = 10); (ii) Rb400 (n = 5); (iii) IR (n = 5); (iv) IR + Rb200 (n = 5); and (v) IR + Rb400 (n = 5). All animal experiments were performed in accordance with the guidelines and were approved by the Institutional Animal Care and Use Committee of the Korea Institute of Radiological and Medical Sciences.

**Irradiation and administration of rebamipide.** Animals were anesthetized with an intraperitoneal injection of 85 mg/kg alfaxalone (Alfaxan®; Careside, Gyeonggi-do, Korea) and 10 mg/kg xylazine (Rompun®; Bayer Korea, Seoul, Korea). They were irradiated with a single exposure to 13-Gy abdominal irradiation at a dose rate of 2 Gy/min using an X-RAD 320 X-ray irradiator (Softex, Gyeonggi-do, Korea). After the radiation exposure, the animals were treated with an oral dose of 200 or 400 mg/kg/day of rebamipide (Mucosta®; Otsuka, Seoul, Korea) daily for 6 days.

**Cell culture.** The HT29 colonic epithelial cell line was purchased from the American Type Culture Collection. HT29 cells were cultured in Dulbecco’s modified Eagle’s medium (Gibco, Grand Island, NY, USA), supplemented with 10% fetal bovine serum (Gibco) and penicillin/streptomycin (Gibco), at 37 °C in a humidified atmosphere containing 5% CO2. Cells were irradiated with 13-Gy irradiation using a 137Cs γ-ray source (Atomic Energy of Canada, Chalk River, ON, Canada) at a dose rate of 3.81 Gy/min and then treated with 0.3 mM rebamipide (Sigma–Aldrich, St. Louis, MO, USA) within 1 h. After 48 h of incubation, the cells were collected, and western blot analysis and real-time reverse transcription–polymerase chain reaction (RT–PCR) were performed.

**Bacterial translocation assay.** Detection of viable bacteria in mouse mLNs, which were harvested under sterile conditions, was performed to evaluate bacterial translocation from the intestinal lumen to mLNs. An aliquot of an mLN homogenate was plated onto MacConkey agar (BD, Franklin Lakes, NJ, USA) and incubated at 37 °C for 24 h. Then, colonies were counted on all plates.

**Histological analysis of the colon.** Colon samples of mice were fixed with a 10% neutral buffered formalin solution, embedded in paraffin wax, and sectioned transversely at a thickness of 4 μm. The sections were stained with hematoxylin and eosin, alcian blue, and the periodic acid-Schiff (PAS) stain. Alcian blue stains carboxylated, sialated, and sulfated acidic mucosubstances, whereas PAS stains neutral mucosubstances.

To detect the expression of Muc2 in colon tissue, slides were subjected to antigen retrieval and then treated with 0.3% hydrogen peroxide in methyl alcohol for 20 min to block the endogenous peroxidase activity. After three washes in phosphate-buffered saline (PBS), the sections were blocked with 10% normal goat serum (Vector ABC Elite kit; Vector Laboratories, Burlingame, CA, USA) and allowed to react with a Muc2 antibody (Abcam, Cambridge, UK). After three washes in PBS, the sections were incubated with a horseradish peroxidase-conjugated secondary antibody (Dako, Carpinteria, CA, USA) within 1 h. After 48 h of incubation, the cells were counted on all plates.

| Species | Protein | Forward (5’–3’) | Reverse (5’–3’) |
|---------|---------|----------------|----------------|
| Mouse   | Zo1     | AGGACACAAAGCAGTGGAG | GGCATTCTGGTCTGTTACA |
| Mmp9    |     | GCCCTGGAACACTCGAC  | TGGAAACTCAACGGCCAGAG |
| Tnfa    |     | AGGCTCTGGCCATAGAACT | CACCAAGCTTTCTGTCTAC |
| Il-1β   |     | GGTCAACAGCTTGAAAGAC | TGTGAAATGCTCCCTTGGAG |
| Muc2    |     | ATGCCAGATCTACATCAAC | GTAGTTTCCGGGAAAGTGA |
| Math1   |     | TGCCCAGATCTACATCAAC | TGGGACAGTTGTTGCT |
| Hes1    |     | GACGCAAGAAGATCGTATAGG | TCGCTAGTGGGAGCC |
| Tfr3    |     | GTGCTCAAGGGTGAGAAGCAT | CAGGCTTGTGGTGGTGGAG |
| β-actin |     | CTTTCACGCCTGGTGGCTTGA | CCGTGAAGTACCCATAGAA |
| Human   | MATH1  | AACTGCTCCATGGAACGACTGT | ATGGCCGACAGATCTATCAACAGG |
| HES1    |     | ATGGGAGAAATATCTGGTCCC | ATGGGAGAAATATCTGGTCCC |
| MUC2    |     | TCTGGTGAAGCAGTCCGTACGAG | GCGAGTCTGGTCTGGTGGAG |
| CLDN3   |     | AGGCTGTACGACTGGTCTGCT | GAAGTCCCAGATATGTTTT |
| CLDN4   |     | CCTCTGCAAGACACTATAAA | CAGGCTGAGTCCAGAGGAA |
| ZO1     |     | GACACGCTGAAGAGACGCT | TCGTTAACCATTGAGCCTG |
| β-Actin |     | TTTAGGATGGCAAGGCATT | GATGAGTTGCGATGGCTTTA |
(Dako) prepared according to the manufacturer’s instructions, and the slides were counterstained with hematoxylin.

**RNA extraction, reverse transcription–polymerase chain reaction, and real-time polymerase chain reaction quantification.** Harvested mouse colon tissues were immediately snap-frozen and stored at $-80 \degree C$ until RNA extraction. Total RNA was isolated from the colon tissues using the TRizol reagent (Invitrogen, Carlsbad, CA, USA), and total RNA from HT29 cells was extracted with the RNeasy mini kit (Qiagen, Hilden, Germany). cDNA was synthesized using the AccuPower RT premix (Bioneer, Daejeon, Korea) according to the manufacturer’s protocol. Real-time RT–PCR was performed using a LightCycler 480 system (Roche, San Francisco, CA, USA). The primer sequences are provided in Table 1. The expression levels of each target gene, determined using the LightCycler 480 system software (Roche), were normalized to those of β-actin. Cycle threshold values were used to calculate the relative mRNA expression using the $2^{-\Delta\Delta CT}$ method.

**Western blot analysis.** Harvested mouse colon tissues were immediately snap-frozen and stored at $-80 \degree C$. Colon tissues from individual mice were homogenized and lysed in a freshly prepared CelLytic™ MT cell lysis reagent (Sigma–Aldrich) containing a complete protease inhibitor cocktail (Roche). HT29 cells were lysed for immunoblotting in RIPA buffer (50 mM Tris–HCl, pH 8.0, 150 mM NaCl, 1 mM ethylenediaminetetraacetic acid, 1% Triton X-100, 0.1% sodium dodecyl sulfate, 1% NP-40, 1%

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**Figure 1** Rebamipide (Rb) treatment attenuates radiation-induced colonic injury. (a) Hematoxylin and eosin-stained colon tissue harvested from control and Rb-treated mice 6 days after 13-Gy abdominal irradiation (IR). (b) The number of colonies grown from mesenteric lymph nodes and (c) mRNA levels of zonula occludens 1 in colon tissue from control and Rb-treated mice after IR. Data are presented as the mean ± standard error of the mean. n = 5 mice for each group. **$P < 0.01$ compared with the control; # $P < 0.05$ and ## $P < 0.01$ compared with the IR group. [Color figure can be viewed at wileyonlinelibrary.com]
sodium deoxycholate, 1 mM dithiothreitol, 1 mM phenylmethylsulfonyl fluoride, and complete protease inhibitor cocktail). Protein samples were separated by sodium dodecyl sulfate–polyacrylamide gel electrophoresis then transferred to membranes, and the membranes were blocked with 5% skim milk in PBS containing 0.1% Tween 20 for 30 min at room temperature. Membranes were incubated with the following antibodies: Muc2 (Abcam), phosphorylated checkpoint kinase 2 (p-CHK2) (Cell Signaling Technology, Danvers, MA, USA), cleaved NOTCH1 (Cell Signaling Technology), and β-actin (Santa Cruz Biotechnology, Dallas, TX, USA). Blots were developed using horseradish peroxidase-conjugated secondary antibodies and visualized by enhanced chemiluminescence (GE Healthcare, Amersham, UK).

**Statistical analysis.** All data are expressed as the mean ± standard error of the mean, and statistical significance of the differences was evaluated by the Student’s t-test. \( P < 0.05 \) was considered statistically significant.

**Results**

**Rebamipide attenuates radiation-induced colon injury.** To investigate the effects of rebamipide on the intestine, we used abdominal irradiation for mice to reduce the radiation-induced bone marrow injury. There are many reports of therapeutic effects of rebamipide on small intestinal injury,22–24; however, reports related to radiation-induced colonic injury are limited. Colitis is a clinical side effect of radiotherapy, which involves the gut microflora and induces colonic endotoxemia.25 Therefore, we examined the colon for histological damage with respect to crypt epithelial damage and inflammatory cell infiltration in rebamipide-treated irradiated mice. Histological analysis showed that irradiated colons displayed epithelial cell loss and crypt damage to the mucosal layer (Fig. 1a). The rebamipide-treated irradiated mice showed attenuation of crypt and epithelial damage (Fig. 1a). Bacterial translocation to lymph nodes indicates that there are defects in the intestinal barrier, and we detected that radiation significantly increased the number of colonies in mLNs compared with that in the control mice (\( P < 0.05 \); Fig. 1b). However, rebamipide treatment of irradiated mice inhibited the bacterial translocation to mLNs (\( P < 0.05 \) in the Rb200 group, \( P < 0.01 \) in the Rb400 group; Fig. 1b). Interestingly, zonula occludens 1 (Zo1), a tight junction (TJ) protein, significantly increased in the irradiation plus rebamipide-200 and rebamipide-400 groups compared with the level in the irradiation group (\( P < 0.05 \) in the Rb200 group, \( P < 0.01 \) in the Rb400 group; Fig. 1c). These results suggested that rebamipide not only attenuated the radiation-induced colon injury but also improved the intestinal barrier dysfunction caused by radiation exposure.

We then evaluated the anti-inflammatory effects of rebamipide using colon samples collected 6 days after abdominal irradiation at 13 Gy. Matrix metalloproteinase 9 (Mmp9), tumor necrosis factor alpha (Tnfα), and interleukin-1β (Il-1β) markedly increased during acute radiation-induced intestinal injury and play pivotal roles in inflammation.23 We analyzed the mRNA levels of Mmp9, Tnfα, and Il-1β in the irradiated colon using real-time RT–PCR. As shown in Figure 2, Mmp9, Tnfα, and Il-1β expression significantly increased in colon tissue of the irradiation group (\( P < 0.05 \); Fig. 2), whereas the rebamipide-treated irradiation groups exhibited attenuated levels of the inflammatory cytokines and Mmp9 (\( P < 0.01 \) in the Rb200 group, \( P < 0.05 \) in the Rb400 group; Fig. 2). Thus, rebamipide treatment of radiation-induced colitis resulted in the recovery of intestinal barrier function and in anti-inflammatory effects.

**Rebamipide improves goblet cell deficiency in the irradiated colon.** Goblet cells are columnar epithelial cells characterized by secretion of mucins, and they function as an intestinal barrier, which protects the epithelium. Application of rebamipide has been shown to increase the proliferation of goblet cells in eye disorders.26,27 We also identified that rebamipide increases goblet cell proliferation in the normal colon through H&E and PAS staining (Fig. 3a,b). To investigate the effects of rebamipide on goblet cells following irradiation-induced injury to the colon, we performed alcian blue and PAS staining of the irradiated colon (Fig. 3c,d). The

![Figure 2](image-url)  
**Figure 2.** Rebamipide (Rb) treatment inhibits the inflammatory response in radiation-induced colitis. Relative mRNA levels of (a) matrix metalloproteinase 9 (Mmp9), (b) tumor necrosis factor alpha (Tnfα), and (c) interleukin-1β (Il-1β) in the colon of Rb-treated irradiated (IR) mice, detected by real-time reverse transcription–polymerase chain reaction. Data are presented as the mean ± standard error of the mean. \( n = 5 \) mice for each group. **\( P < 0.01 \) compared with the control; ###\( P < 0.001 \) and #\( P < 0.05 \) compared with the IR group.
irradiation group showed a significant decrease in positively stained goblet cells, which was consistent with the decreased expression of mucins compared with that in the control group ($P < 0.01$; Fig. 3c–e). The rebamipide-treated irradiation groups showed higher expression of acidic and neutral mucins and higher numbers of goblet cells per crypt in the colon than the irradiation group ($P < 0.05$ in the Rb200 group, $P < 0.01$ in the Rb400 group; Fig. 3c–e). These results suggested that rebamipide treatment alleviated the radiation-induced colitis and led to the recovery of goblet cells, which protect the intestinal epithelium.

**Rebamipide improves goblet cell differentiation in the irradiated colon.** Because rebamipide effectively increased the number of goblet cells, according to histological analysis, we sought to confirm the effect of rebamipide on goblet cell differentiation. Muc2 is the major mucin synthesized and secreted by goblet cells in the colon. First, we found that the irradiation group had lower $\text{Muc2}$ mRNA and protein levels in the colon than those in the control group ($P < 0.05$; Fig. 4a,b). Immunohistochemistry showed that Muc2-positive cells appeared large and their number decreased in the irradiated colon (Fig. 4c).
Rebamipide treatment of the irradiation group significantly restored the mRNA and Muc2 protein levels in the colon compared with those in the untreated irradiation group ($P < 0.01$; Fig. 4a,b). The results demonstrated that Muc2-positive cells increased in the rebamipide-treated irradiated mice compared with their numbers in the irradiated mice (Fig. 4c).

Differentiation of intestinal stem cells into the goblet cell lineage is facilitated by mouse atonal homolog 1 (Math1), a target gene repressed by hairy and enhancer of split 1 (Hes1). We identified that rebamipide regulates Math1 and Hes1 genes and induces Muc2 expression in the colon of normal mice (Fig. 5a). Otherwise, mRNA of Math1 was downregulated and that of Hes1 was upregulated in the irradiated colon ($P < 0.05$; Fig. 5b, c). Trefoil factor 3 (Tff3), another goblet cell differentiation marker, was repressed in the irradiation group compared with its level in the control group ($P < 0.05$; Fig. 5d). Rebamipide treatment increased the Math1 mRNA levels ($P < 0.05$; Fig. 5b) and reduced those of Hes1 in the colons of the irradiated mice ($P < 0.01$; Fig. 5c). Consistent with the upregulation of Muc2 expression in the rebamipide-treated irradiated mice, Tff3 also increased in IR + Rb400 group ($P < 0.05$; Fig. 5d). Thus, rebamipide induced the goblet cell differentiation through upregulation of the Math1 gene in the radiation-induced colitis mice.

**Rebamipide inhibits NOTCH1 activation and promotes barrier function in irradiated colonic epithelial cells.** Because rebamipide effectively promoted the goblet cell differentiation in the mouse colon, we examined its effects on HT29 colonic epithelial cells (a human colon adenocarcinoma cell line). HT29 cells are commonly used in the research of cell differentiation because they display characteristics of pluripotent intestinal cells. Irradiation induced DNA damage in HT29 cells, which usually activates the CHK2 protein, whereas rebamipide-treated cells exhibited decreased p-CHK2 expression (Fig. 6a). In addition, rebamipide rescued the loss of Claudin (CLDN) 3, CLDN 4, and ZO1 caused by irradiation of colonic epithelial cells (Fig. 6e–g). We demonstrated that rebamipide treatment attenuates loss of Muc2 in the irradiated colon through upregulation of Math1 gene. Consistent with these results, rebamipide upregulated the expression of MATH1 and MUC2 genes in irradiated HT29 cells (Fig. 6b,d). However, we did not find the alteration of HES1 gene in irradiated epithelial cell (Fig. 6c). We also found that activated NOTCH1 was inhibited by rebamipide in irradiated colonic epithelial cells (Fig. 6a). These results suggested that the inhibition of NOTCH1 caused by rebamipide treatment might regulate the MUC2 synthesis in epithelial cells. Rebamipide reduced the loss of TJs and improved the synthesis of MUC2 through inhibition of NOTCH1 activation.

**Discussion**

Exposure of the abdominal region to radiation causes significantly increased bacterial growth and bacterial translocation to extraintestinal sites by destroying the intestinal mucosal barrier. Because colonic epithelial junctional complexes and barrier functions are highly sensitive to radiation, radiation-induced colitis is a common clinical problem associated with radiotherapy and accidental exposure to ionizing radiation. The condition may also lead to alterations of the gut microbiota and induce colonic endotoxemia. Therefore, we focused on the effects of rebamipide against colonic injury using a GI-ARS model.

To evaluate the effects of rebamipide on radiation-induced colitis, we performed histological analysis and an intestinal barrier function assay. The analysis revealed that rebamipide...
attenuated the colonic injury by increasing the levels of Zo1, one of TJ components, and by inhibiting bacterial translocation. TJs, which are highly specialized intercellular junctions, are responsible for epithelial barrier functions in the gastrointestinal tract. An irradiated colonic epithelium displayed a rapid redistribution of tight junctional complexes in the acute phase. However, in this in vivo and in vitro study, rebamipide was able to prevent the irradiation-induced destruction of TJs in the colonic epithelium. These findings suggested that the TJ recovery upon rebamipide treatment attenuated the radiation-induced colonic damage.

Rebamipide showed inhibition of inflammatory cytokines and chemokines such as TNFα and IL-1β, as well as inhibition of MMP9 in the irradiated colon. MMP9 is released from intestinal epithelial cells in response to proinflammatory cytokines and is responsible for the degradation of TJs, with a subsequent loss of mucosal integrity. MMP9 can activate NOTCH1, induce the loss of MUC2 synthesis, and increase bacterial adhesion to epithelial cells. The reduction of MMP9 levels in the damaged colon treated with rebamipide indicated the restoration of intestinal integrity related to the attenuation of TJ loss. These results suggested that rebamipide treatment could alleviate inflammation and improve mucosal integrity in radiation-induced colitis.

We also investigated the effects of rebamipide treatment in irradiated mice with increased numbers of flawed goblet cells in the irradiated colon. Mucins, glycoproteins secreted by goblet cells, form a thick mucus gel layer and maintain the integrity of the gastrointestinal mucosal surface. Mice with genetic deficiencies for goblet cell differentiation are dramatically susceptible to Salmonella infection, develop severe barrier disruption, and show higher mortality rates compared with wild-type mice. In addition, the mucus acts as a protection, lubrication, and transport medium between the luminal contents and epithelial lining. Inflammatory bowel disease patients are characterized by flawed goblet cells and intestinal barrier disruptions. In our study, radiation exposure resulted in damage to the colonic epithelial barrier, including defects in goblet cells, increased bacterial translocation, and inflammation responses in colonic tissue. The application of rebamipide attenuated the radiation-induced colitis by recovering defective goblet cells and inhibiting bacterial translocation.

![Figure 5](image_url)

Figure 5  Rebamipide (Rb) treatment induces goblet cell differentiation. mRNA levels of (a) mouse atonal homolog 1 (Math1) (Con, Rb400), (b) hairy and enhancer of split 1 (Hes1), and (c) mucin2 (Muc2) in the colons of control and Rb400-treated mice. mRNA levels of (a) Math1, (b) Hes1, and (c) trefoil factor 3 (Tff3) in the colons of control and Rb-treated irradiated (IR) mice, determined by real-time reverse transcription–polymerase chain reaction. Data are presented as the mean ± standard error of the mean. n = 5 mice for each group. *P < 0.05 compared with the control; **P < 0.01 compared with the IR group.
translocation. Rebamipide stimulated goblet cell differentiation in the irradiation-impaired intestinal barrier.

NOTCH1 activation regulates the transcription of downstream target genes such as the HES1 gene.35,36 HES1 is a basic helix–loop–helix transcriptional repressor,36,37 whereas MATH1 is another basic helix–loop–helix transcription factor, which is suppressed by HES1.28,38 The MATH1 gene is involved in the differentiation of intestinal stem cells into the goblet cell lineage.28,39,40 Inhibition of NOTCH signaling attenuated intestinal inflammation by regulating MATH1 and MUC2 expression in a dextran sodium sulfate-induced colitis model.31 We found that rebamipide treatment increased the level of MATH1 and promoted goblet cell differentiation in the colons of irradiated mice. Irradiated colonic epithelial cells showed higher MUC2 expression upon rebamipide treatment. In particular, rebamipide inhibited the expression of activated NOTCH1 in HT29 cells. Therefore, we suggest that rebamipide inhibits the activation of NOTCH1, which regulates the differentiation of goblet cells and improves the colon mucosal barrier in radiation-induced colitis.

In conclusion, the present study demonstrates that rebamipide treatment can attenuate the colon damage in irradiated mice, and its effects are due to the inhibition of TJ damage, anti-inflammatory activity, and stimulation of goblet cell differentiation. Therefore, rebamipide treatment may provide a therapeutic strategy for managing radiation-induced colitis.

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