

CIRMM/CIBiS

Taniguchi LAB.

[Integrative Comprehension of Innate Immune Responses]

Immunology Social Cooperation Program

Max Planck-The University of Tokyo Center for Integrative Inflammation

<http://www.iis.u-tokyo.ac.jp/~mol-immu/>

<http://mputc.com/index.html>

Our research interests are molecular mechanisms that underlie the regulation of gene expression and signal transduction in immune system. Given various molecules have been reported to have regulatory functions in immune system and involved in tissue homeostasis and disease pathologies, we focus on these immune regulatory molecules to elucidate mechanisms for tissue homeostasis and disease, such as inflammation, cancer and autoimmune diseases and develop therapeutic targets for these diseases. We are intensively studying the following immune regulatory molecules ranging from nucleic acids to proteins, sugar and lipid; inflammation-inducing protein HMGB1, small nuclear RNA that is involved in the pathology of autoimmune diseases, surfactant protein-D (SP-D) that contributes to the maintenance of microbiota composition and dead cell-derived lipid prostaglandin E2 (PGE2) that inhibits inflammation. We are also searching for new immune regulatory molecules.

Innate immune receptor, such as Toll-like receptors, C-type lectin receptors (CLRs) and cytosolic receptors, recognize not only pathogen-associated molecular patterns but also self-molecules derived of dead cells or cancer cells and activates immune cells. We have discovered Dectin-1, one of CLRs, recognizes tumor-derived glycan structure leading to enforced tumor-killing by NK cells. Recently, we also found that Dectin-2 and MCL are required for the suppression of liver tumor metastasis. Studies for other CLRs are also on-going.

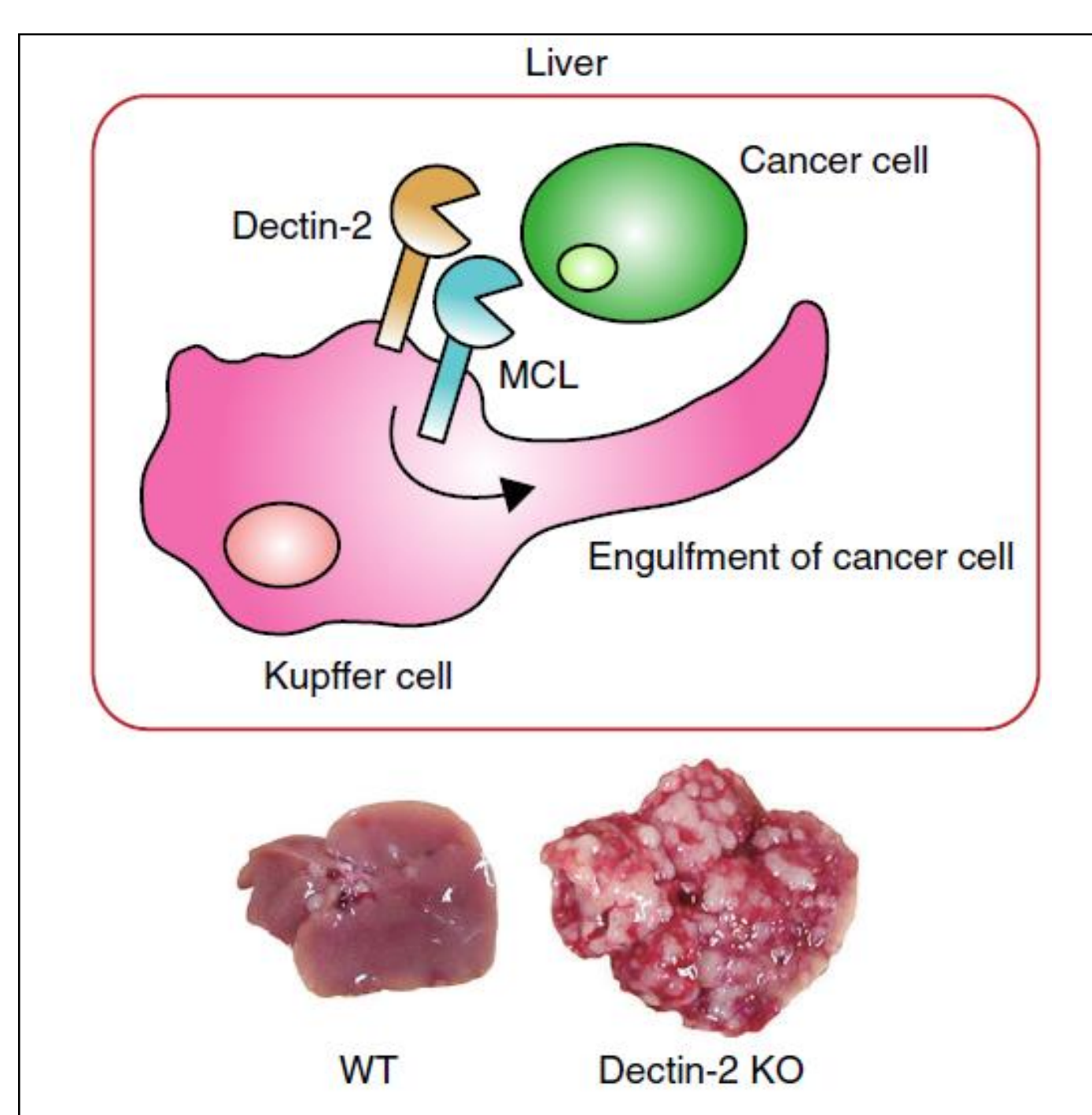
On the other hand, it has been emerging that commensal microorganisms make enormous impacts on our immune system. We are now investigating effects of intestinal microorganisms on hosts' immune cells to delineate mechanisms for homeostasis of immune system and tissue as well as disease pathogenesis.

For the current research projects listed below, utilizing advanced molecular biology techniques and several gene-deficient mouse strain, we strive to establish the molecular basis towards conquest of infection, autoimmune and inflammatory diseases, and cancers.

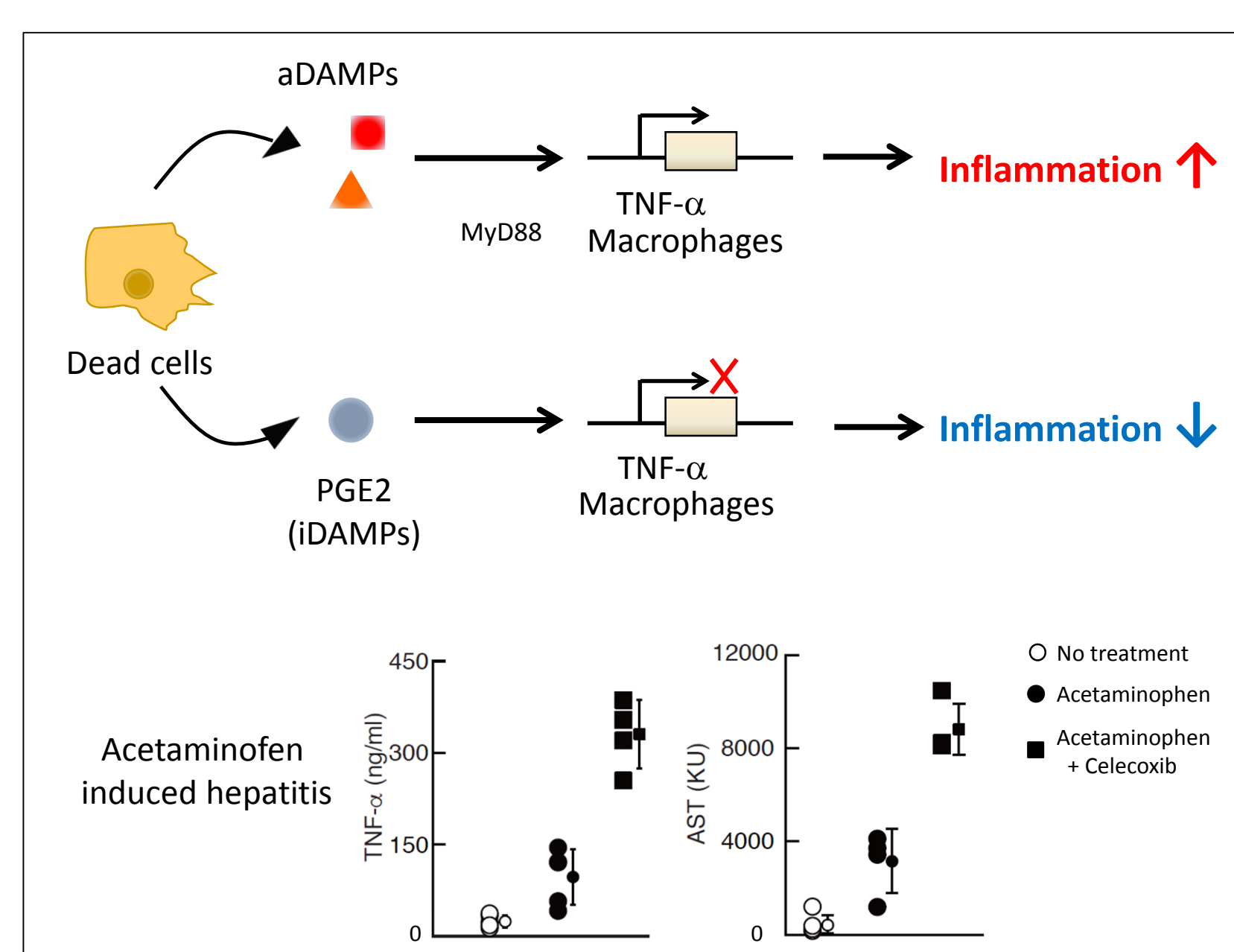
We now also engage in Max Planck-The University of Tokyo Center for Integrative Inflammation and also in a graduate student's education program.

(Current Projects)

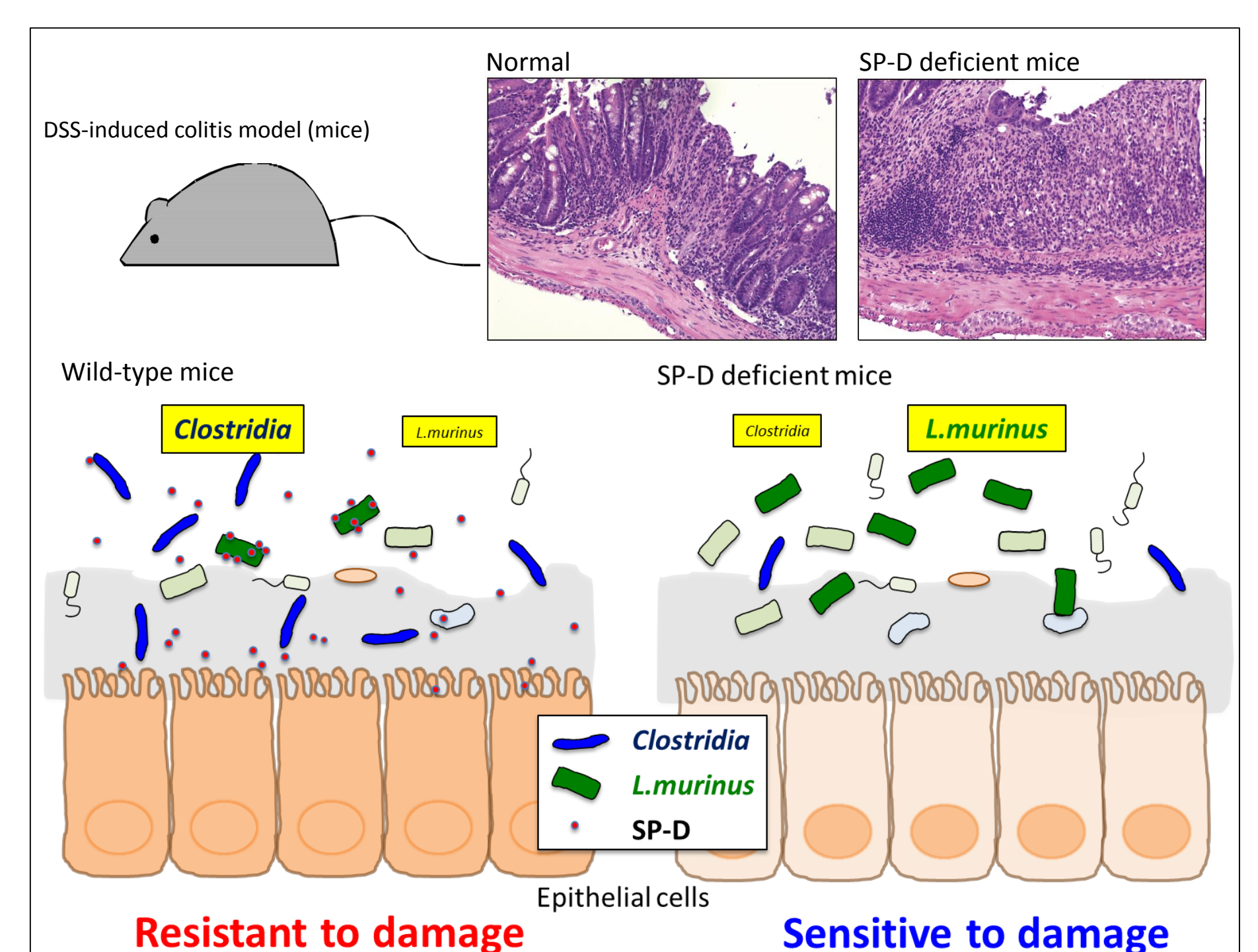
- ◆ Development of new immune-regulatory molecules for inflammation, autoimmunity and cancer
- ◆ Identification of dead cell-derived molecules activating/suppressing immune responses
- ◆ Elucidation of mechanisms of intestinal homeostasis by symbiosis with microorganisms
- ◆ Analysis of newly synthesized compounds with anti-tumor activity



(Fig.1) A C-type lectin receptor Dectin-2 promotes the engulfment of cancer cells by liver-residing macrophages, namely Kupffer cells, contributing to the suppression of liver metastasis. MCL, a C-type lectin receptor known for forming complex with Dectin-2, is also essential for such anti-tumor response (upper panel). Liver metastasis is aggravated in Dectin-2-deficient mice (lower panel). (PNAS 113: 14097-14102, 2016)



(Fig.2) Dead cells release damage-associated molecular patterns (DAMP) to activate immune cells to provoke inflammation. This study have shown the dead cells at the same time secrete PGE2 which suppress inflammation by inhibits TNF α transcription. We propose to name the former activating DAMP (aDAMP) and the latter inhibitory DAMP (iDAMP). Prostaglandin Our immune system is homeostatically controlled by balance of aDAMP and iDAMP. (PNAS 113: 3844-3849, 2016)



(Fig.3) Surfactant protein D (SP-D)-deficient mice are more sensitive to dextran sulfate sodium-induced colitis than wild-type mice (upper panel). SP-D inhibits extreme proliferation of *L.murinus* and other bacteria in wild-type mice. However, their proliferation is not regulated in the absence of SP-D, leading to alteration of microbiota composition and more severe colitis. SP-D contributes to the maintenance of intestinal homeostasis by balancing of microbiota composition (lower panel).