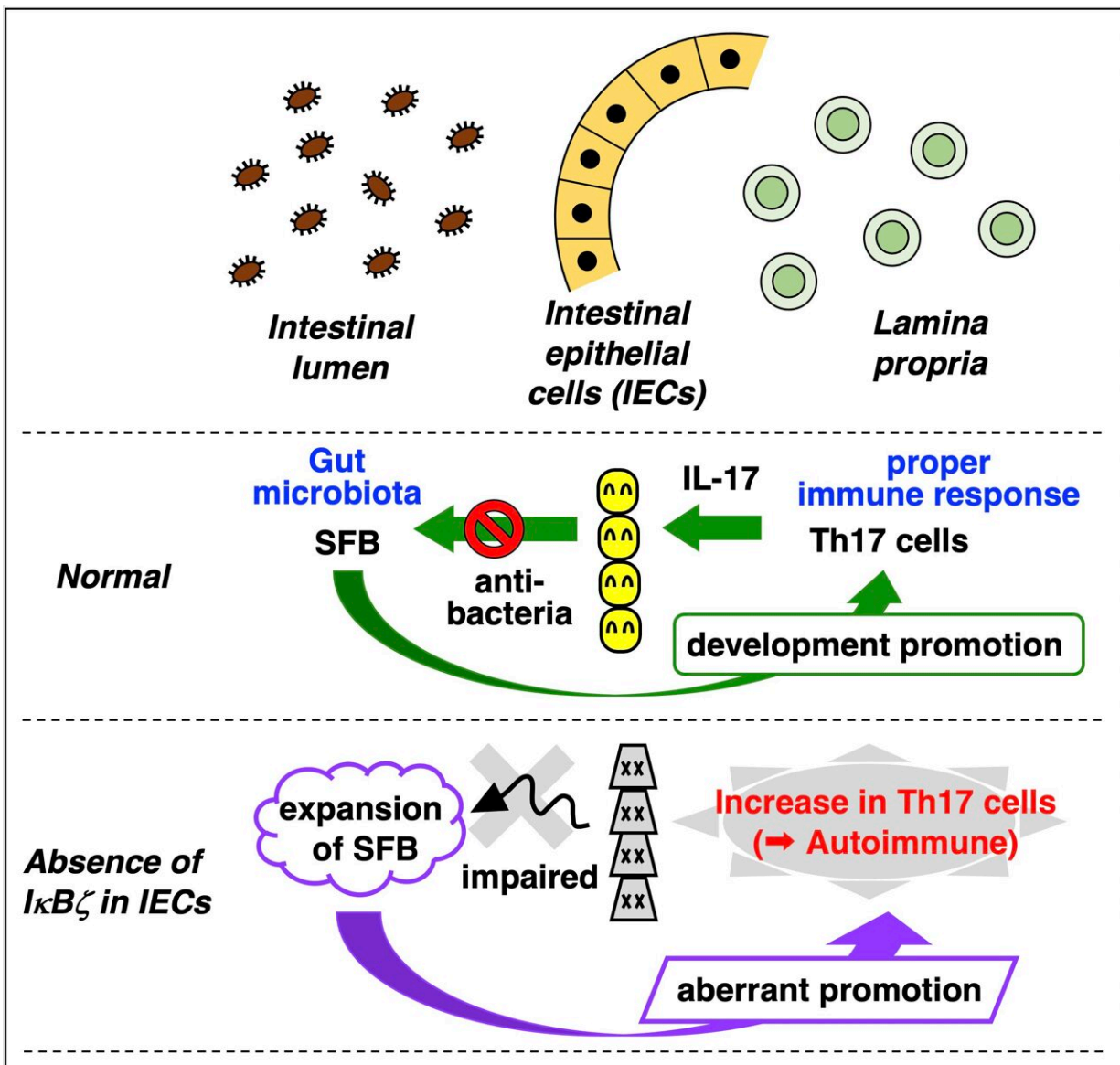


# Keeping balance inside and outside the small intestine

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In the normal intestine, IECs control gut bacteria by releasing anti-microbial

factors in response to IL-17. Because increase in SFB leads to up-regulation of IL-17 by promoting Th17 cell generation, the numbers of SFB and Th17 cells are maintained constant. In contrast, lack of  $\text{I}\kappa\text{B}\zeta$  in IECs results in expansion of both SFB and Th17 cells, which can cause the development of autoimmune diseases. Credit: Soh Yamazaki

In the normal small intestine, the levels of SFB and Th17 cells are both maintained as they counterbalance each other. Th17 cells release IL-17 to limit unwanted expansion of SFB, whereas a decrease in the number of SFB eases the restrictive action of Th17 cells. The research group found that this elaborate control system owes to the presence of healthy IECs.

IECs that lack  $\text{I}\kappa\text{B}\zeta$  gene fail to exert anti-bacterial effects in response to IL-17 even though the cytokine is plentifully produced by increased Th17 cells. They demonstrated that lack of  $\text{I}\kappa\text{B}\zeta$  in IECs leads to impairment in the two IL-17-mediated defense machineries in the gut: the production of IgA and the maintenance of Paneth cell integrity.

"Gut [epithelial cells](#) are aligned as a single layer. This thin layer is beneficial for nutrient absorption, but vulnerable to invasion. It requires a strong defense mechanism against invasive pathogens. Besides, these cells have to control the growth of microbes in a flexible manner as needed," said the lead author of the paper, Soh Yamazaki, Ph.D., Associate Professor of the Toho University School of Medicine.

"We hope that our study will lead to the development of a novel strategy to treat [inflammatory diseases](#) by manipulating the function of  $\text{I}\kappa\text{B}\zeta$ ," said the last author Hiroyasu Nakano, M.D., Ph.D. Professor of the Toho University School of Medicine.

The finding was published in the journal *Mucosal Immunology*.

**More information:** Soh Yamazaki et al, I $\kappa$ B $\zeta$  controls IL-17-triggered gene expression program in intestinal epithelial cells that restricts colonization of SFB and prevents Th17-associated pathologies, *Mucosal Immunology* (2022). [DOI: 10.1038/s41385-022-00554-3](https://doi.org/10.1038/s41385-022-00554-3)

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