Gastric lesion is a predominantly precancerous disease [1,2], but fails to be the heated scientific research focus since therapeutic application to inhibit gastric acid secretion was developed [1]. Unfortunately, despite of this kind of treatment application, the morbidity of gastric cancer cannot be curbed, especially in China [3] and other Asian countries [4]. We analyzed the phenomena and found that the current treatment used in clinic does not drop the reoccurrence of gastric lesion due to lack of mucosal repairment strategy for patients [5].

Short Chain Fatty Acids (SCFAs), including acetate, propionate and butyrate, are the metabolites of anaerobic bacteria, not only produced in intestinal tract but also present in fermented foods, which are important for maintaining the integrity of intestinal mucosa [6]. In a series of studies, attention was focused on the effects of SCFAs on gastric mucosal lesion in the mouse model induced by ethanol. We originally reported that probiotic Clostridium butyricum [7] and its metabolite, butyrate [5], can protect gastric mucosa from lesion. Recently, we have published a paper named “Short Chain Fatty Acid Acetate Protects against Ethanol-induced Acute Gastric Mucosal Lesion in Mice” on BIOL PHARM BULL. In this study, acetate and propionate were used to treat gastric lesion. Previously, the most extensively studied and best-documented functions of acetate and propionate are their effect on Inflammatory Bowel Diseases (IBDs) [8,9]. However, our data indicated that only acetate was protective in this experiment and we have applied for a patent (NO. 201610204569.9) using these results.

It has been shown that SCFA acetate attenuated the inflammation and oxidation in the IBD study. Therefore, the underlying mechanisms of acetate protection for gastric mucosa were investigated from these two aspects and we got some supportive data. But given the limited experiment condition, we did not do further investigation in the paper. It was reported that acetate activated its special receptor, GRP43, to inhibit inflammation and oxidation [10]. GRP43, also known as Free Fat Acid Receptor 2 (FFAR2) [11], is a Gi/o-coupled G Protein-Coupled Receptor (GPCR) [12]. The primary endogenous agonists of GRP43 are acetate [13], propionate and butyrate [14]. But, given the propionate effect on gastric mucosal lesion, GRP43 should not be activated by propionate. The studies based on FFAR2/-/- mouse have implicated the receptor in the regulation of energy metabolism [12] and IBD [15]. However, discrepancies of the pathways activated by FFAR2 agonists in different studies have been observed [16,17]. In the other experiment, acetate has also been documented to regulate gene expression to inhibit inflammation as a Histone Deacetyltranferase (HDAC) inhibitor [18]. As a typical HDACi, SCFA butyrate has been widely used in different kinds of studies [19]. Acetate and propionate were shown to increase the histone acetylation by Park et al. [18] in the study of effects of SCFAs on T cells. However, they did not investigate the mechanism in detail and other researchers did not report the similar results. Therefore, the experiment should be designed to make sure whether acetate can acetylate histone to induce gastric mucosal protection in the next step. Based on the results of previous studies, more novel mechanisms for the gastric mucosal protection of acetate remain to be explored in further studies as shown in Figure 1.

SCFA acetate is widely used in our daily life, especially in food additives. Our result is likely to reveal the reason for the character of gastric cancer morbidity. It is also been noticed that animal model of chronic gastric ulcer was conventionally induced by local injection of acetic acid in gastric wall [20]. In the following study, it is suggested to modify the model using diluted HCl instead of acetic acid, according to our finding.

The protective effects of SCFA acetate on gastric lesion was shown in our study, although much remains to be done to understand the details. We deeply believe that SCFAs studies on stomach will be invaluable in reducing the incidence and recurrence rate of gastric ulcer, and preventing stomach cancer.
References