Taniguchi Lab.

[Integrative comprehension of innate immune responses]

Immunology Social Cooperation Program

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

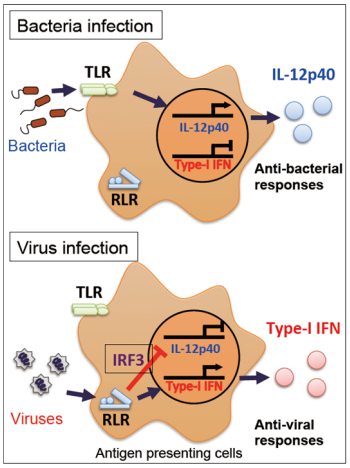
Graduate School of Medicine, Faculty of Medicine, Cooperative Chair

Our research interests within the fields of cellular and molecular immunology are focused on the molecular mechanisms of host defense against viral and bacterial infection and involve the extensive analysis of the mechanisms that underlie the regulation of gene expression and signal transduction in host defense systems. Among these mechanisms, the interferon (IFN) system is one of the most important in controlling infections. It was during the course of our studies on the IFN system that we discovered the interferon regulatory factor (IRF) family of transcription factors. Subsequent research carried-out by us and others have revealed a remarkable functional diversity of this family, particularly as key regulators in the control of immune responses and oncogenesis. While the core of our current research is aimed at clarifying the functions of IRF family members in the context of immunity, the broad scope of our scientific interests encompass a number of areas including those pertaining to innate immune system activation, inflammation, autoimmunity, and oncogenesis. One recent and new focus of our laboratory is to understand how molecules derived from dead cells, such as HMGB1, contribute to the regulation of inflammation and immunity. 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.

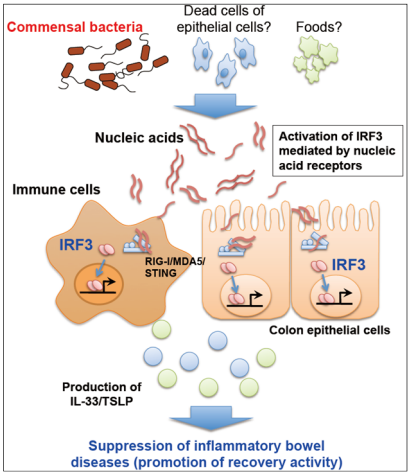
We now also engage in a graduate student's education program as a cooperative chair of Graduate School of Medicine, and Faculty of Medicine.

(Current Projects)

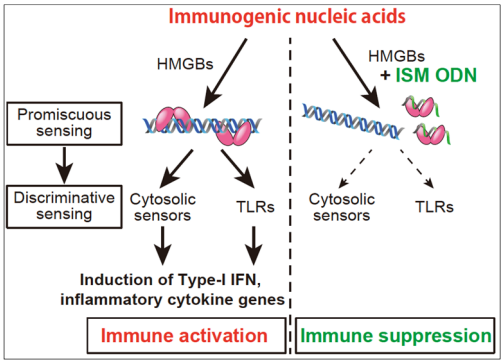
- ◆Signal cross-interferences between innate receptors
- ◆Analysis of signaling complex activated by newly identified nucleic acid recognition receptor
- ◆Role of HMGB1 in autoimmune and inflammatory diseases
- ◆IRF family transcription factors in tumor-associated immune regulatory mechanism
- ◆Analysis of newly synthesized compounds with anti-tumor activity
- ◆Identification of dead cell-derived molecules responsible for the activation and suppression of immune responses
- ◆Role of commensal bacteria in the regulation of innate and adaptive immunity
- ◆Development of new immune-regulatory agents for inflammation, autoimmunity, cancer
- ◆Role of T cell repertoires in mucosal immunity



(Fig.1) Bacterial infection activates TLRs and induces IL-12p40 gene, which promotes anti-bacterial responses (Upper). On the other hands, virus infection-activated IRF3 suppresses the IL-12p40 gene induction evoked by bacteria infection (Lower).(Nat. Immunol. 13: 659-666, 2012)



(Fig.2) IRF3 is activated by intestinal contents involving nucleic acids and activate IL-33 and TSLP genes, which promotes the suppression of colitis. (PNAS 109: 21016-21021, 2012)



(Fig.3) All immunogenic nucleic acids exposed in the cytosol are sensed by High-mobility group box (HMGB) proteins (Nature 462: 99-103, 2009)。The complex of HMGB proteins and the exposed nucleic acids is recognized by Toll-like receptors in endosomes and cytosolic nucleic acid sensors, which activates IRF and NF-κB transcription factors to induce type-I IFNs and inflammatory cytokine genes. ISM ODN which we developed binds very strongly to HMGB proteins and suppress nucleic acid-mediated innate immune responses. (PNAS 108: 11542-11547, 2011)