O-8. *Toxoplasma Gondii* Effectors TgIST and TgGRA15 Differentially Target Host IDO1 to Antagonize the IFN-γ-induced Anti-*T. Gondii* Response in Human Cells

Hironori BANDO[1,2], Yasuhiro FUKUDA[1], Masahiro YAMAMOTO[2] and Kentaro KATO[1]

[1]Graduate School of Agricultural Science, Tohoku University
[2]Department of Immunoparasitology, RIMD Osaka University

Toxoplasma is an important intracellular pathogen that causes lethal toxoplasmosis in humans and animals. Interferon-γ (IFN-γ) is critical for anti-*T. gondii* responses in both human and mice. Recent extensive studies using the mouse as a model organism have revealed that IFN-γ-inducible GTPases play critical roles, and also revealed that virulent *T. gondii* can inhibit IFN-γ-mediated host immune response. Thus, the relation between host immunity and *T. gondii* virulence is well established in mice. On the other hand, IFN-γ-induced anti-*T. gondii* responses in human is not completely clear because the IFN-γ-inducible GTPase-mediated anti-*T. gondii* responses may not be major in human. Therefore, *T. gondii* virulence strategy to resist IFN-γ-induced anti-*T. gondii* responses in human also largely remains unclear. Here, at first, we generate various human cells lacking IFN-γ-inducible gene, and show that IDO1 is required for IFN-γ-induced response in various types of human cells. Then, we focus on *T. gondii* virulence mechanisms in human cell. In this study, we focus on distinct *T. gondii* virulence mechanisms involving TgIST and TgGRA15 to suppress IFN-γ-dependent immunity in human cells. We generate TgIST or TgGRA15-deficient *T. gondii* by CRISPR/Cas9 system, and show that IDO1 mRNA induction is inhibited TgIST-dependently in various types of IFN-γ-stimulated human cells, and also show that IDO1-dependent anti-*T. gondii* response is inhibited TgGRA15-dependently in secondly infected cells. Taken together, we demonstrate that *T. gondii* possesses at least two differential virulence mechanisms targeting IDO1 by TgIST and TgGRA15 to antagonize IFN-γ-induced anti-*T. gondii* responses in human cells.