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TLR-independent control of innate immunity in Caenorhabditis elegans by the TIR domain adaptor protein TIR-1, an ortholog of human SARM

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Both plants and animals respond to infection by synthesizing compounds that directly inhibit or kill invading pathogens. We report here the identification of infection-inducible antimicrobial peptides in Caenorhabditis elegans. Expression of two of these peptides, NLP-29 and NLP-31, was differentially regulated by fungal and bacterial infection and was controlled in part by tir-1, which encodes an ortholog of SARM, a Toll–interleukin 1 receptor (TIR) domain protein. Inactivation of tir-1 by RNA interference caused increased susceptibility to infection. We identify protein partners for TIR-1 and show that the small GTPase Rab1 and the f subunit of ATP synthase participate specifically in the control of antimicrobial peptide gene expression. As the activity of tir-1 was independent of the single nematode Toll-like receptor, TIR-1 may represent a component of a previously uncharacterized, but conserved, innate immune signaling pathway.