Cathelicidin LL-37 binds to bacterial cell wall

Hains, DS., Jassal, B., Jupe, S., Stephan, R., Warner, D.

European Bioinformatics Institute, New York University Langone Medical Center, Ontario Institute for Cancer Research, Oregon Health and Science University.

21/04/2021

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).

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. ↗

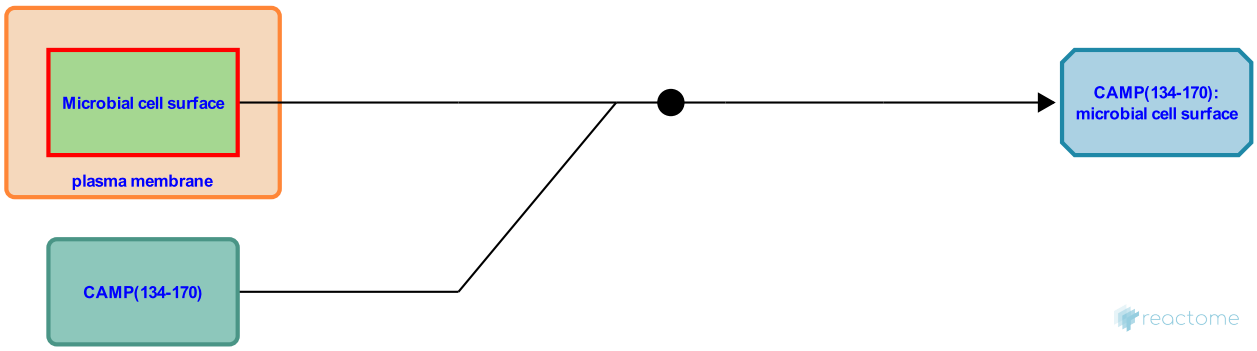
Fabregat, A., Korninger, F., Viteri, G., Sidiropoulos, K., Marin-Garcia, P., Ping, P. et al. (2018). Reactome graph database: Efficient access to complex pathway data. *PLoS computational biology, 14*, e1005968. ↗

Cathelicidin LL-37 binds to bacterial cell wall ↗

Stable identifier: R-HSA-1222685

Type: binding

Compartments: extracellular region, plasma membrane



Human cathelicidin antimicrobial peptide (hCAP18, also known as CAMP) is synthesized as 18-kDa pro-protein (Sorensen O et al. 1997, 2001; Yang D et al. 2000; Mendez-Samperio P 2010). The proform hCAP18 is stored within vesicles such as specific granules of neutrophils. Upon inflammation or injury hCAP18 undergoes proteolytic cleavage to produce the mature antimicrobial 37-amino acid-long peptide LL-37 (CAMP(134-170)) which is secreted outside the cells (Sorensen O et al. 1997, 2001; Yang D et al. 2000; Mendez-Samperio P 2010). LL-37 has a net positive charge and is thought to interact with bacteria via electrostatic attraction toward the negatively charged bacterial membrane (Wang G et al. 2012, 2014; Kuroda K et al. 2015). LL-37 is amphiphilic in nature and is comprised of hydrophobic and hydrophilic residues aligned on opposite sides of the peptide (Braff MH et al. 2005; Wang G 2008; Wang G et al. 2012, 2014). The hydrophobic domain may facilitate the peptide penetration through phospholipid bilayers of bacteria (Shai Y 1999).

LL-37 has direct microbicidal activities against Gram-positive bacteria (S. aureus, Group A Streptococcus, Bacillus megaterium), Gram-negative bacteria (E. coli, P. aeruginosa, Salmonella minnesota) and fungi such as C. albicans (Yang D et al. 2000; Nagaoka I et al. 2005; Braff MH et al. 2005; Wang G et al. 2012). LL-37 also has antiviral activities against herpes simplex virus, HIV-1, and vaccinia virus (Yasin B et al. 2000; Steinstraesser L et al. 2005; Howell MD et al. 2006; Gordon YJ et al. 2005). LL-37 may have the potential to prevent sepsis or septic shock associated with pathogenic bacterial infection by inhibiting the release of toxic components such as LPS and lipoteichoic acid (LTA) that cause excess tissue damage and inflammation (Larrick JW et al. 1995)

LL-37 expression was found to correlate with an activation of TLR2, TLR4 and TLR9 signaling pathways in M. tuberculosis-stimulatied human monocyte-derived macrophages, alveolar macrophages and neutrophils (Rivas-Santiago et al. 2008).

Literature references

van der Does, AM., Bergman, P., Agerberth, B., Lindbom, L. (2012). Induction of the human cathelicidin LL-37 as a novel treatment against bacterial infections. *J. Leukoc. Biol., 92*, 735-42. ↗

Rivas-Santiago, B., Hernandez-Pando, R., Carranza, C., Juarez, E., Contreras, JL., Aguilar-Leon, D. et al. (2008). Expression of cathelicidin LL-37 during Mycobacterium tuberculosis infection in human alveolar macrophages, monocytes, neutrophils, and epithelial cells. *Infect Immun, 76*, 935-41. ↗

Editions

2011-01-10	Authored	Stephan, R.
2011-02-28	Edited	Jassal, B.
2012-04-30	Reviewed	Warner, D.
2016-04-15	Reviewed	Jupe, S.
2016-08-02	Reviewed	Hains, DS.