Impromptu Seminar #2-1

Keio University School of Medicine

JKiC 1F seminar room
at the north end of the campus

Mon, December 11th, 2017

15:30-16:45

Noah W. Palm

Assistant Professor of Department of Immunobiology
Yale University School of Medicine

"Establishing Causal Roles for the Gut Microbiota in Human Disease"

(Host: K. Honda, Professor of Microbiology and Immunology)

The composition of the gut microbiota is thought to have dramatic effects on the development and progression of a variety of diseases, including Inflammatory Bowel Disease (IBD), autoimmunity, and metabolic syndrome. However, identifying the specific bacteria that preferentially affect disease susceptibility and severity in humans remains a major challenge. In response to this problem, we developed a novel technology that uses the host's own immune response to the microbiota as a guide to identify specific members of the gut microbiota that preferentially modulate disease development. This approach specifically identified known disease-causing intestinal bacteria in a mouse model of microbiota-driven colitis. Furthermore, we were able to use this approach to identify specific bacterial strains from IBD patients that selectively conferred susceptibility to severe colitis when transplanted into germ-free mice. These studies thus: (i) establish a new strategy for the identification of disease- and immune-modulating members of the microbiota in humans; (ii) identify potentially disease-driving members of the intestinal microbiota in humans with IBD; and (iii) begin to establish causal, rather than correlative, connections between specific changes in the microbiota and human disease. Future studies using similar approaches will allow us to elucidate the full spectrum of reciprocal interactions between the microbiota and the host immune system. These studies will lead to a more complete understanding of the role of microbiota composition in human health and disease and will eventually enable the development of novel and specific microbiota-targeted therapeutics.

Impromptu Seminar #2–2

Keio University School of Medicine

JKiC 1F seminar room
at the north end of the campus

Mon, December 11th, 2017

16:45-18:00

Daniel Mucida

Assosiate Professor of Laboratory of Mucosal Immunology
Rockefeller University

"Intestinal Epithelial and Intraepithelial T Cell Crosstalk Mediates a Dynamic Response to Infection"

(Host: K. Honda, Professor of Microbiology and Immunology)

Intestinal intraepithelial lymphocytes (IELs) are located at the critical interface between the intestinal lumen, constantly exposed to food and microbes, and the core of the body. Using high-resolution microscopy techniques and intersectional genetic tools, we investigated the nature of IEL response to luminal microbes. We observed that TCR$\gamma\delta^+$ IELs exhibit a distinct location and movement pattern in the epithelial compartment that is microbiome-dependent and quickly altered upon enteric infection. Infection-induced IEL changes include increased inter-epithelial cell (EC) scanning behavior, which is associated with enhanced anti-microbial gene expression and glycolysis. Conversely, direct modulation of the glycolytic status is sufficient to change IEL behavior and the susceptibility to early pathogen invasion. Both, IEL behavioral and metabolic changes are dependent on EC pathogen sensing. Our results uncover a coordinated EC–IEL response to enteric infections that modulates lymphocyte energy utilization and dynamics, helping the maintenance of epithelial barrier.

Support: NIH and Helmsley Charitable Trust (DM), Colitis and Crohn's Foundation of America (DM and BSR).