reactome

SARM binds viral dsRNA:TLR3:TICAM1

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Introduction

Reactome is open-source, open access, manually curated and peer-reviewed pathway database. Pathway annotations are authored by expert biologists, in collaboration with Reactome editorial staff and cross-referenced to many bioinformatics databases. A system of evidence tracking ensures that all assertions are backed up by the primary literature. Reactome is used by clinicians, geneticists, genomics researchers, and molecular biologists to interpret the results of high-throughput experimental studies, by bioinformaticians seeking to develop novel algorithms for mining knowledge from genomic studies, and by systems biologists building predictive models of normal and disease variant pathways.

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Literature references

Fabregat, A., Sidiropoulos, K., Viteri, G., Forner, O., Marin-Garcia, P., Arnau, V. et al. (2017). Reactome pathway analysis: a high-performance in-memory approach. *BMC bioinformatics, 18*, 142. ↗

Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

Fabregat, A., Jupe, S., Matthews, L., Sidiropoulos, K., Gillespie, M., Garapati, P. et al. (2018). The Reactome Pathway Knowledgebase. *Nucleic Acids Res, 46*, D649-D655. ↗

Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

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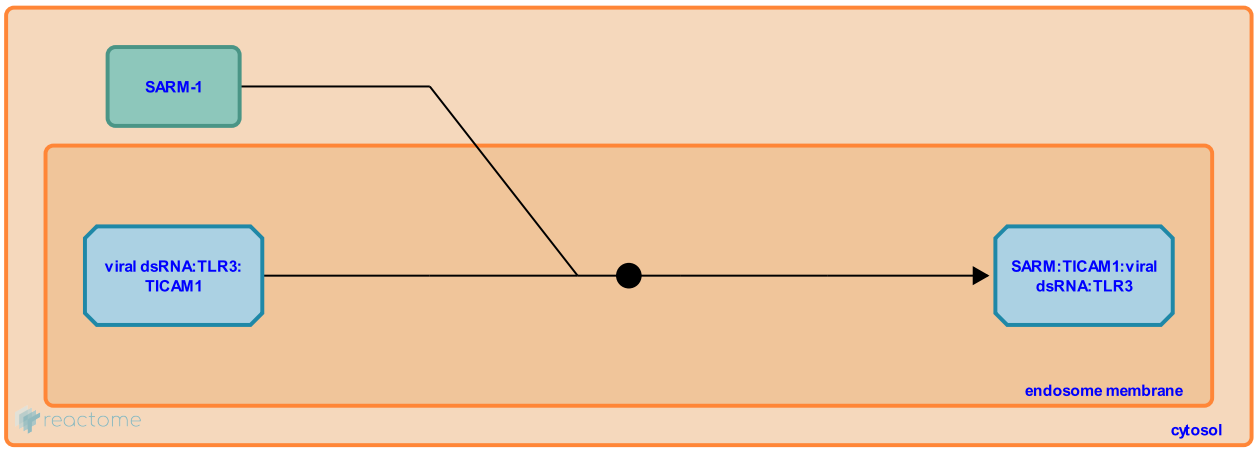
Stable identifier: R-HSA-9014320

Type: binding

Compartments: endosome membrane, cytosol



SARM (sterile alpha-and armadillo-motif-containing protein) is a TIR-domain-containing adaptor, which functions as a negative regulator of TRIF (TICAM1)-dependent Toll-like receptor signaling in humans. A pairwise yeast two-hybrid assay demonstrated that SARM is capable of binding directly to TICAM1 (Carty M et al. 2006). GST pulldown studies suggest that protein-protein interactions occur between the TIR domains of SARM and TICAM1 (Carlsson E et al. 2016). The complex of TICAM1:SARM is thought to inhibit downstream TRIF signaling by preventing the recruitment of TRIF effector proteins (Carty M et al. 2006).

SARM expression was shown to inhibit poly(I:C)-induced TICAM1-dependent NFkappaB activaion, RANTES production and IRF activation in human embryonic kidney HEK293 cells (Carty M et al. 2006). Moreover, suppression of endogenous SARM expression by siRNA led to enhanced TLR3- and TLR4-dependent gene induction in both transformed HEK293 and primary PBMC cells (Carty M et al. 2006), Thus, SARM associates with TICAM1 via its TIR and sterile-alpha motif (SAM) domains to block the induction of proinflammatory genes downstream TLR3.

Literature references

Schröder, M., Stack, J., Moynagh, PN., Carty, M., Bowie, AG., Goodbody, R. (2006). The human adaptor SARM negatively regulates adaptor protein TRIF-dependent Toll-like receptor signaling. *Nat. Immunol., 7*, 1074-81.

Editions

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