

MyD88 TIR domain higher-order assembly interactions revealed by serial femtosecond crystallography

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MyD88 and MAL are Toll-like receptor (TLR) adaptors that signal to induce pro-inflammatory cytokine production. We previously observed that the TIR domain of MAL (MAL^{TIR}) forms filaments in vitro and induces formation of crystalline higher-order assemblies of the MyD88 TIR domain (MyD88^{TIR}). Due to their crystal size, conventional crystallography proved to be challenging. However, through serial femtosecond crystallography (SFX) we were able to determine the structure of MyD88 crystals. Here, we present the SFX structure of the MyD88^{TIR} assembly, which revealed a biological relevant two-stranded higher order assembly arrangement of TIR domains analogous to that seen previously for MAL^{TIR}. Our study provides structural and mechanistic insights into TLR signal transduction¹.

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