tablet in terms of amelioration of chronic oxidative stress in the colonic mucosa in UC patients.

According to literatures, there have been no definition for the term, “functional foods” in the US until recently [27-29]. This situation has been the same in Japan. However, Martirosyan et al. from the Functional Food Center in the US, recently proposed a new definition for functional foods, as follows [27-29]. They proposed that functional foods are “natural or processed foods that contain biologically active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms." We believe that this concept is very important when we consider developing new functional foods products, which show obvious benefit for human health in clinical practice. Regarding the previous studies on broccoli sprouts, numerous reports have shown that broccoli sprouts are natural foods that contains precursor of biologically active components, sulforaphane [7-8]. Furthermore, our data from the present study clearly show that dietary approach with non-toxic amounts of broccoli sprouts provides beneficial effects on colonic mucosal inflammation in UC patients, which is evaluated quantitatively by a specific biomarker, fecal calprotectin, induces better management of their symptoms, reduces risk of UC recurrence, and presumably prevents occurrence of colitis-associated colon cancer in the future. Taken together, we believe that our data provide strong evidence for broccoli sprouts as one of the functional foods, which clearly promotes human health.

Finally, we would like to emphasize that this is the first study to demonstrate that dietary intake of sulforaphane-rich broccoli sprouts mitigates colonic mucosal inflammation in patients with ulcerative colitis. The present study further suggests dietary approach with antioxidant food, such as sulforaphane-rich broccoli sprouts, not only mitigates colonic inflammation, but also contributes to keep remission in mesalazine-treated ulcerative colitis patients, indicating that dietary approaches by functional foods in combination with medical drugs could provide most beneficial effects on chronic inflammatory diseases.

Study Limitations: To start, the sample size in this trial fell short of the initially calculated requirement, which suggests that the data may still be preliminary. Consequently, we should consider planning another BS intervention study that involves a larger cohort of UC patients. Additionally, Second, while this study has suggested that BS increases the composition of the butyrate-producing microbiota, we need to examine if it specifically increases the butyrate level in the colonic lumen. Third, although this study was performed in a double-blinded fashion, BS and AS have minute differences that some participants may have been able to identify. Therefore, we must recognize that this study was not conducted in a completely double-blinded fashion. In addition, other dietary components may have affected the data during the trial period. Thus, another clinical trial using pure SFN, such as via glucoraphanin tablets, instead of using BS, must be conducted. However, most importantly, we were able to ameliorate colonic mucosal inflammation in UC patients by a dietary approach with SFN-rich BS.

Conclusion: This study demonstrated that a dietary approach with SFN-rich BS mitigates colonic inflammation in human UC patients treated with mesalazine. Our findings indicate that the positive effects of SFN-rich BS may be driven by the activation of the Nrf2-dependent antioxidant system, which helps combat chronic oxidative stress.

Abbreviations: AS: alfalfa sprouts**,** BS: broccoli sprouts**,** CAI: clinical activity index**,** SD: standard deviation, SFN:

sulforaphane**,** UC: ulcerative colitis

Authors Contribution: Akinori Yanaka designed the protocol of this study, obtained research funds, submitted proposal to ethical committees in the hospitals, analyzed the obtained data, and wrote the manuscript. Toshihide Ohmori, Masanori Ochi, and Hideo Suzuki checked the original protocol and the manuscript, and made some helpful comments. All the authors contributed to participants recruitment and conducted the clinical trial.

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