Supporting Information

Sarkar *et al.* 10.1073/pnas.0804956105

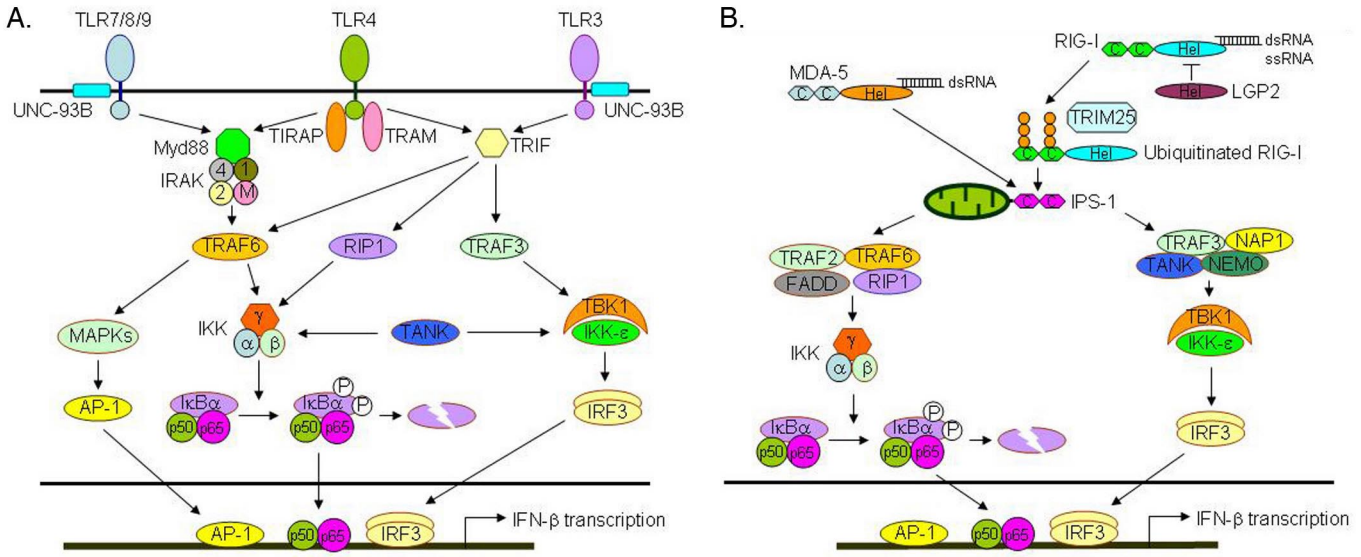

Fig. S1. An overview of induction of type I IFN. (*A*) Type I IFN induction by Toll-like receptors (TLRs). Five TLRs (TLR3, TLR4, TLR7, TLR8, and TLR9) have been shown to induce the production of type I IFNs. TLR7, TLR8, and TLR9 trigger the classical Myd88-dependent TLR pathway, via the TIR-containing cytosolic adapter Myd88. TLR3 triggers the alternative Myd88-independent, TIR domain-containing adapter, inducing the IFN-β (TRIF)-dependent pathway. TLR4 triggers the Myd88-dependent pathway via the TIRAP-Myd88 interaction and triggers the Myd88-independent pathway via the TRIF-related adapter molecule (TRAM)-TRIF interaction. The Myd88-dependent pathway results in the activation of both NF-κB and MAPKs via the IL-1 receptor associated kinase (IRAK) complex, which comprises two active kinases (IRAK-1 and IRAK-4) and two noncatalytic subunits (IRAK-2 and IRAK-M). The Myd88-independent pathway results in the activation of IRF3 via two kinases: NF-κB kinase ε (IKK-ε) and TANK-binding kinase-1 (TBK-1). TRAF family member-associated NF-κB activator (TANK) interacts with NF-κB essential modulator (NEMO; IKK-γ), TBK1 and IRF3 and may therefore form a liaison between the Myd88-dependent and Myd88-independent pathways. (*B*) Type I IFN production by MDA-5 and RIG-I. ssRNA with a 5′-triphosphate group and dsRNA are detected by the RIG-I and MDA-5. Activation of RIG-I involves lysine-63-linked ubiquitination (Ub) by the ubiquitin ligase TRIM25. This activation is inhibited by LGP2. Both MDA-5 and RIG-I activate the adapter proteins IPS-1 via CARD domain (C) interactions. IPS-1 then induces signaling pathways that result in the activation of the transcription factors IRF3 and NF-κB.

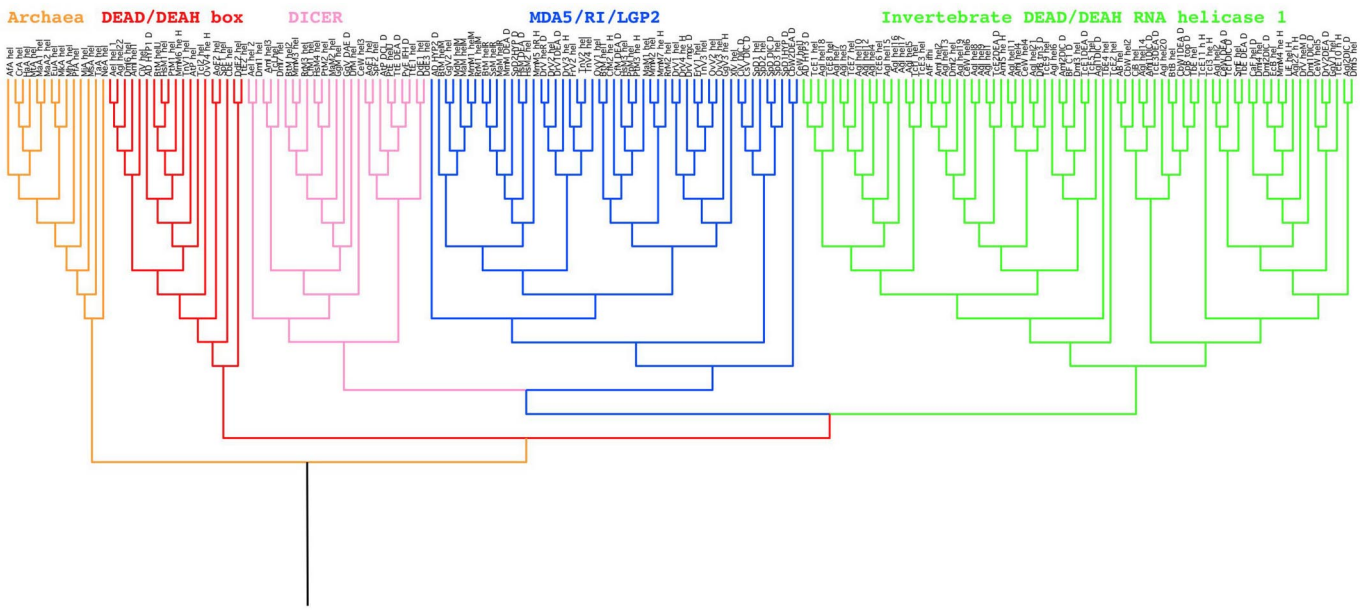

Fig. S2. Phylogenetic tree showing the relationships of helicases. This is the same tree in Fig. 2*A* of the main text, provided here to magnify and observe the gene names. See main text for details. Accession numbers for all sequences used in this tree are in Table S1.

Other Supporting Information Files

Table S1 (PDF)
Table S2 (PDF)
Table S3 (PDF)
Table S4 (PDF)