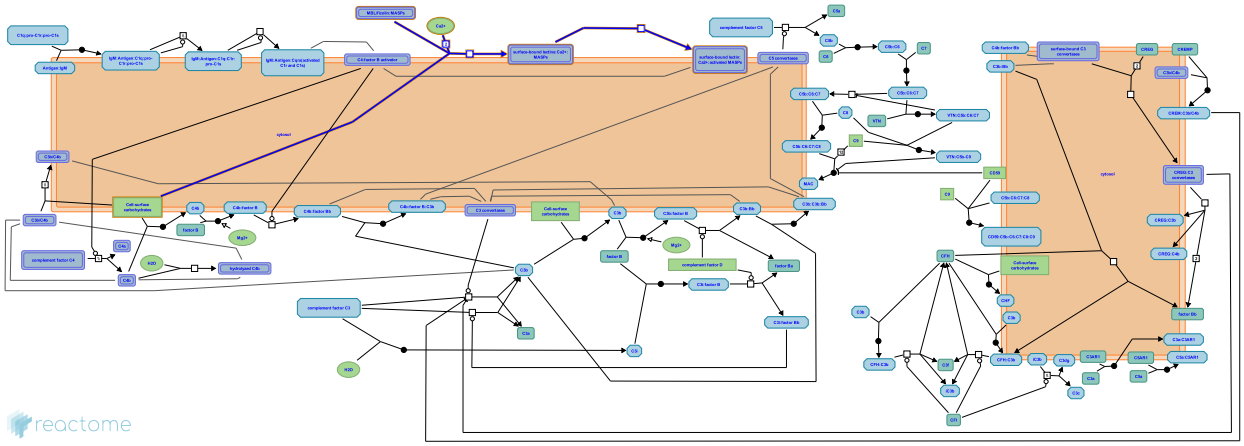
Lectin-mediated initiation of complement cascade



D'Eustachio, P., Jupe, S., Shamovsky, V.

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

20/04/2021

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. ↗

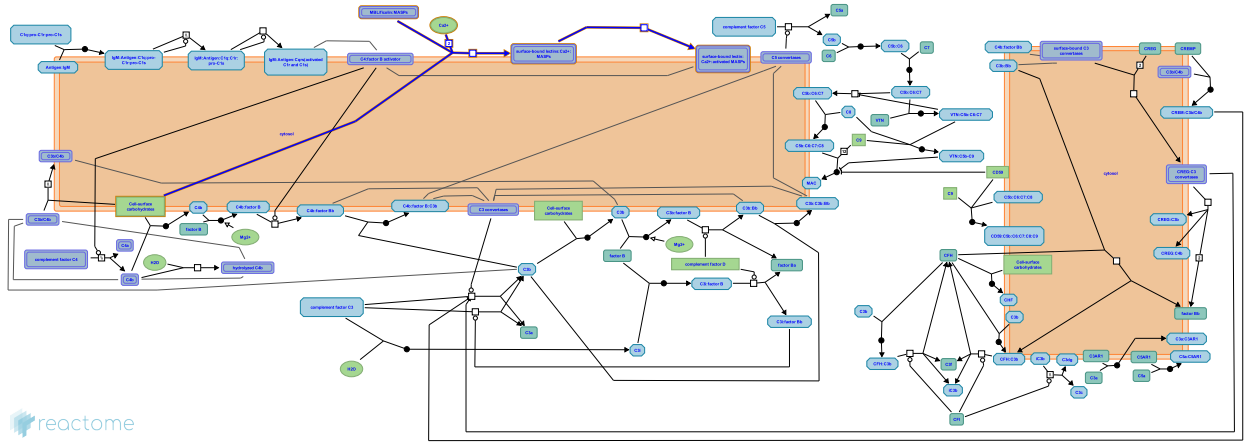
Sidiropoulos, K., Viteri, G., Sevilla, C., Jupe, S., Webber, M., Orlic-Milacic, M. et al. (2017). Reactome enhanced pathway visualization. *Bioinformatics, 33*, 3461-3467. ↗

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. ↗

Lectin-mediated initiation of complement cascade ↗

Stable identifier: R-GGA-2132270



Activation of lectin pathway begins when mannan-binding lectin (MBL, also called mannose-binding protein, MBP) or ficolins bind to cell-surface carbohydrates on the target cell in the presence of Ca2+. Surface bound lectins are assembled with MBL-associated serine proteases (MASPs) [Turner MW et al 1996, Fujita T et al 2004]. The lectin-MASP complex cleaves C4 and C2 complements to generate their active fragments. The active fragments - C4b and C2b, form C3 convertase [Wallis R et al 2007].

Most of the components of chicken lectin pathway (MBL, ficolin, MASP2, MASP3, MAp19) have been mapped, cloned and characterized (Laursen SB and Nielsen OL 2000; Lynch NJ et al 2005).

Literature references

Lambris, JD. (2008). Structure and Function of Ficolins, Current Topics in Complement.

Norup, LR., Juul-Madsen, HR. (2007). An assay for measuring the mannan-binding lectin pathway of complement activation in chickens. *Poult Sci, 86*, 2322-6. ↗

Wallis, R., Dodds, AW., Mitchell, DA., Sim, RB., Reid, KB., Schwaeble, WJ. (2007). Molecular interactions between MASP-2, C4, and C2 and their activation fragments leading to complement activation via the lectin pathway. *J Biol Chem, 282*, 7844-51. ↗

Fujita, T., Matsushita, M., Endo, Y. (2004). The lectin-complement pathway--its role in innate immunity and evolution. *Immunol Rev, 198*, 185-202. ↗

Fujita, T. (2002). Evolution of the lectin-complement pathway and its role in innate immunity. *Nat Rev Immunol, 2*, 346-53. ↗

Editions

2012-11-07	Reviewed	D'Eustachio, P.
2012-12-20	Authored	Shamovsky, V.
2013-01-31	Reviewed	Jupe, S.
2013-11-20	Edited	Shamovsky, V.

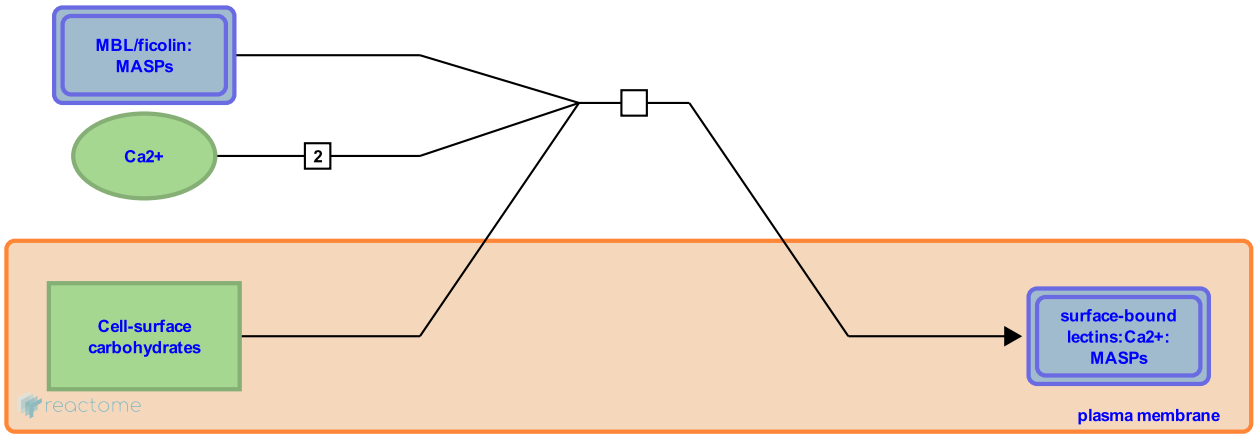
MBL or ficolin binds an oligosaccharide pattern on the target cell surface ↗

Location: Lectin-mediated initiation of complement cascade

Stable identifier: R-GGA-2132187

Type: transition

Compartments: extracellular region, plasma membrane



Both mannose-binding lectin (MBL) and ficolins are lectins, that circulate in plasma as oligomers of structural subunits. Each subunit is composed of three identical peptides and contains an amino-terminal cysteine-rich region, a collagen-like domain, a neck region and a carboxy-terminal carbohydrate-binding domain. However, the carbohydrate-binding domains of MBL and ficolins are quite different. A carbohydrate-recognition domain (CRD) is in MBL and a fibrinogen-like domain is in ficolins [Holmskov U et al 2003; Endo Y et al 2006; Thiel S and Gadjeva M 2009]. MBL recognizes certain carbohydrates such as mannose and GlcNAc. Mammalian ficolins like MBL possess carbohydrate-binding activity. Different ficolins have distinct recognition specificities [Matsushita M et al 1996; Lu J and Le Y 1998; Gout E et al 2009].

Mammals usually possess two MBL genes and two or three ficolin genes, but only one of each has been found in the chicken genome. Several studies investigated the function of chicken MBL upon avian viral infections with infectious laryngotracheitis virus (ILTV), infectious bursal disease virus (IBDV) and infectious bronchitis virus (IBV) [Nielsen OL et al 1998, 1999; Laursen SB and Nielsen OL 2000; Juul-Madsen HR et al 2003, 2007]. Similar to mammals, chickens produce MBL in the hepatocytes, secrete it into the blood, and upregulate the production during acute stages of virus infections. The serum concentration of chicken MBL increased two- to three-fold in virus-infected chickens compared with noninfected controls, indicating that chicken MBL is a minor acute phase mediator. Chicken MBL was also reported to mediate host response against bacterial infection such as Pasteurella multocida [Schou TW et al 2010]. The ability of chicken MBL to activate the complement cascade was tested in a heterologous system by deposition of human C4 on the chicken MBL:MASP complex in response to infection with avian IBV. The complement activation was directly associated with the concentration of MBL in serum [Laursen SB and Nielsen OL 2000; Juul-Madsen HR et al 2003, Norup LR and Juul-Madsen HR 2007].

Followed by: MASPs activation

Literature references

Laursen, SB., Nielsen, OL. (2000). Mannan-binding lectin (MBL) in chickens: molecular and functional aspects. *Dev Comp Immunol, 24*, 85-101. ↗

Fujita, T., Matsushita, M., Endo, Y. (2004). The lectin-complement pathway--its role in innate immunity and evolution. *Immunol Rev, 198*, 185-202. ↗

Kishore, U. (2009). Humoral Pattern Recognition Molecules: Mannan-Binding Lectin and Ficolins, Target Pattern Recognition in Innate Immunity.

Holmskov, U., Thiel, S., Jensenius, JC. (2003). Collections and ficolins: humoral lectins of the innate immune defense . *Annu Rev Immunol, 21*, 547-78. ↗

Matsushita, M., Endo, Y., Taira, S., Sato, Y., Fujita, T., Ichikawa, N. et al. (1996). A novel human serum lectin with collagen- and fibrinogen-like domains that functions as an opsonin. *J Biol Chem, 271*, 2448-54. ↗

Editions

2012-11-07	Reviewed	D'Eustachio, P.
2012-12-20	Authored	Shamovsky, V.
2013-01-31	Reviewed	Jupe, S.
2013-11-20	Edited	Shamovsky, V.

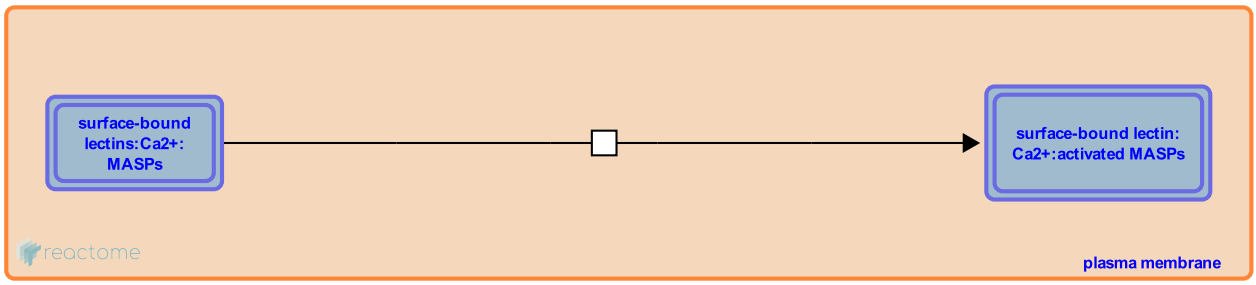
MASPs activation ↗

Location: Lectin-mediated initiation of complement cascade

Stable identifier: R-GGA-2132206

Type: transition

Compartments: plasma membrane



MBL and ficolins circulate as complexes with MBL-associated serine proteases (MASPs), which become activated upon lectin binding to the target cell surface. Although three different mammalian MASPs (-1, -2, and -3) were reported to associate with MBL and ficolins, only MASP-2 has a clearly defined role in complement activation [Wallis R et al 2006]. It cleaves C4 and C2 to produce C4a, C4b and C2a,C2b fragments. C2b and C4b form the catalytic component of the C3 convertase (C4b2b). The other two mammalian MASPs (-1 and -3) are alternatively spliced products of a single structural gene. MASP-1 cleaves C2 but not C4 [Chen CB and Wallis R 2004]. MASP-1 may function as MASP-2 activator [Heja D et al 2012]. MASP-3 is not autoactivated. Rather, it is probably activated through the action of an unknown protease [Zundel S et al 2004].

MASPs have a modular structure consisting of an N-terminal CUB domain, a Ca2+-binding EGF-like domain, a second CUB domain, two complement control protein (CCP) modules and a C-terminal serine protease domain. The CUB1-EGF-CUB2 region mediates homodimerization and binding to MBL. The minimal functional unit for complement activation is a MASP homodimer bound to two MBL trimeric subunits [Feinberg H et al 2003; Teille F et al 2008].

Orthologues of human MASP2, MASP3 and MAp19 were identified in the chicken genome [Lynch NJ et al 2005]. MASP1 is considered to be absent in birds. Despite the lack of MASP-1-like enzymatic activity in sera of chicken and other birds, avian lectin pathway complexes efficiently activated C4. The amino-acid sequence of chicken MASP-2 is 54% identical with those of the human and mouse MASP-2, and the organization of the gene is the same as in mammals. Chicken MASP-3 shares approximately 75% of its amino-acid residues with human and Xenopus MASP-3.

Preceded by: MBL or ficolin binds an oligosaccharide pattern on the target cell surface

Literature references

Wallis, R., Dodds, AW., Mitchell, DA., Sim, RB., Reid, KB., Schwaeble, WJ. (2007). Molecular interactions between MASP-2, C4, and C2 and their activation fragments leading to complement activation via the lectin pathway. *J Biol Chem, 282*, 7844-51. ↗

Chen, CB., Wallis, R. (2004). Two mechanisms for mannose-binding protein modulation of the activity of its associated serine proteases. *J Biol Chem, 279*, 26058-65. ↗

Zundel, S., Cseh, S., Lacroix, M., Dahl, MR., Matsushita, M., Andrieu, JP. et al. (2004). Characterization of recombinant mannan-binding lectin-associated serine protease (MASP)-3 suggests an activation mechanism different from that of MASP-1 and MASP-2. *J Immunol, 172*, 4342-50. ↗

Feinberg, H., Uitdehaag, JC., Davies, JM., Wallis, R., Drickamer, K., Weis, WI. (2003). Crystal structure of the CUB1-EGF-CUB2 region of mannose-binding protein associated serine protease-2. *EMBO J, 22*, 2348-59. ↗

Teillet, F., Gaboriaud, C., Lacroix, M., Martin, L., Arlaud, GJ., Thielens, NM. (2008). Crystal structure of the CUB1-EGF-CUB2 domain of human MASP-1/3 and identification of its interaction sites with mannan-binding lectin and ficolins. *J Biol Chem, 283*, 25715-24. ↗

Editions

2012-11-07	Reviewed	D'Eustachio, P.
2012-12-20	Authored	Shamovsky, V.
2013-01-31	Reviewed	Jupe, S.
2013-11-20	Edited	Shamovsky, V.

Table of Contents