GSDMD (1-275) binds PIPs

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28/08/2021

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.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751), University of Toronto (CFREF Medicine by Design), European Union (EU STRP, EMI-CD), and the European Molecular Biology Laboratory (EBI Industry program).

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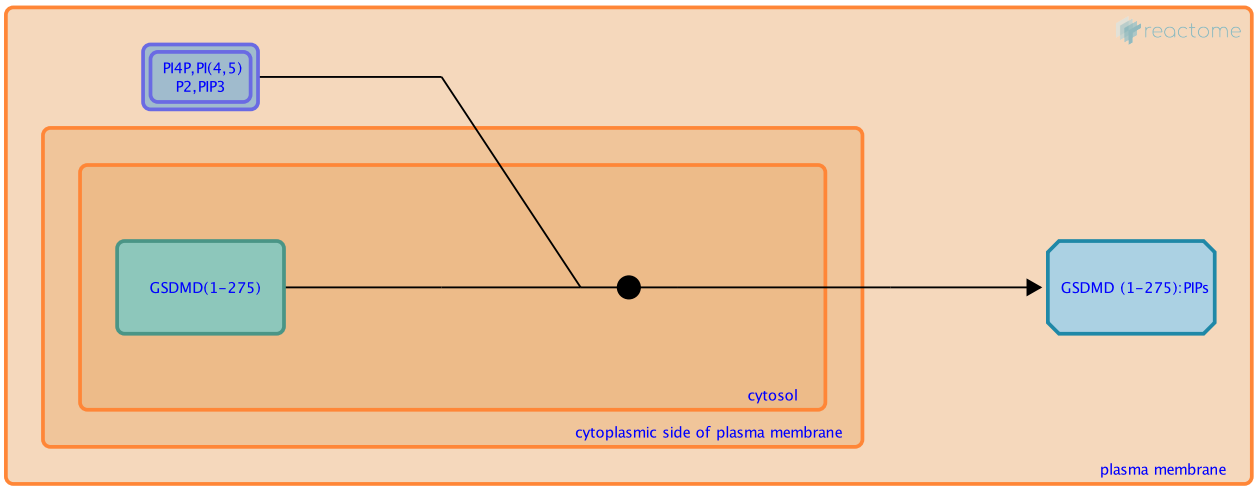
Stable identifier: R-HSA-9647631

Type: binding

Compartments: cytosol, plasma membrane



Human gasdermin D (GSDMD) is a member of the gasdermin (GSDM) protein family, which is processed by inflammatory caspases and cleaved into N□terminal (GSDMD(1□275)) and C□terminal (GSDMD(276□484)) fragments (Shi et al. 2015). The N□terminal fragment of GSDMD (1□275) by itself caused pyroptosis when expressed ectopically in human embryonic kidney HEK293 cells, whereas the overexpression of the GSDMD C□terminus was found to block pyroptosis (Shi et al, 2015). The N□terminal fragment, GSDMD (1□275), targets and permeabilizes cellular membranes by assembling transmembrane pores (Ding et al, 2016; Liu X et al, 2016; Sborgi et al, 2016; Mulvihill et al. 2018). High-resolution (≤ 2 nm) atomic force microscopy (AFM) showed that the N□terminal fragment of GSDMD inserts into various lipid membranes (Mulvihill E et al. 2018). The lipid composition of the membrane was found to directly influence the ability of GSDMD to permeabilize liposomes (Ding et al, 2016; Liu et al, 2016; Mulvihill et al. 2018). Whereas phosphoinositides (PIPs) facilitated binding of GSDMD (1□275), cholesterol reduced insertion of GSDMD (1□275) and pore formation (Ding et al, 2016; Sborgi et al, 2016; Mulvihill et al. 2018). Once inserted, GSDMD (1□275) assembles arc-, slit-, and ring-shaped oligomers (Ding et al, 2016; Liu et al, 2016; Sborgi et al, 2016; Mulvihill et al. 2018).

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Editions

2020-11-09	Authored	Shamovsky, V.
2021-02-17	Reviewed	D'Eustachio, P., Kanneganti, TD.
2021-02-17	Edited	Shorser, S.
2021-04-22	Reviewed	Shao, F.