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Project Title	Studying roles of Toll-like receptor 9 in autoimmune diseases
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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. Here, we will study roles of TLR9 in activation, proliferation, and differentiation of monocyte/macrophages and dendritic cells in steady and disease states. We will use *Tlr9*$^{-/-}$, *Pld3*$^{-/-}$, and *Dnase1*$^{-/-}$ mice, where TLR9 drives autoimmune responses. TLR9-dependent alteration in tissue macrophages in these mice will be studied. We will ask whether some tissue macrophages are increased in *Dnase1*$^{-/-}$ and *Pld3*$^{-/-}$ mice. If TLR9-dependent increase in tissue macrophages are confirmed, roles of the increased tissue macrophages in tissue damages found in these mice will be studied. In parallel, molecular mechanisms behind TLR9-dependent increase in monocytes/macrophages will be studied. We hypothesize that TLR9 directly drives proliferation and differentiation of tissue macrophages. In 2019, we have already established the Ba/F3 line which proliferate in TLR9-dependent manner. In 2020, we conducted FACS analyses of tissue macrophages in *Dnase1*$^{-/-}$, and *Dnase1*$^{-/-}$ *Tlr9*$^{-/-}$ mice to identify the monocyte subset that increased in TLR9-dependent manner. Unfortunately, we could not find any alteration in monocytes/macrophages. On the other hand, we generated *Pld3*$^{-/-}$ mice and now are crossing them with *Tlr9*$^{-/-}$ mice. *Pld3*$^{-/-}$ mice will be studied in near future.