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REPLY TO LETTER

Reply to comment on: Dietary yeasts reduce inflammation in central nervous system via microflora

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Dear Editor

We thank Perricone et al. for their interest in and comments on our manuscript.[1] Diet, intestinal microflora, and metabolites produced by this microflora are important because they exert positive effects on human health through intestinal immunity. Several bacteria and their components exert positive effects against experimental autoimmune encephalomyelitis (EAE); however, limited information is available on the effects of yeasts such as *Saccharomyces*, *Candida*, and *Aspergillus*, which are constituents of fermented foods, on EAE.[2] Our study is significant because we found that *Candida kefyr* ameliorated EAE; in addition, our study suggested that not all yeasts exerted the same effect on immunity, as mentioned by Perricone et al. Furthermore, the effects of *C. kefyr* seem to be some immune-mediated diseases specifically depending on the underlying pathology.

Anti-*Saccharomyces cerevisiae* antibodies (ASCAs) are interesting molecules. High levels of ASCAs in patients with Crohn's disease suggest that this yeast contributes to intestinal immunity.[3] ASCAs are also found in patients with some autoimmune diseases of the central nervous system (CNS). Levels of ASCAs are significantly higher in AQP4-seropositive patients with neuromyelitis optica than in healthy controls.[4] Thus, it seems likely that *S. cerevisiae* affects the autoimmune diseases of the CNS. In our study, oral administration of *C. kefyr* reduced the proportion of *Bacteroides* and microbiome transfer from *C. kefyr*-treated mice reduced the proportion of *Bacteroides* and ameliorated EAE and dextran sulfate sodium-induced colitis. However, oral administration of *S. cerevisiae* did not reduce the proportion of *Bacteroides* or clinical severities in both animal models.[2] These results suggested that modification of microbiome by *C. kefyr* reduced inflammation.

Because many kinds of yeasts reside in intestine and each yeast may exert different effects on human health, further studies should be performed to determine the exact roles of these yeast, as pointed out by Perricone et al.

Conflict of Interest

K. T., T. O., M. K., T. K., J. H., S. S., T. S., H. M., and Y. N. have nothing to declare. T. T., M. T., and K. H. are relevant persons of Kyorin Pharmaceutical Co., Ltd.

References

1. Perricone C, Rinaldi M, Shoenfeld Y. Comment on dietary yeasts reduce inflammation in central nerve system via microflora. Ann Clin Transl Neurol 2015; doi: 10.1002/acn3.256. In press.
2. Takata K, Tomita T, Okuno T, et al. Dietary yeasts reduce inflammation in central nerve system via microflora. Ann Clin Transl Neurol 2015;2:56–66.
3. Iliev ID, Funari VA, Taylor KD, et al. Interactions between commensal fungi and the C-type lectin receptor Dectin-1 influence colitis. Science 2012;336:1314–1317.
4. Banati M, Csecsei P, Koszegi E, et al. Antibody response against gastrointestinal antigens in demyelinating diseases of the central nervous system. Eur J Neurol 2013;20:1492–1495.