The TNF receptor associated factors (TRAF1-6) are major signal transducers for the TNF receptor (TNFR) superfamily and the IL-1 receptor (IL-1R)/Toll-like receptor (TLR) superfamily. As a first step towards understanding this signal transduction, we determined the crystal structures of the TRAF domain of human TRAF2, both alone and in complex with several receptor peptides, revealing a conserved trimeric self-association of TRAF2 and a symmetrical interaction with the receptor. We also determined the crystal structure of the complex between the TRAF domain of TRAF2 and TRADD. In conjunction with biochemical and cellular studies, we revealed a novel mechanism of TRAF signaling. Recently, we determined the crystal structures of TRAF6, alone and in complex with receptor peptides from CD40 and TRANCE-R. These structures revealed a distinct molecular mechanism for TRAF6 to initiate signal transduction of both the TNFRs and the IL-1R/TLRs.

**Keywords:** TRAF, SIGNAL TRANSDUCTION, CRYSTAL STRUCTURES