reactome

RNASEs bind bacterial LPS, PGN

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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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Reactome database release: 77

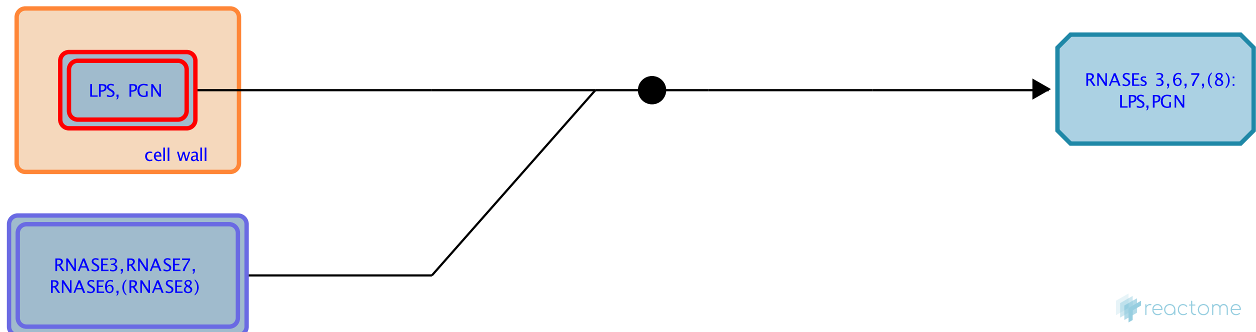
This document contains 1 reaction (see Table of Contents)

RNASEs bind bacterial LPS, PGN ↗

Stable identifier: R-HSA-6803063

Type: binding

Compartments: extracellular region, cell wall



Ribonucleases (RNase) 3, 6 and 7, which belong to the RNase A superfamily and are secreted upon infection, interact with the components of the bacterial cell wall (Torrent M et al. 2010; Pulido D et al. 2016a, b).

RNase A family is a vertebrate-specific gene family (Goo SM & Cho S 2013). Members of RNase A family share specific elements of sequence homology, a unique disulfide-bonded tertiary structure, and the ability to hydrolyze polymeric RNA (Beintema JJ & Kleineidam RG 1998; Rosenberg HF 2008). Eight catalytically active members are found in humans: RNase1 (pancreatic RNase), RNase2 (eosinophil derived neurotoxin/EDN), RNase3 (eosinophil cationic protein/ECP), RNase4, RNase5 (angiogenin), RNase6, RNase7 (skin-derived RNase), and RNase8 (divergent paralog of RNase7) (Sorrentino S 2010). Analysis of human genome sequence has revealed the existence of five additional RNases named as RNases 9-13, although they appear to lose enzymatic activity (Devor EJ et al. 2004; Castella S et al. 2004; Cho S et al. 2005). All human RNase A family members encode relatively small polypeptides of 14 to 16kDa containing signal peptides of 20 to 28 amino acids for protein secretion. Mature RNases contain 6 to 8 cysteine residues that are crucial to hold the overall tertiary structure (Sorrentino S 2010). Apart from the ribonuclease activity the RNase A family members have been implicated in a wide variety of biological actions including antipathogen and immunomodulatory activities (Harder J & Schroder JM 2002; Rudolph B et al. 2006; Boix E et al. 2008; Boix and Nogués, 2007; Spencer JD et al. 2011; Becknell B et al. 2015; Rosenberg HF 2015). Evidence of antimicrobial properties displayed by distantly related members ascribed to the family an ancestral role in host defence (Pizzo E & D'Alessio G 2007; Rosenberg HF et al. 2008).

RNase3, RNase6 and RNase7 have been identified as the most potent human antibacterial ribonucleases with a broad antimicrobial action against Gram-positive and Gram-negative bacteria (Pulido D et al. 2013, 2016; Zhang J et al. 2003; Boix E et al. 2008; Torrent M et al. 2010). Mutagenesis analysis revealed that ribonuclease-inactive RNase7 protein exhibited similar anti-microbial activity against P. aeruginosa, E. faecium and E. coli as the wild-type protein suggesting that RNase7 may kill bacteria independently of its ribonuclease catalytic activity (Huang YC et al. 2007; Koten B et al. 2009). Similar results were reported on microbicidal effect of ribonuclease-inactive RNase3 and 6 proteins against S. aureus (Rosenberg HF 1995; Pulido D et al. 2016a). Being cationic proteins with a high pI, RNase3, 6 and 7 interact with anionic components of biological membranes (Zhang J et al. 2003; Boix E et al. 2008; Torrent M et al. 2010; Boix E et al. 2012; Pulido D et al. 2016a). RNase3, 6 and 7 present, respectively, a high number of either Arg, His or Lys surface-exposed residues that may contribute to their distinct bactericidal mechanisms of action (Torrent M et al. 2010; Prats-Ejarque G et al. 2016). RNase3 displays a membrane disruption capacity that is dependent on both surface exposed hydrophobic and cationic residues. RNase3 can bind and partially in-

sert into the lipid bilayers, promoting its aggregation and final lysis, following a carpet-like mechanism. The RNase3 agglutination process precedes the bacterial death and lysis event. The antimicrobial properties of the RNase6 are comparable to its RNase3 homolog and correlate to the bacterial cell damage and agglutination activities (Pulido D et al. 2016a). In contrast, RNase7 has no significant membrane aggregation capacity (Torrent M et al. 2010). RNase7 binds and permeabilizes the bacterial membrane displaying a much higher leakage capacity compared to RNase3 (Torrent M et al. 2010; Huang YC et al. 2007). Membrane permeabilization by RNase7 required four clustered lysine residues but no catalytic residues (Huang YC et al. 2007). Binding to PGN and LPS has been reported for RNases 3 and 7 (Torrent M et al. 2010; Pulido D et al. 2016b). Studies using a battery of progressively truncated LPS-defective E. coli strains correlated the LPS interaction with the protein cell agglutination and bactericidal activities (Pulido D et al. 2012). Further work indicated that RNase3 and RNase 6 high cell agglutination activity towards Gram negative species is retained by their respective N-terminus peptides (Torrent M et al. 2012, 2013; Pulido D et al. 2016c). In particular, the RNase3 N-terminus encompasses a specific patch (Y33-R36) required for LPS binding and an hydrophobic aggregation prone region (A8-I16) that mediates the protein self amyloid- like aggregation and promotes the cell death.

Literature references

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