SFTPA/SFTPD binds TLR4:LY96

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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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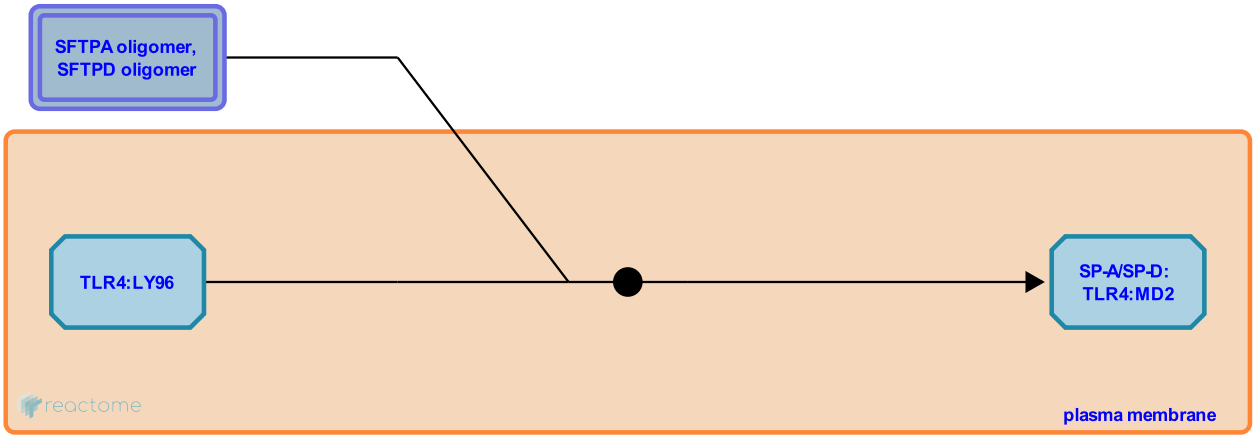
Stable identifier: R-HSA-5432852

Type: binding

Compartments: extracellular region, plasma membrane



The hydrophilic pulmonary surfactant proteins SP-A (SFTPA) and SP-D (SFTPD) belong to the C-type lectin family. Members of the C-type lectin family contain an N-terminal collagen-like domain and a C-terminal carbohydrate recognition domain (CRD) (Kishore U et al. 2006). The CRD allows binding to various components, including carbohydrates, phospholipids or charge patterns found on microbes, allergens and dying cells, while the collagen region can interact with receptor molecules present on immune cells in order to initiate clearance mechanisms (Kishore U et al. 2006). SP-A and SP-D are known to bind to a range of microbial pathogens that invade the lungs (Eggleton P & Reid KB 1999; Crouch E & Wright JR 2001; McCormack FX1 & Whitsett JA 2002; Nayak A et al. 2012; Jakel A et al. 2013). SP-A and SP-D form large oligomeric structures to orchestrate the pulmonary innate immune defense by mechanisms that may involve binding and agglutinating pathogens (Kuan SF et al 1992; Griese M & Starosta V 2005; Yamada C et al. 2006; Kishore U et al. 2006; Zhang L et al. 2001). The direct interaction of SP-A with macrophages was shown to promote phagocytosis of Klebsiella pneumoniae, Escherichia coli, Staphylococcus aureus, and Pseudomonas aeruginosa (Van Iwaarden JF et al. 1994; Hickman-Davis JM et al. 2002; Ding J et al. 2004; Mikerov AN et al. 2008; Gil M et al. 2009).

SP-A and SP-D were found to bind to the recombinant soluble form of extracellular TLR4 domain (sTLR4) and MD2 in a Ca2+ -dependent manner, with involvement of the CRD region (Yamada et al. 2006; Yamazoe M et al. 2008). SP-A was also shown to interact with CD14 (Sano H. et al. 1999). Studies involving gene knock-out mice, murine models of lung hypersensitivity and infection together with functional characterization of cell surface receptors revealed both pro- and anti-inflammatory functions of SP-A and SP-D in the control of lung inflammation in mammals (Guillot L et al. 2002; Madan T et al. 2001, 2005, 2010; Wang JY & Reid KB 2007; Yamada et al. 2006; Yamazoe M et al. 2008; Wang G et al. 2010). Anti-inflammatory effects of SP-A caused inhibition of NF-kB activation and accumulation of inhibitory protein I kappa B-alpha (IkB-alpha) in LPS-challenged alveolar macrophages (AM) (Wu Y et al. 2004). SP-A also inhibited tumor necrosis factor-alpha (TNFalpha) expression induced by smooth LPS but not by rough LPS in the human macrophage-like cell line U937 cells (Sano H. et al. 1999). In addition, SP-A attenuated cell surface binding of smooth LPS and subsequent NF-kB activation in TLR4/MD2 expressing human embryonic kidney (HEK293) cells (Yamada et al. 2006). Like SP-A, SP-D bound to complex of sTLR4:MD2 was found to down regulate a secretion of TNFalpha and activation of NF-kB in LPS-stimulated AM and TLR4/MD-2-transfected HEK293 cells (Yamazoe M et al. 2008). SP-A and SP-D are thought to prevent LPS-elicited inflammatory responses by altering LPS binding to its receptors, TLR4:MD2 or CD14 (Sano H. et al. 1999; Yamada et al. 2006; Yamazoe M et al. 2008).

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Editions

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