SFTPA/SFTPD binds TLR2:TLR1

D'Eustachio, P., Granucci, F., Shamovsky, V., Zanoni, I.

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

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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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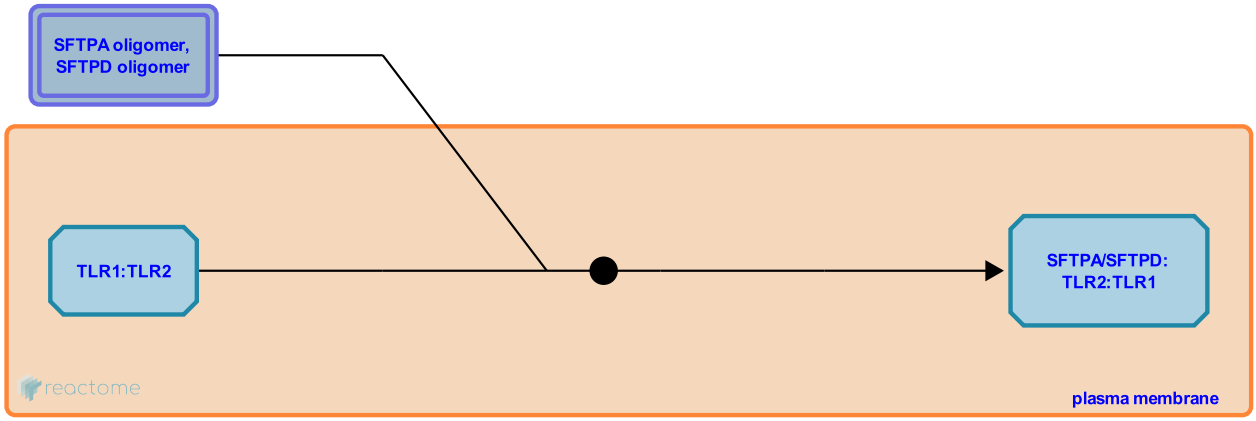
Stable identifier: R-HSA-5432814

Type: binding

Compartments: extracellular region, plasma membrane



The lung surfactant proteins SP-A (also known as SFTPA) and SP-D (SFTPD) have been implicated in the regulation of pulmonary host defense and inflammation. SP-A and SP-D were found to bind to the recombinant soluble form of extracellular TLR2 domain (TLR2) via its C-terminal carbohydrate recognition domain (CRD) in a Ca(2+)-dependent manner (Murakami S et al. 2002; Ohya M et al. 2006). SP-A downregulated TLR2-mediated signaling and tumor necrosis factor alpha (TNFalpha) secretion in TLR2-transfected human embryonic kidney 293 (HEK293) cells upon stimulation with TLR2 ligands such as fungal cell surface component zymosan or bacterial peptidoglycan (PGN) (Murakami S et al. 2002; Sato M et al. 2003). Similarly, SP-A significantly reduced PGN-elicited TNFalpha secretion by human leukemic monocyte lymphoma U937 cell line and rat alveolar macrophages (Murakami S et al. 2002). In primary human monocyte-derived macrophage SP-A regulated TLR2 and TLR4 activity by diminishing proinflammatory cytokine production as the result of a decreased phosphorylation of a key regulator of NFkB, IkBalpha. Nuclear translocation of NFkB-p65 (RELA) was also inhibited (Henning LN et al. 2008). SP-A downregulated kinases upstream of IkBalpha by decreasing the phosphorylation of Akt and MAPKs in response to either LPS (TLR4 ligand) or Pam3Cys (TLR2 ligand) (Henning LN et al. 2008). In addition, SP-A upregulated surface protein expression of TLR2 on macrophages, while it did not affect TLR4 surface expression. The increased TLR2 expression is thought to enhance pathogen recognition by TLR2, while SP-A mediated inhibition of TLR signaling may protect from an overreactive inflammatory response (Henning LN et al. 2008).

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Editions

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