Complex endosymbiotic system of mealybugs
Impact on biological concepts such as genome, cell and individual

The smallest reported bacterial genome belongs to *Tremblaya princeps*, a β-proteobacterial symbiont of the mealybug *Planococcus citri* (PCIT). Strikingly, *Tremblaya* of PCIT also possesses its own γ-proteobacterial endosymbiont, *Moranella endobia*. Genome and transcriptome analyses, including genome sequencing of a *Tremblaya* lineage containing no intracellular bacteria, revealed that the extreme genomic degeneracy of PCIT *Tremblaya* likely resulted from acquiring *Moranella* as an endosymbiont. In addition, we found that at least 22 horizontally transferred genes from multiple diverse bacteria are expressed in the mealybug genome, likely complementing missing symbiont genes. However, none of these horizontally transferred genes are derived from *Tremblaya*, indicating that genome reduction in this symbiont has entailed no gene transfers to the host nucleus. Our results suggest that the functioning of this three-way symbiosis is dependent on genes from at least six lineages of microorganisms and reveal a path to intimate endosymbiosis distinct from that followed by organelles.

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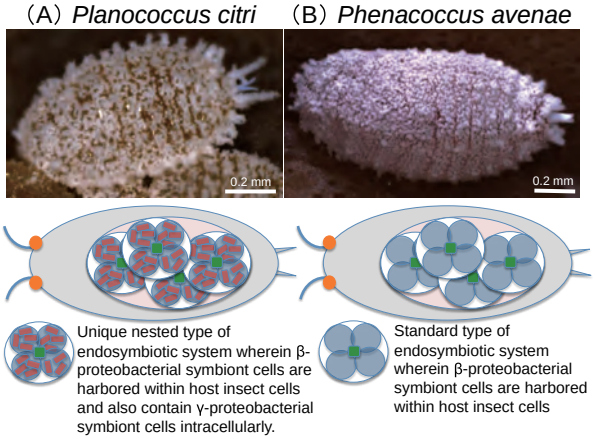

Schematic illustration of endosymbiotic systems in the citrus mealybug *Planococcus citri* (A) and the bulb mealybug *Phenacoccus avenae*

Anti-inflammatory mechanisms characteristic of lactic acid bacteria
Double-stranded RNA in LAB triggers production of protective interferon-β

The fermentative lactic acid bacteria (LAB) are aerobic and abundant in the environment and food and they consequently compose a major part of our small intestinal commensal flora. Therefore, LAB affect maturation of host immune cells and maintenance of intestinal immune homeostasis under normal steady-state conditions. However, molecular mechanisms for protective and anti-inflammatory effects induced by LAB were illusive. We discovered that LAB trigger interferon-β (IFN-β) production from dendritic cells and protect mice from experimental colitis. The LAB-induced IFN-β production was diminished by double-stranded RNA (dsRNA) digestion or treatment with endosomal inhibitors. Moreover, the protective effects induced by LAB were abrogated by neutralizing IFN-β. These results identify TLR3 as a sensor to small intestinal commensal bacteria and suggest that dsRNA in LAB contributes to anti-inflammatory and protective immune responses. These findings shed light on the clinical application of LAB and commensal bacteria for prevention and treatment of inflammatory diseases.

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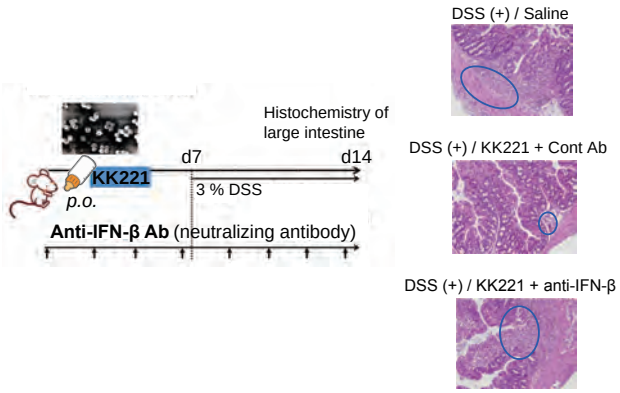

Anti-inflammatory effects of interferon-β on experimental colitis
Oral administration of LAB (KK221) suppressed infiltration of inflammatory cells by IFN-β induction.