Internship Proposal 2014-2015

Laboratory: Division of Innate Immunity, The Institute of Medical Science, The University of Tokyo (IMSUT)

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Internship project: Mechanisms controlling TLR responses (Sep-Dec, 2014)

What we do

Toll-like receptors (TLRs) recognize the pathogen-associated molecular patterns (PAMPs) and induce immune response. TLRs recognize not only PAMPs but also host-derived ligands in the disease state. TLR activation has to be under the tight control to avoid hazardous inflammation. We focus on the mechanism controlling TLR activation with the techniques in molecular biology, cell biology, and mouse genetics. We generate monoclonal antibody (mAb) to detect endogenous TLRs (Onji et al., 2013; Kannno et al., 2013). We also generate knockout and knockin mice to see *in vivo* outcomes when TLRs is out of control. The D34A mutation of the TLR transporter Unc93 homolog B1 (Unc93B1) enhances TLR7 response and attenuates TLR9 response. Knockin mice harboring this mutation show lethal systemic inflammation (Fukui et al., 2011). TLRs have been shown to have pathogenic roles not only in infectious diseases but also in autoimmune disease. We are trying to use mAbs to TLRs for therapeutic intervention in autoimmune diseases.

Publication

1. Onji et al., An essential role for the N-terminal fragment of Toll-like receptor 9 in DNA sensing. Nat Commun. 2013
2. Kanno and Yamamoto et al., Essential role of Toll-like receptor 7 (TLR7)-unique cysteines in an intramolecular disulfide bond, proteolytic cleavage and RNA sensing. Int Immunol. 2013
3. Fukui et al., Unc93B1 restricts systemic lethal inflammation by orchestrating Toll-like receptor 7 and 9 trafficking. Immunity. 2011