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Identification of a nuclear receptor/coactivator developmental signaling pathway in the nematode parasite Strongyloides stercoralis

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Abstract

DAF-12 is nematode-specific nuclear receptor that has been proposed to govern development of the infectious stage of parasitic species, including Strongyloides stercoralis. Here, we identified a parasite-specific coactivator called DIP-1 that is required for DAF-12 ligand-dependent transcriptional activity. DIP-1 is found only in Strongyloides spp. and selectively interacts with DAF-12 through an atypical receptor binding motif. Using CRISPR-Cas9 directed mutagenesis, we demonstrate that DAF-12 is required for the requisite developmental arrest and the ligand-dependent reactivation of infectious S. stercoralis iL3 larvae, and that these effects require the DIP-1 coactivator. These studies reveal the existence of a distinct nuclear receptor/coactivator signaling pathway that governs parasite development.