Broader function of TIR domains in Arabidopsis immunity.

Calcium signaling is essential for immune responses in Arabidopsis. TIRs (Toll Interleukin-like R genes) are an ancient family of NAD-degrading enzymes functioning in immune signaling in prokaryotes, plants, and mammals. In Arabidopsis, a class of TIR domain containing immune receptors, the so-called TNLs, activates the EDS1 module (Enhanced Disease Susceptibility 1), which in turn triggers RNL-driven (CC-R NLR [Nucleotide binding Leucine rich repeats]) calcium influx leading to defense and cell death induction. We found that the TNL SADR1 [Suppressor of ADR1-L2 (Activated Disease Resistance 1-like 2) 1] was required for immune signaling downstream of the RNL ADR1-L2. SADR1 was involved in PAMP signaling, in "runaway cell death" and, together with RNLs, regulated gene expression during bacterial infection, likely in a non-autonomous way. This defense system controlled by RNLs was triggered by effectors and was essential to limit the systemic propagation of the pathogen. SADR1 was not required for immune signaling initiated by other TNLs but potentiated ADR1-L2 signaling partially independently of EDS1. This potentiation activity was not specific to SADR1 as the auto-active TNL *snc1* could partially compensate SADR1 loss of function. Inhibiting TIR enzymatic activity with high concentration of nicotinamide, a product of NAD cleavage known to inhibit NADase activity in humans, resulted in decreased calcium influx, pathogen growth restriction and host cell death following PRR and TNL or CNL activation. Overall, TIR domains potentiate calcium influx and defense and are broadly required for Arabidopsis immunity.