Center for Animal Disease Models

Members

Since 2012 April

◇ Immunological Disease Research Group

Yoichiro Iwakura	Chairman, RIBS, Prof.
Masato Kubo	RIBS, Prof.
Daisuke Kitamura	RIBS, Prof.
Chiharu Nishiyama	Fac. Indust. Sci. Tec., Prof.
Yoichiro Isohama	Fac. Pharm. Sci., Prof.
Tomokatsu Ikawa	RIBS, Asso. Prof.
Haruo Kozono	RIBS, Asso. Prof.
Shuhei Ogawa	RIBS, Junior Asso. Prof.
Yohsuke Harada	Fac. Pharm. Sci., Junior Asso. Prof.
Soo-Hyun Chung	RIBS, Assis. Prof.
Sachiko Kubo	RIBS, Technician
Ce Tang	RIBS, Project Researcher
Hsi-Hua Chi	RIBS, Postdoc
Xi Fu	RIBS, Postdoc

◇ Organ Regeneration Research Group

Ryo Goitsuka	RIBS, Prof.
Tomoko Masaike	Fac. Sci. Tec., Junior Asso. Prof.
Shunsuke Kon	RIBS, Junior Asso. Prof.

◇ Mental/Neurological Disorder Research Group

Teiichi Furuichi	Fac. Sci. Tec., Prof.
Takehi Nakamura	RIBS, Prof.

◇ Cancer Research Group

Kouji Matsushima	RIBS, Prof.
Kazunori Akimoto	Fac. Pharm. Sci., Prof.
Tatsunobu Mizuta	RIBS, Associate Prof.
Naoko Nakano	RIBS, Associate Prof.
Mitsutoshi Tsukimoto	Fac. Pharm. Sci., Asso. Prof.
Mahito Sadaie	Fac. of Sci. Tec., Asso. Prof.
Satoshi Ueha	RIBS, Asso. Prof.
Yuya Terashima	RIBS, Junior Asso. Prof.
Masayuki Sakurai	RIBS, Junior Asso. Prof.

◇ Advisory Board Member

Makoto Asashima	Teikyo Univ., Prof.
Kazuhiko Yamamoto	RIKEN, Team leader
Ken-ichi Yamamura	Kumamoto Univ., Prof.
Kensuke Miyake	Univ. of Tokyo, Prof.
Yoshikazu Higami	Fac. Pharm. Sci., Prof.
Hiroyasu Esumi	RIBS, Prof.

Objectives

- Elucidation of pathogenic mechanisms of diseases such as immune diseases, neuro-mental diseases, developmental diseases and cancer using gene-modified mice.
- Development of new drugs, functional foods, and vaccines to treat or prevent diseases by organizing interdisciprinary research groups and understanding disease pathogenesis.
- Support for researches by generating gene modified mice and improving infrastructure.

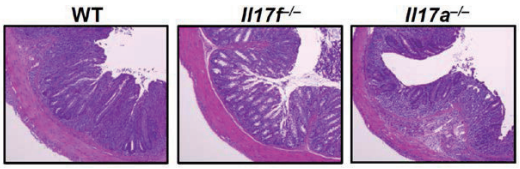
Research Topics

- Immunological Disease Research Group: Using gene-modified mice related to inflammatory cytokines, innate immunity receptors and signaling molecules, we aim to develop novel drugs, functional foods, and vaccines for autoimmune, allergic, and infectious diseases.
- Organ Regeneration Research Group: The molecular mechanisms of organogenesis, organ maintenance, and cell and organella movement during organogenesis and tumorigenesis will be investigated by generating gene-modified mice to develop novel therapeutics to treat diseases caused by abnormalities in these processes.
- Mental/Neurological Disorder Research Group: The pathogenic mechanisms of mental and neurological disorders will be investigated by using animal disease models to develop new therapeutics for the treatment of these diseases.
- Cancer Research Group: To know the pathogenesis and develop anti-cancer therapy, the mechanism of cancer development at the molecular, cellular, organ, and body levels will be investigated using gene-modified mice.

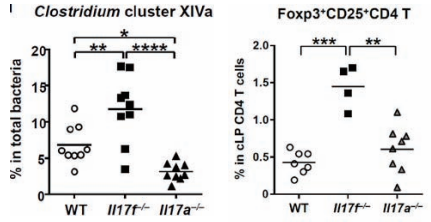
Current state and future perspective

This Center was established in 2013 as a branch of RIBS, and this year, the center has restarted as a member of the Research Institute for Science & Technology together with many new members. Through cooperation among different biological research groups in Noda area, the Center functions as a hub for the biomedical researches in TUS and Japan.

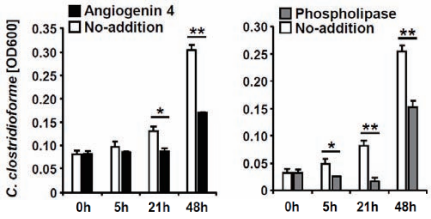
① IL-17F-deficient mice exhibit milder colitis.



② Regulatory T cells and commensal *Clostridium* XIV are over- expanded in the colon of IL-17F-deficient mice.

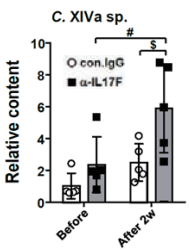


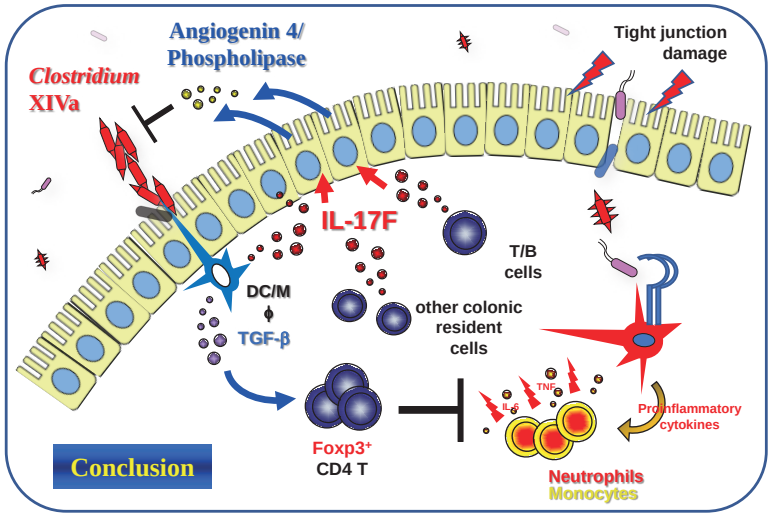
③ IL-17F inhibits the growth of *Clostridia* by inducing antimicrobial Angionenin4 and Phospholipase.



Tang C. et al., *Nat Immunol.* 2018, 19:755-765.

④ Treatment of anti-IL-17F antibody facilitates the expansion of *Clostridium* XIV and suppresses the colitis development.

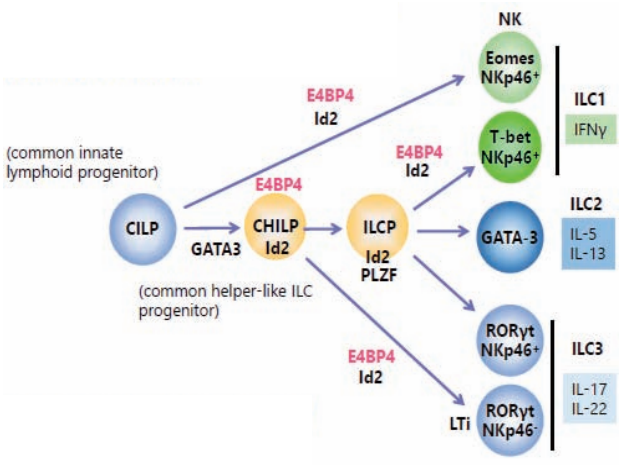




In this study, we found that IL-17F, but not IL-17A, gene knockout mice develop milder colitis, accompanied by over-colonization of regulatory T cell-inducing commensal *Clostridium* XIVa in the colon. IL-17F is produced by various colon resident cells, and induces a series of antimicrobial proteins to suppress the growth of *Clostridia*. Treating mice with anti-IL-17F antibody facilitates the colonization of *Clostridia* and inhibits mouse colitis.

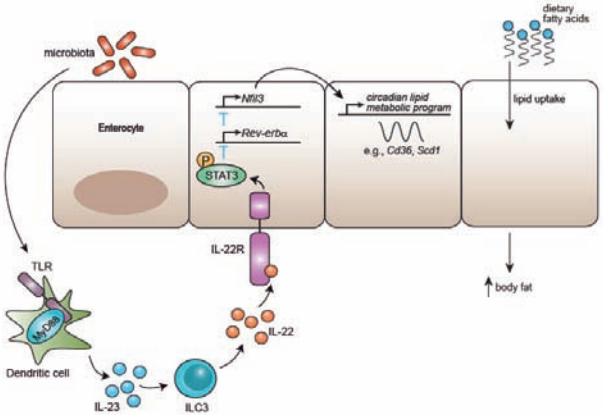
The circadian transcription factor E4BP4 regulates innate lymphoid cells and the lipid metabolism

E4BP4 regulates development of innate lymphoid cells (ILCs)



E4BP4 regulates the lipid metabolism in the gut

The intestinal microbiota has been identified as an environmental factor that markedly affects energy storage and body-fat accumulation in mammals, yet the underlying mechanisms remain unclear. Here we show that the microbiota regulates body composition through the circadian transcription factor E4BP4 (also called NFIL3). Nfil3 transcription oscillates diurnally in intestinal epithelial cells, and the amplitude of the circadian oscillation is controlled by the microbiota through group 3 innate lymphoid cells, STAT3 (signal transducer and activator of transcription 3), and the epithelial cell circadian clock. E4BP4 controls expression of a circadian lipid metabolic program and regulates lipid absorption and export in intestinal epithelial cells. These findings provide mechanistic insight into how the



Motomura et al. **Nat. Immunol**. 2011
Firth, M.A. et al. **J. Exp. Med.** 2013,
Di Santo, J.P., Veiga-Fernandes, H., et al. **Cell report** 2015 Wang et al., **Science** 357, 912–916, 2017