

Study of *Shigella* infectious strategy for the intestinal barrier

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【Outline of survey】

The intestinal lumen is covered by epithelial monolayer, which acts an intrinsic defensive barrier against microbial invaders. Nevertheless, many pathogenic bacteria, including *Shigella*, are capable of colonizing the intestinal epithelium by circumventing the various host barrier functions. In the present study, we investigate how the bacterial pathogens such as *Shigella* colonize the intestinal epithelium and how they can evade host innate defense system. In brief, we focus on the role of subset of effectors secreted via the type III secretion system from intracellular *Shigella* in the middle of stage of infection of intestinal epithelium, and investigate their biological activities and roles of each of the effectors in promoting bacterial survival and colonization. Based on the results with each of the effectors together, we envisage to unveil the novel bacterial infectious system, which will also provide some important insight into understanding the sophisticated bacterial infectious strategies shared with many other bacterial pathogens.

【Expected results】

When we will achieve the goals of the research proposal, we expect the following outcomes; (i) our study will provide clue and idea to elucidate other bacterial infectious systems and the host-cellular responses, (ii) our study will allow us to evaluate the impact of each barrier function lying in the intestinal epithelium on bacterial infection, (iii) we will get some insight into understanding the molecular basis for determining the human-specificity of *Shigella*, and (iv) we will translate the knowledge obtained through this study into development of safer *Shigella* vaccine, and animal model.

【References by the principal researcher】

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- Iwai H., Kim, M., Ashida H., Ogawa M., Fujita Y., et al. A bacterial effector targets Mad2L2, an APC inhibitor, to modulate host cell cycling. *Cell.* 130: 611-623. 2007.
- Yoshida S., Handa Y., Suzuki, T., Ogawa M., Suzuki M., et al. Microtubule-severing activity of *Shigella* is pivotal for intercellular spreading. *Science.* 314: 985-989. 2006.
- Ogawa, M., Yoshimori, T., Suzuki, T., Sagara, H., Mizushima, N., et al. Escape of intracellular *Shigella* from autophagy. *Science.* 307: 727-731. 2005.

【Term of project】 FY2008—2012

【Budget allocation】

152,800,000 yen (direct cost)

【Homepage address】

<http://www.ims.u-tokyo.ac.jp/bac/hp/mainpage.html>