



Supplemental Figure 1. A model depicting the proposed mechanism for TRAF6 regulation by optineurin.

Optineurin is a new binding partner of IRAK-1, preventing the NF- κ B signaling pathway. Stimulation of TLR/IL-1 β receptor recruits MyD88 through the Toll/interleukin-1 receptor (TIR) domain. Then, MyD88 interacts with IRAK4 through their death domains (DD). Due to autophosphorylation and activation, IRAK4 enables its DD to bind the DD of the related kinase IRAK1. The MyD88-IRAK complex further binds to the ubiquitin ligase TRAF6, which undergoes autoubiquitination. Polyubiquitination of TRAF6 is key to TAB2/3 recruitment and NF- κ B signaling. Optineurin binds to IRAK1 and inhibits TRAF6 polyubiquitination by recruiting the deubiquitinase CYLD.