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SUMMARY of
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Research Title		Structural anaylsis of NOD1 and NOD2 LRR domain and binding mode of their ligands.
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	Present Title	Structural anaylsis of NOD1 and NOD2 LRR domain and binding mode of their ligands.
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Summary

The innate immune system detects the invasion of pathogens, acts as the first barrier until acquired immune system is activated and induces successive host defense mechanisms. Various pathogens present in the environment develop the tools to escape from innate immunity. The host innate immunity has also evolved customized PRRs for pathogenic molecules that cannot be altered. The peptidoglycan, a major component of bacterial cell wall, is one of the well characterized PAMPs recognized by NOD molecules. NOD1 and NOD2 are a cytoplasmic muropeptide sensor that recognizes the ligands taken up through various routes. Once NOD1 is activated by its appropriate substrates, sequential signal transduction results in the first host defense. NOD1 recognizes the DAP-containing part like L-Ala--D-Glu-meso-diaminopimelic acid (Tri-DAP) present in the peptidoglycan of Gram negative bacteria and some Gram positive bacteria whereas NOD2 recognizes muramyl dipeptide (MDP) in the peptidoglycan of Gram positive bacteria. It was reported that the leucine-rich-repeat (LRR) variants of these two intracellular peptidoglycan-sensing receptors are very closely related in asthma, inflammatory bowel disease (IBD), Crohn's disease and Blau syndrom. Here, we succeeded crystallization of LRR domain in NOD1 and NOD2.

It is difficult to express only the LRR domains of NLR family in *E. coli* system. We designed fusion proteins which contain N-terminal LRR motif that increases solubility and expression in *E. coli* and C-terminal LRR motif of NLR family such as NOD1, NOD2 and NOD3. 3 fusion proteins are well purified and 3 crystals are finally obtained and diffracted into the resolution of 2.4 Å, 2.7 Å and 1.95 Å, respectively. There is a molecule in an asymmetric unit of hNOD1 fusion protein crystals and it belonged to orthorhombic space group C2221, with unit cell parameters a = 84.18 Å, b = 151.06 Å, c = 78.57 Å. In the case of hNOD2 fusion protein, we have known the crystals belonged to monoclinic space group P21, with unit cell parameters a = 109.632 Å, b = 126.283 Å, c = 110.536 Å. Also, the crystal of hNOD3 belonged to monoclinic space group p21 with unit cell parameters a = 73.097 Å, b = 66.137 Å, c = 106.706 Å.

Just as other LRR motif, LRR domain of human NOD1 (hNOD1) makes horseshoe-shaped structure. Total 8 repeats of leucine rich repeat are included in the hNOD1 LRR motif. Interestingly, unidentified metal atom is found in the C-terminal LRR motif. In the case of hNOD2 and hNOD3, unidentified electron density is found in the concave surface that is possible ligand binding site.

The innate immunity is more common than adaptive immunity, and the research is expected to continue in the future. Innate immunity is an immune system that is older than adaptive immunity and exists in a wider variety of organisms. For example, the plant's immune system and the innate immune system of humans have the same LRR structure and understanding how their pattern recognition mechanisms evolve has a great academic value.