

Poster Presentation

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Structural studies of nucleic acid sensing Toll-like receptor

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Toll-like receptors (TLRs) sense pathogen-associated molecular patterns originating from invading microorganism and evoke innate immune responses. Among TLRs, TLR3, TLR7, TLR8, and TLR9 are localized to endosomal membranes and are responsible for the recognition of nucleic acids. TLR7 and TLR8 recognize single stranded RNA. In addition, TLR7 and TLR8 are activated by small chemical compounds. TLR9 recognizes DNA containing Cytosine-phosphate-Guanine motif. These nucleic acid sensing TLRs are attractive therapeutic targets for the modulation of immune responses in the viral and bacterial infections and in the pathogenesis of autoimmune diseases. However, the structural basis for the nucleic acid recognition and signaling mechanisms remains to be elucidated. Therefore, we conducted crystallographic studies of these TLRs. Recently, we have determined the crystal structures of the extracellular domain of human TLR8 in the unliganded form and in the liganded forms with chemical ligands (Tanji et al., 2013). Both unliganded and liganded forms of TLR8 were dimer. Ligands were located at two equivalent positions in the dimerization interface. The ligand binding induced the reorganization of the preformed dimer to the activated dimer such that the C-terminal regions of the two protomers are in close proximity to enable the subsequent dimerization of the intracellular signaling domains and its interactions with adaptor proteins.

[1] H. Tanji, U. Ohto, T. Shibata et al., *Science*, 2013, 339, 1426-1469.

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