

## Intestinal barrier regulation by dietary polyphenols

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Gastrointestinal epithelium provides a physical barrier against external environment. Barrier defects resulting in the permeation of luminal inflammatory substances induce an abnormally robust inflammatory response. The barrier integrity depends on the coordinated expression and interaction of proteins in cell-cell junctional complexes, including the tight junctions (TJs). Recently, we have demonstrated that some dietary polyphenols have potentials to regulate the intestinal TJ barrier. Among the polyphenols tested, a citrus polyphenol, naringenin, promotes and protects the intestinal TJ barrier in human epithelial Caco-2 cells and a murine model of colitis. In Caco-2 cells, naringenin enhances the intestinal TJ barrier, indicated by epithelial electrical resistance and dextran permeability. Immunoblot analysis and confocal microscopy demonstrate that naringenin increases the assembly of TJ proteins, ZO-2, occludin, claudin-1, and claudin-4, at TJs. The increased claudin-4 by naringenin is mediated by its transcriptional regulation. Luciferase reporter assays with mutagenesis and pharmacological inhibitors show that the naringenin-mediated claudin-4 up-regulation occurs in part through a transcriptional factor, Sp-1. The naringenin-induced occludin assembly correlates with its phosphorylation, indicating the important role of the occludin phosphorylation. In a murine model of colitis, the naringenin ingestion suppresses the colon damage and inflammation, indicated by clinical score, colon shortening, and inflammatory cytokine expression. This naringenin-mediated suppression occurs simultaneously with protection of TJ barrier in colons. Taken together, some polyphenols such as naringenin have roles in intestinal barrier regulation and that the supplemental feeding might provide us with an alleviative effect on diseases associated with the intestinal barrier defect.

### Biography

Takuya Suzuki has completed his Ph.D. at the age of 31 years from Hokkaido University, Japan and postdoctoral studies from Hokkaido University and University of Tennessee Health Science Center. He is the associate professor in Hiroshima University, Japan. He has published more than 45 papers in reputed journals and has recently received Japan Prize in Agricultural Sciences, Achievement Award of Young Scientists.