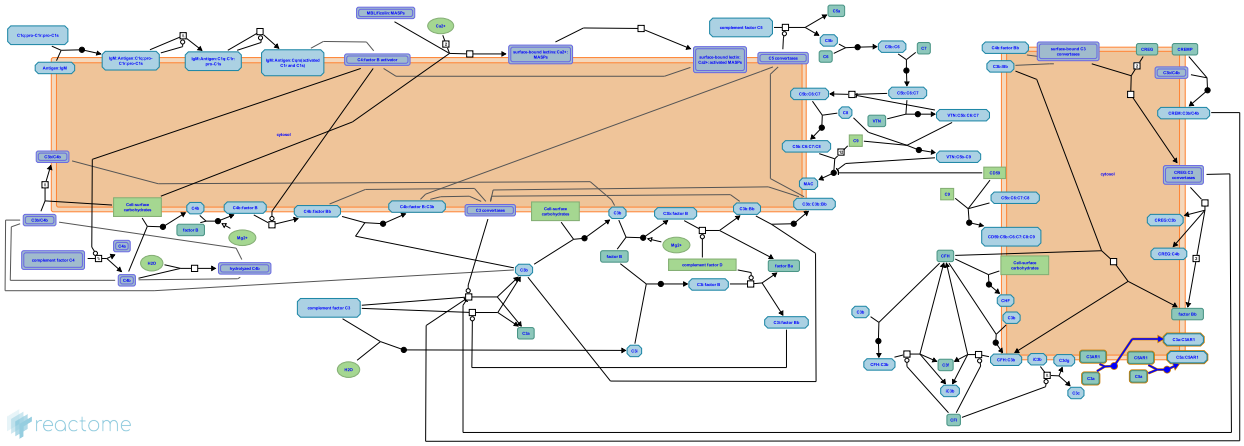
Anaphylatoxins initiate inflammatory responses



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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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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. ↗

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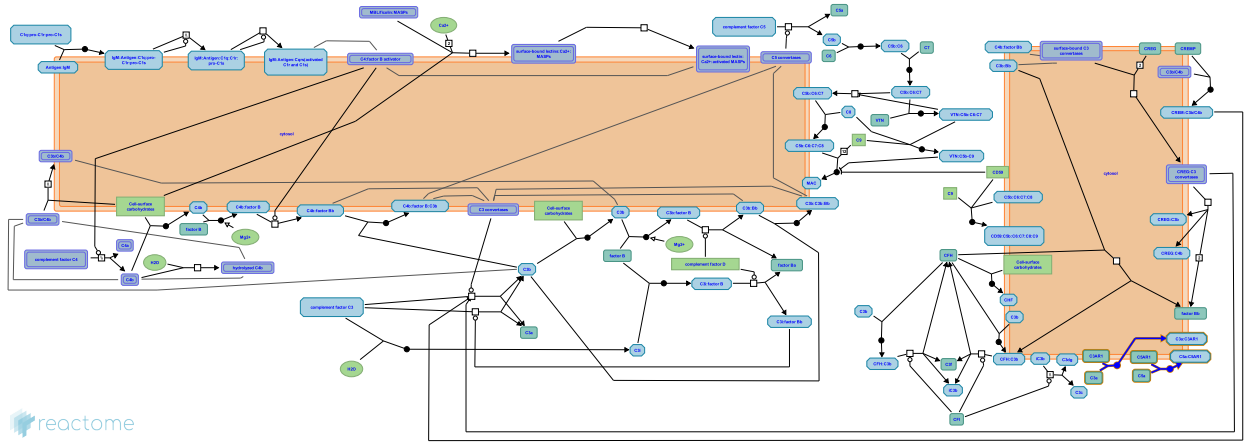
Anaphylatoxins initiate inflammatory responses

Stable identifier: R-GGA-2173345



Anaphylatoxic peptides C3a and C5a function as mediators of host inflammatory response in mammals. These molecules are generated during complement activation and bind to their specific G protein coupled receptors (GPCR), which are expressed on granulocytes, monocytes, mast cells and activated lymphocytes (Peng Q et al. 2009; Haas PJ and van Strijp J 2007).

Expression of both C3 and C5 as well as C3aR and C5aR was detected in chicken liver and eye tissues (Haynes T et al. 2013). Moreover, chicken C3a was shown to stimulate chick retina regeneration through MAPK-STAT3 activation in a C3aR-dependent manner (Haynes T et al. 2013). In addition, functionally active anaphylatoxins and their receptors were found in teleost fish and Xenopus (Rottland J et al. 2004; Boshra H et al. 2004; Holland MC and Lambris JD 2004; Boshra H et al. 2005; Carmona-Fontaine C et al. 2011). The studies in those species suggested that the basic structure and function of anaphylatoxins and their receptors have been conserved for more than 300 million years (Sunyer JO et al. 2005). Taken together, the observations above suggest that the chicken complement signaling may release active fragments C3a and C5a, which associate with C3a and C5a receptors respectively.

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Haynes, T., Luz-Madrigal, A., Reis, ES., Echeverri Ruiz, NP., Grajales-Esquivel, E., Tzekou, A. et al. (2013). Complement anaphylatoxin C3a is a potent inducer of embryonic chick retina regeneration. *Nat Commun, 4*, 2312.

Carmona-Fontaine, C., Theveneau, E., Tzekou, A., Tada, M., Woods, M., Page, KM. et al. (2011). Complement fragment C3a controls mutual cell attraction during collective cell migration. *Dev Cell, 21*, 1026-37.

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Boshra, H., Li, J., Peters, R., Hansen, J., Matlapudi, A., Sunyer, JO. (2004). Cloning, expression, cellular distribution, and role in chemotaxis of a C5a receptor in rainbow trout: the first identification of a C5a receptor in a nonmammalian species. *J Immunol, 172*, 4381-90.

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.

C3a anaphylatoxin binds C3a receptor ↗

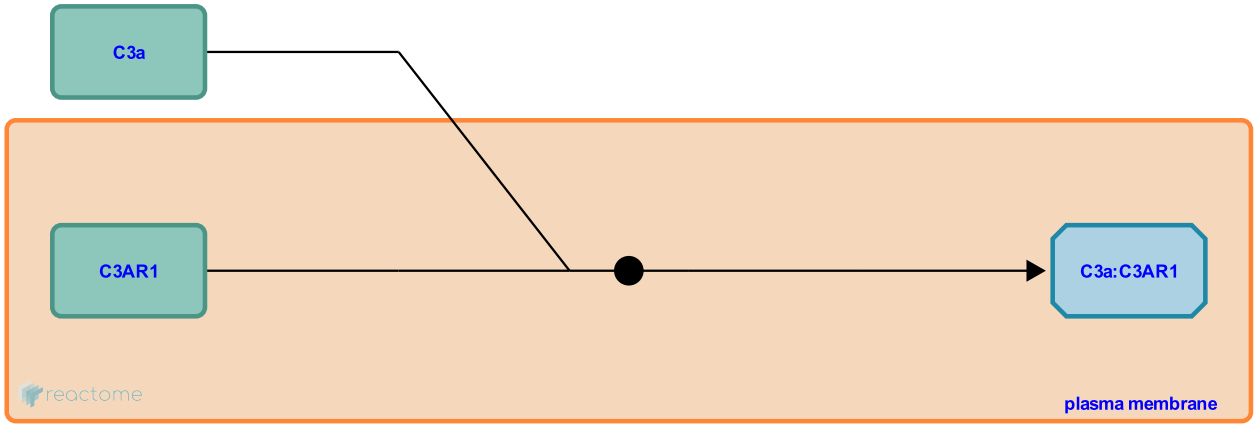
Location: Anaphylatoxins initiate inflammatory responses

Stable identifier: R-GGA-2173317

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: C3a receptor binds anaphylatoxin C3a (Homo sapiens)



In mammals, complement C3a receptor (C3aR) is a member of the G protein-coupled receptor family (G-PCRs) (Crass T et al. 1996). C3aR is activated upon binding of complement fragments C3a. C3aR transduces signals through multiple pathways, leading to the inhibition of adenylyl cyclase, activation of MAP kinase, phosphoinositol accumulation and calcium mobilization (Sayah S et al. 2003; Ricklin D et al. 2010).

Upon complement activation chicken C3 is cleaved into fragments that resemble mammalian C3a and C3b (Laursen I and Koch C 1989). Chicken C3 and its cleavage products were detected in liver, plasma and different eye tissues (Haynes T et al. 2013). In addition to C3 activation fragments, chicken C3aR mRNA and protein were found in eye tissues at E4 (embryo's stage at which retinectomies are performed). Histological analysis in combination with immuno-histochemical and western blotting procedures using post-retinectomy samples revealed that the treatment with chicken C3a induced chick retina regeneration via MAPK-STAT3 signaling in a C3aR-dependent manner (Haynes T et al. 2013).

Literature references

Ricklin, D., Hajishengallis, G., Yang, K., Lambris, JD. (2010). Complement: a key system for immune surveillance and homeostasis. *Nat Immunol, 11*, 785-97. ↗

Sayah, S., Jauneau, AC., Patte, C., Tonon, MC., Vaudry, H., Fontaine, M. (2003). Two different transduction pathways are activated by C3a and C5a anaphylatoxins on astrocytes. *Brain Res Mol Brain Res, 112*, 53-60. ↗

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Editions

2012-11-07	Reviewed	D'Eustachio, P.
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2013-11-20	Edited	Shamovsky, V.

C5a anaphylatoxin binds C5a receptor ↗

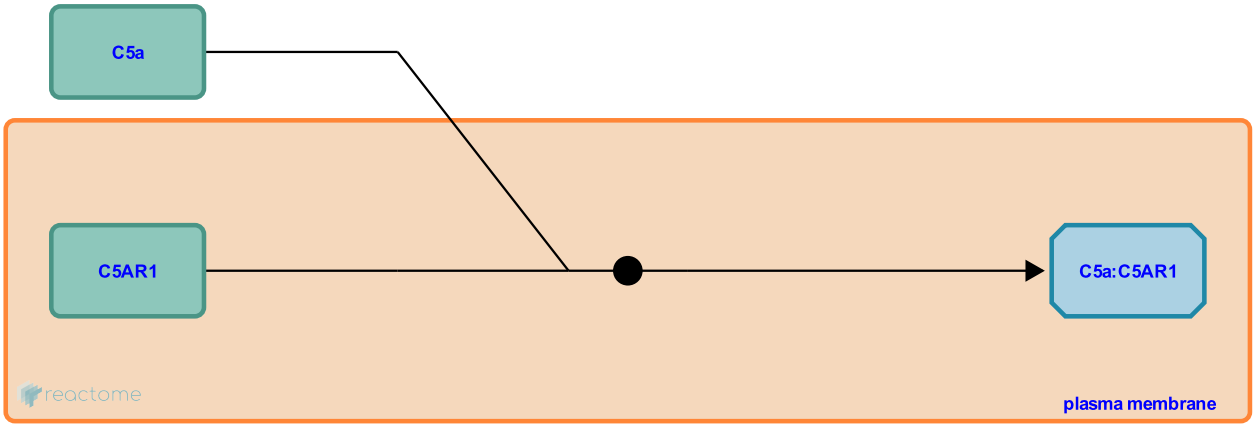
Location: Anaphylatoxins initiate inflammatory responses

Stable identifier: R-GGA-2173318

Type: binding

Compartments: plasma membrane, extracellular region

Inferred from: C5a receptor binds C5a anaphylatoxin (Homo sapiens)



In mammals, complement C5a receptor (C5aR) is a member of the G protein-coupled receptor family (G-PCRs) (Boulay et al. 1991; Gerard NP and Gerard C 1991). C5aR is activated upon binding of complement fragment C5a. C5aR transduces signals through multiple pathways, leading to the inhibition of adenylyl cyclase, activation of MAP kinase, phosphoinositol accumulation and calcium mobilization [Sayah S et al 2003; Ricklin D et al 2010; Wrann CD et al 2007].

Chicken C5aR mRNA was detected in liver and in various eye tissues (Haynes T et al. 2013). The binding of chicken C5a to C5aR has not been verified experimentally but is inferred from properties of the orthologous human proteins.

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Ricklin, D., Hajishengallis, G., Yang, K., Lambris, JD. (2010). Complement: a key system for immune surveillance and homeostasis. *Nat Immunol, 11*, 785-97. ↗

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