

TOLL receptor Serial Femtosecond Crystallography structure

Understanding the dynamics of biological processes provides new insight into treating disease. X-ray crystallography reveals what proteins look like at the atomic scale and has been key for developing new therapeutics. TOLL-like receptors are activated by pathogens, which results in a string of protein interactions within the cell producing an immune response. Two responses can occur, immunity, or inflammation. Inflammation is associated with several pathological states, including infectious, autoimmune, inflammatory, cardiovascular, and cancer-related disorders which makes them an important biological target. TOLL like receptor adaptor proteins when mixed can oligomers into highly ordered structures. Using X-ray Free Electron Laser (XFEL) facilities and their extremely intense sources of X-rays Serial Femtosecond Crystallography (SFX) data was collected on these oligomers. Using SFX methods we have solved the first biological relevant structure of Myeloid differentiation primary response gene 88 (MYD88), a Toll-like receptor (TLR) adaptor protein, which plays an important role in inflammatory disease. The data generated at the Linac Coherent Light Source provided structural and mechanistic insight into TLR signal transduction.

References:

1. Clabbers, M., Holmes, S. et.al. MyD88 TIR domain higher-order assembly interactions revealed by micro-crystal electron diffraction and serial femtosecond crystallography Nature Communications, Nature communications 12 (1), 1-14, 2021.

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