GSDME (1-270) binds cardiolipin

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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

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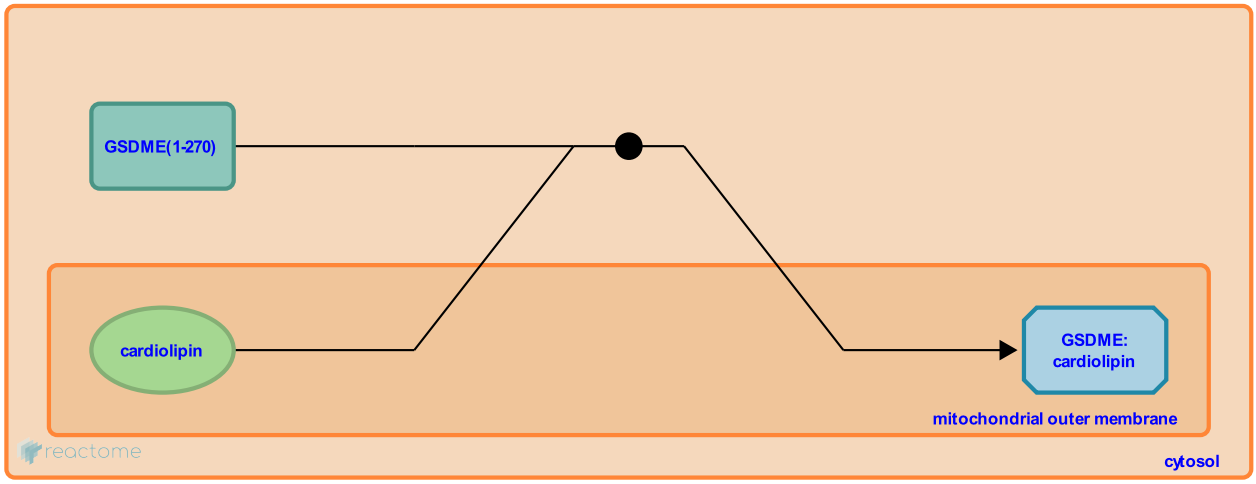
Stable identifier: R-HSA-9710354

Type: binding

Compartments: cytosol, mitochondrial outer membrane



Gasdermin E (GSDME) is cleaved by caspase 3 (CASP3) at D270 in response to apoptotic stimuli (Rogers C et al. 2017; Wang Y et al. 2017). The released N-terminal fragment of GSDME (1-270) targets the plasma membrane to drive pyroptosis in GSDME-expressing cells (Wang Y et al. 2017). In addition, the N-terminal fragment of mouse GSDME binds to cardiolipin liposomes causing severe leakage (Wang Y et al. 2017). Although cardiolipin is primarily located in the inner mitochondrial membrane, the outer mitochondrial membrane also contains around 10-20% cardiolipin and cardiolipin translocates in a regulatable manner between the compartments (Liu J et al. 2003; reviewed in Dudek J 2017). Confocal microscopy and biochemical analysis revealed that tagged-GSDME (1-270) localized to mitochondria and triggered release of proapoptotic proteins such as cytochrome c (CYCS) upon ectopic expression in human HeLa cells or human embryonic kidney 293T (HEK293T) cells (Rogers C et al. 2019). Endogenous GSDME (1-270) also localized to the mitochondrial fraction during apoptosis in TNFα plus actinomycin D (TNFα/actD)-treated human lymphoid CEM-C7 cells. Apoptotic stimuli-triggered cleavage of GSDME (1-270) induced CYCS release and ROS production in CEM-C7 cells (Rogers C et al. 2019). These data suggest that the N-terminal fragment of GSDME (1-270) can permeabilize the mitochondria in response to apoptotic stimuli (Rogers C et al. 2019), however, the physiological relevance of this event remains to be determined.

This Reactome event describes the GSDME (1-275) binding to mitochondrial cardiolipin leading to CYCS release from the mitochondria.

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Editions

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