ID No.	K3001	
Project Title	Studying roles of Toll-like receptor 9 in autoimmune diseases	
Principal Investigator	Eicke Latz	(Prof., Univ. Bonn)
Project Members IMSUT Host	Kensuke Miyake	(Prof., IMSUT)
Researcher Members	Tatjana Reuter	(PhD Student, Univ. Bonn)
	Takuma Shibata	(Assistant Prof., IMSUT)
	Ryota Sato	(Project Assistant Prof., IMSUT)

Report

Toll-like receptors (TLRs) are expressed in immune cells and sense pathogen components to mount defense responses. Although TLR9 basically responds to microbial single-stranded DNA (ssDNA), TLR9 responses to self-derived ssDNA have been implicated in a variety of autoimmune diseases. We studied roles of TLR9 in activation, proliferation, and differentiation of monocyte/macrophages and dendritic cells in steady and disease states. We examined *Dnase1*$^{-/-}$, *Dnase1l1*$^{-/-}$, *Dnase1l2*$^{-/-}$, *Dnase1l3*$^{-/-}$, *Pld3*$^{-/-}$, *Pld4*$^{-/-}$ mice to study the role of TLR9 in autoimmune responses. TLR9-dependent alteration in tissue macrophages were studied in these mice. Unfortunately, we could not find any monocytosis in these single mutant mice and therefore studied double mutant mice. We finally found monocytosis in *Pld3*$^{-/-}$ *Pld4*$^{-/-}$ double mutant mice. Ly6Chigh monocyte/macrophages increased in the spleen and the circulation. Monocytosis was also found in the liver, brain, and salivary glands. Characterization of macrophages in these organs is now ongoing. To ask whether the monocytosis is dependent on TLR9, we crossed *Pld3*$^{-/-}$ *Pld4*$^{-/-}$ mice with *Tlr9*$^{-/-}$ mice. Our results suggest that PLD3 and PLD4 negatively regulates NA-sensing TLRs by degrading their ligands.