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Gene Section

Review

PYCARD (PYD and CARD domain containing)

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Abstract

Review on PYCARD, with data on DNA/RNA, on the protein encoded and where the gene is implicated.

Identity

Other names: ASC, CARD5, TMS, TMS-1, TMS1

HGNC (Hugo): PYCARD

Location: 16p11.2

DNA/RNA

Description

3 exons spanning 1.4 kb, with a CpG island surrounding exon 1 (Conway et al., 2000; Gerhard et al., 2004; Ota et al., 2004). Exon 1 encodes a pyrin domain (PYD), exon 2 encodes a proline and glycine-rich (PGR) domain, and exon 3 encodes a caspase recruitment domain (CARD) (Masumoto et al., 1999; Matsushita et al., 2009).

Protein

Description

PYCARD is composed of two protein-protein interaction domains: an N-terminal pyrin domain (PYD) and a C-terminal caspase-recruitment domain (CARD). The PYD and CARD domains are structurally independent six-helix bundle motifs connected by a 23-residue proline and glycine-rich (PGR) linker domain (Martinon et al., 2000; Bertin et al., 2001; de Alba, 2009; Matsushita et al., 2009).
There are 4 transcripts (splice variants) including the canonical PYCARD (PYCARD1) (Matsushita et al., 2009; Bryan et al., 2010). Correlating to four transcript splice variants are four protein isoforms.
In addition to the canonical PYCARD protein (also known as isoform 1, fASC), three additional isoforms display unique capabilities with respect to their function as part of the inflammasome, with one of the isoforms even showing an inhibitory effect. Isoforms 1 and 2 are the activating isoforms of ASC and co-localize with intracellular nucleotide oligomerization domain-like receptors (NLRs) and caspase-1. Isoform 2 (also known as ASC-b, vASC) lacks a PGR domain and may not be needed for caspase activation but is involved in direct regulation of IL-1β processing.
The inhibitory isoform (isoform 3, ASC-c) co-localizes only with caspase-1, but not with NLRP3. Isoform 4 (ASC-d) does not co-localize with NLRP3 or with caspase-1 and lacks the ability to function as an inflammasome adaptor.
It may not be a functional protein product and its precise function and relation to PYCARD is unknown (Matsushita et al., 2009; Bryan et al., 2010).
PYD is also known as the domain in apoptosis and interferon response (DAPIN) or the pyrin, AIM, ASC death-domain-like (PAAD) domain. It is an 80-100 residue domain with alpha-helical secondary structure located on the N-terminus of the protein. Like CARD, it is a member of the death domain-fold superfamily of proteins.
Strong dipole moments in PYD suggest that electrostatic interactions play an important role for the binding between PYDs.
The function of PYD is to bind other PYD-containing proteins and is also associated with domains such as CARD, leucine-rich repeat (LRR), dual specificity spore lysis A (splA) protein kinase and ryanodine receptor (SPRY), caspase, or zinc-finger B-box (Martinon et al., 2001; Pawlowski et al., 2001; Liepinsh et al., 2003).

CARD is a subclass of protein motif known as the death fold, which features an arrangement of six to seven antiparallel alpha helices with a hydrophobic core and an outer face composed of charged residues. The CARD structure of PYCARD reveals two distinctive characteristics; helix 1 is not fragmented as in all other known CARDs; and it demonstrates a uniform distribution of positive and negative charges, whereas these are commonly separated into two areas in other death domains (de Alba, 2009).

CARD mediates the interaction between adaptor proteins participating in apoptosis by regulating caspases. CARD-containing proteins are also involved in inflammation through their regulation of nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB). The mechanisms by which CARDs activate caspases and NF-κB involve the assembly of multi-protein complexes, which can facilitate dimerization or serve as scaffolds on which proteases and kinases are assembled and activated. Domains associated with CARD include: PYD, Apoptotic protease activating factor-1 (Apaf-1) domains [including LRR, Tryptophan-Aspartic acid (WD or beta-transducin) repeats, nucleotide binding and oligomerization (NB-ARC or NOD) domains and ATPase domains], sarcoma (Src) tyrosine kinase proto-oncogene homology domains, death domain (DD) and the proform of caspases (e.g., CASP-9) (Hofmann et al., 1997; Bouchier-Hayes and Martin, 2002; Reed et al., 2004).

The PGR linker adopts a residual structure in order to maintain a back-to-back orientation of the PYD and CARD domains, which avoids steric interference of one domain with the binding site of the other. NMR relaxation experiments show that the linker is flexible despite the residual structure (de Alba, 2009).

Expression

Silencing of PYCARD correlates with hypermethylation of the CpG island surrounding exon 1. Breast cancer cell lines exhibit complete methylation of PYCARD and do not express PYCARD mRNA, whereas overexpression of PYCARD inhibits the growth of breast cancer cells (Conway et al., 2000).

In normal fibroblasts, the CpG island of the PYCARD gene is composed of an unmethylated domain with distinct 5-prime and 3-prime boundaries. De novo or aberrant methylation of the PYCARD CpG island in cells is accompanied by localized hypoacetylation of histone H3 and H4 and gene silencing (Stimson and Vertino, 2002).

Localisation

Cytoplasm, endoplasmic reticulum, mitochondrion, nucleus.

PYCARD forms hollow spherical aggregates near the perinuclear space of apoptotic cells (McConnell and Vertino, 2000). PYCARD also tends to self-aggregate during in vitro apoptosis induced by retinoids, etoposide and other anti-tumor drugs (Masumoto et al., 1999).

PYCARD is localized primarily in the nucleus in resting monocytes/macrophages but rapidly redistributes to the cytoplasm, perinuclear space, endoplasmic reticulum and mitochondria upon pathogen infection and subsequent inflammasome activation (Bryan et al., 2009; Zhou et al., 2011).

Function

PYCARD is known to interact with a variety of inflammatory and cell death-related genes including NLRs (NLRP1-14, NLRC4 [IL-1β converting enzyme protease-activating factor (IPAF)], Absent in Melanoma 2 (AIM2); caspase-1, caspase-2, caspase-3, caspase-5, caspase-8, caspase-9, caspase-12; pyrin; pyrin-only protein (POP) 1 and pyrin-only protein (POP) 2; cAMP-dependent protein kinase type I-alpha regulatory subunit (PRKAR1A); AP-1; serum response factor. There are 75 genes known to be induced by PYCARD. A large proportion of them are related to transcription (23%), inflammation (21%), or cell death (16%) (Hasegawa et al., 2009).

Inflammation

PYCARD is an adaptor protein involved in the structure and function of inflammasomes. Inflammasomes are pattern recognition receptors characteristically composed of an NLR, ASC and caspase-1 and are responsible for production of pro-inflammatory cytokines, in particular IL-1β and IL-18. There are several subtypes of inflammasomes that recognize a diverse array of microbial, endogenous, and environmental danger signals (Agostini et al., 2004; Mariathasan et al., 2004; Muruve et al., 2008; Fernandes-Alnemri et al., 2009; Hornung et al., 2009; Zhou et al., 2011; Dunn et al., 2012).

Mounting evidence indicates that inflammasomes and PYCARD also elicit non-overlapping inflammatory functions. PYCARD interaction with NLRC4 regulates both apoptosis via caspase-8 and NF-κB activation via PYD. PYCARD can inhibit or activate NF-κB through PYD interactions with the NF-κB IKK complex (Stehlik et al., 2002; Masumoto et al., 2003; Sarkar et al., 2006; Fernandes-Alnemri et al., 2007; Hasegawa et al., 2009; Hornung et al., 2009; Taxman et al., 2011).

PYCARD is also associated with inflammasome-independent transcriptional activation of cytokines and chemokines via activator protein-1 (AP-1), NF-κB, mitogen activated protein kinase (MAPK) and caspase-8 (Taxman et al., 2006). In pathogen-infected cells, PYCARD regulates MAPK

phosphorylation by pathogens and Toll-like receptor (TLR) agonists via suppression of the dual-specificity phosphatase (DUSP10/MKP5), and independent of caspase-1 and IL-1β; thus demonstrating a function for ASC that is distinct from the inflammasome in modulating MAPK activity and chemokine expression (Taxman et al., 2011).

Adaptive immunity

PYCARD may play an inflammasome-independent role in driving dendritic cells to stimulate T-cell priming for the induction of antigen-specific cellular and humoral immunity. Dendritic cell maturation stimuli activate caspase-1 in human dendritic cells. Inhibition of PYCARD and cathepsin B markedly diminishes the capacity of mature dendritic cells to stimulate antigen-specific T cells. The defective ability of PYCARD or cathepsin B-deficient dendritic cells to stimulate T cells is independent of inflammasome-mediated processing of inflammatory cytokines or priming of dendritic cells with pre-processed lipopolysaccharide (Guo and Dhodapkar, 2012).

On the other hand, PYCARD may also play an inflammasome-independent role in antigen-specific inflammatory disease. Mice genetically modified to lack both PYCARD alleles [ASC (-/-)] are protected from collagen-induced arthritis, whereas mice lacking Nlrp3 and caspase-1 are susceptible to collagen-induced arthritis. This may result from an inability of dendritic cells to facilitate antigen-specific activation of lymphocytes in mice lacking PYCARD. Furthermore, antigen-induced proliferation of purified T cells lacking PYCARD [ASC (-/-)] is restored upon incubation with wild type dendritic cells, but not when cultured with ASC (-/-) dendritic cells (Ippagunta et al., 2010).

Cell death (apoptosis, pyroptosis, necrosis)

PYCARD promotes caspase-mediated inhibition of cellular proliferation, DNA fragmentation and apoptosis via caspases including caspase-2/3/8 and 9 to activate the mitochondrial apoptotic pathway. The mechanism likely involves mitochondrial translocation of BAX, proteolytic maturation of BID and upregulation of the p53 response to cell stress or genotoxic insult (McConnell and Vertino, 2000; Ohtsuka et al., 2004; Hasegawa et al., 2007). PYCARD may also increase the susceptibility of leukemia cell lines to apoptotic stimuli by anticancer drugs (Masumoto et al., 1999).

PYCARD is involved in macrophage pyropoptosis (inflammatory cell death) which is characterized by potassium efflux and/or decreased intracellular potassium. The interaction of AIM2 with PYCARD leads to the formation of the pyroptosome, which induces pyroptotic cell death in response to cytoplasmic DNA in cells containing caspase-1 (Fernandes-Alnemri et al., 2007; Fernandes-Alnemri et al., 2009).

PYCARD also mediates cellular necrosis (pyronecrosis) in concert with NLRP3 and cathespin to cause programmed necrotic cell death that is independent from pyroptosis and does not require caspase-1 (Willingham et al., 2007; Satoh et al., 2013).

Implicated in

Cancer

Anti-cancer immunity

Note

ATP released by dying tumor cells activates P2RX7 receptors on dendritic cells, which triggers NLRP3/ASC (PYCARD)/ caspase-1 inflammasome-dependent IL-1β production and subsequent dendritic cell-mediated priming of tumor antigen-specific CD8+ T-cell production of IFN-γ (Aymeric et al., 2010).

Melanoma

Note

ASC has a dual role in melanoma progression via differential regulation of NF-κB activity and IL-1β processing. In primary melanoma, relatively high levels of ASC expression inhibit NF-κB activity and IL-1β transcription, with net inhibition of tumorigenesis. In metastatic melanoma, however, aberrant methylation results in decreased levels of ASC. The relative paucity of ASC protein in these cells, as well as assembly of a constitutionally active ASC-dependent inflammasome, may result competition among various pathways for a limited supply of ASC, with a net result of decreased inhibition of NF-κB, a positive feedback loop of IL-1 signalling and a pro-tumorigenic effect (Guan et al., 2003; Okamoto et al., 2010; Liu et al., 2013).

Skin squamous cell carcinoma

Note

ASC expression is reduced in squamous cell carcinoma. Tissue-specific analysis of a murine model of squamous cell carcinoma reveals that ASC has opposing functions: ASC acts as an inflammasome-independent p53-dependent tumor suppressor in keratinocytes while functioning as an inflammasome-dependent tumor promoter in dendritic cells (Drexler et al., 2012).

Colorectal cancer

Note

ASC expression sensitizes colorectal cancer cells to chemotherapeutic agents, resulting in inflammasome-independent cell death via mitochondrial reactive oxygen species and janus-kinase signalling. Methylation and silencing of ASC in colorectal cancer cells confers resistence to cell death by DNA-damaging chermotherapeutics (Riojas et al., 2007; Hong et al., 2013).

NLRP3/ASC-dependent caspase-1 activity is critical for IL-18-mediated IFN-γ-dependent STAT1 tumor suppression of colorectal cancer triggered by chronic inflammation (Allen et al., 2010; Dupaul-Chicoine et al., 2010; Zaki et al., 2010).
On the other hand ASC-dependent caspase-1 activity has a tumorigenic effect via IL-6 and STAT3 in response to microbial induction of aryl hydrocarbon receptors in the cecum (Ikuta et al., 2013).

Breast cancer

Note
Epigenetic silencing of TMS1 (PYCARD, ASC) results in failure of breast cancer cells to undergo BIM- and caspase-8-dependent apoptosis (anoikis) after detachment from the extra-cellular matrix (Parsons and Vertino, 2006; Parsons et al., 2009).

Prostate cancer

Note
Interferons induce expression of the cytosolic DNA-sensing AIM2/ASC inflammasome in normal human prostate cells. AIM2 mRNA levels are higher in benign prostate hyperplasia (BPH) cells than in normal prostate tissue. AIM2 mRNA levels are lower, however, in prostate cancer cells relative to BPH cells (Ponomareva et al., 2013).
Aberrant methylation and reduced expression of ASC occurs in prostate cancer cell lines and is associated with more aggressive disease (Collard et al., 2006; Das et al., 2006).

Glioblastoma

Note
Glioblastoma astrocytes aberrantly methylate ASC resulting in decreased ASC expression relative to normal human brain tissue. Decreased ASC expression may be associated with decreased patient survival and progression from grade III to grade IV glioma (Stone et al., 2004).

Lung cancer

Note
Hypermethylation of the ASC promoter with reduced ASC expression occurs in primary lung cancer and is correlated with progression and metastasis of human lung adenocarcinoma. ASC hypermethylation in sputum DNA correlates with a high risk of lung cancer (Machida et al., 2006).

Promyelocytic leukemia

Note
Promyelocytic leukemia protein (PML) limits ASC function and relegates ASC to the nucleus, limiting inflammasome activation and IL-1β production in bone marrow macrophages (Dowling et al., 2014). Another study, using a genetically distinct murine model, found that PML enhances NLRP3 inflammasome assembly and production of IL-1β, but did not specifically examine interactions between PML and ASC (Lo et al., 2013).

Inflammatory diseases

Atopic dermatitis

Note
Downregulation of NLRP3/ASC inflammasome function in atopic dermatitis may predispose patients to Staphylococcus aureus superinfection (Niebuhr et al., 2014).

Psoriasis

Note
AIM2, ASC, caspase-1, and caspase-5 expression is upregulated in psoriatic skin lesions (Dombrowski et al., 2011; Kopfnagel et al., 2011; Salskov-Iversen et al., 2011).

Contact dermatitis

Note
Ultraviolet (UV) light triggers cutaneous production of uric acid with demonstrated effects on the NLRP3/ASC/caspase-1 inflammasome and varying impact on immunity and carcinogenesis. The NLRP3/ASC inflammasome contributes to a caspase-dependent IL-1β hypersensitivity response (Watanabe et al., 2007).
Allopurinol (a xanthine oxidase inhibitor of uric acid production) prevents UV-induced NLRP3 upregulation but not UV-induced ASC downregulation (Leighton et al., 2013).

Pyogenic arthritis, pyoderma gangrenosum, and acne (PAPA) syndrome

Note
Alterations in ASC as well as upstream and downstream components of the inflammasome pathway are involved in a variety of inflammatory skin diseases.
Hereditary mutations in proline serine threonine phosphatase-interacting protein [PSTPIP1, or CD2-binding protein 1 (CD2BP1)], which regulates pyrin and is involved in filament organization, may activate NLRP3-independent ASC/caspase-1 activity, resulting in the persistent IL-1β secretion implicated in PAPA syndrome (Shoham et al., 2003; Waite et al., 2009).

Familial mediterranean fever

Note
Similar to the PAPA syndrome, gain of function mutations in the pyrin-encoding MEFV gene result in ASC-dependent, NLRP3-independent, caspase-1-mediated activation of IL-1β (Waite et al., 2009; Chae et al., 2011; Franchi and Núñez, 2011).

Inflammatory bowel disease

Note

ASC triggers caspase-driven enteric neuronal cell death in response to inflammatory driven ATP activation of P2X7R and pannexin channels (Gulbransen et al., 2012).

Alterations in the NLRP6 inflammasome pathway including ASC, caspase-1 and IL-18 may contribute to the etiology of human inflammatory bowel disease (Elinav et al., 2011).

Metabolic diseases including: gout, rheumatoid arthritis, diabetes mellitus and atherosclerosis

Note

Macrophages, TLRs, NLRs and other components of the innate immune system play a role in the etiology of a variety of metabolic inflammatory diseases.

Dysregulated ATP, lipid, urate and glucose metabolism disrupts microtubule polymerization, inflammasome assembly and proinflammatory cytokine production. Tubulin polymerization is critical for mitochondrial transport and inflammasome assembly by allowing for juxtaposition of ASC with NLRP3 in the cytosol (Martinon et al., 2006; Griffith et al., 2009; Ippagunta et al., 2010; Wen et al., 2011; Lu et al., 2012; Wen et al., 2012; Akira et al., 2013; Benetti et al., 2013; Grant and Dixit, 2013; Jourdan et al., 2013; Lee et al., 2013).

Infectious diseases

Anthrax

Note

Anthrax lethal toxin triggers the formation of ASC-dependent NLRC4, NLRP3 and AIM2, but not NLRP1-dependent processing of caspase-1 with subsequent autoproteolysis and IL-1β secretion in murine macrophages (Nour et al., 2009; Lu et al., 2012; Van Opdenbosch et al., 2014). The 7-desacetoxy-6,7-dehydrogedunin (7DG) small molecule has been shown to protect macrophages from anthrax lethal toxin. 7DG inhibits protein kinase R, which is has a role in ASC assembly, caspase-1 activation and macrophage pyroptosis (Hett et al., 2013).

Chlamydia trachomatis

Note

Chlamydia trachomatis, an obligate intracellular bacteria, triggers secretion of IL-1β secretion in human trophoblasts via Nod1 but independent of Nalp3 (NLRP3) inflammasomes (Kavathas et al., 2013). Murine macrophages lacking ASC display prolonged courses of infection with Chlamydia muridarum, associated with reduced IL-18 production as well as T cell recruitment and proliferation but exhibit normal levels of IL-1β secretion and no change oviduct pathology, suggesting ASC has an IL-1-independent role in adaptive immunity during genital chlamydial infection (Nagarajan et al., 2012).

Cervical epithelial cells, however, are the preferred host medium for Chlamydia trachomatis and these cells do not normally produce IL-1β.

Infection by Chlamydia trachomatis activates NLRP3/ASC/caspase-1 which instead alters lipid metabolism by caspase mediated fragmentation of the Golgi apparatus diversion of Golgi lipids to the Chlamydia intracellular inclusion.

This provides an optimal growth environment for intracellular chlamydia and blocking casapase-1 in these cells can inhibit chlamydial infection by ~60% (Abdul-Sater et al., 2009).

Chlamydia pneumonia

Note

Chlamydia pneumonia is a significant cause of atypical pneumonia and inflammatory diseases including asthma and COPD, infects alveolar macrophages. IL-1β secretion depends on Chlamydia pneumonia entry into murine macrophages with subsequent protein synthesis resulting in mitochondrial dysfunction, NLRP3/ASC/Caspase-1 activation, and IL-1β secretion.

This suggests an important role for ASC in clearing Chlamydia pneumonia infection as well as chronic inflammatory diseases affecting the airway (He et al., 2010; Shimada et al., 2011).

Escherichia coli

Note

Enterohemorrhagic E. coli (EHEC) O157:H7 enterohemolysin (Ehx) triggers NLRP3/ASC/caspase-1-dependent production of IL-1 in THP-1 macrophages (Zhang et al., 2012). As with salmonella, double-stranded RNA-dependent protein kinase (PKR, EIF2AK2) interacts with ASC and other inflammasome components including NLRP3, NLRP1, NLRC4 and AIM2 to trigger caspase-1-dependent IL-1β production and pryopoptosis in E. coli-infected macrophages IL-1β (Lu et al., 2012).

Extracellular infection, however, requires ATP co-stimulation of the P2X7 receptor and potassium efflux for NLRC4/ASC-driven caspase-1 activation in macrophages (Franchi et al., 2007a).

HSV

Note

The nuclear promyelocytic leukemia (PML) protein limits formation of cytosolic ASC dimers in HSV-infected bone marrow macrophages with subsequent decreases in IL-1β secretion (Dowling et al., 2014).

Legionella

Note

Legionella avoids caspase-1 activation through downregulation of NLRC4 and ASC expression through an unknown mechanism (Abdelaziz et al., 2011; Pereira et al., 2011).

Listeria

Note

The AIM2/ASC inflammasome senses cytosolic double strand DNA from intracellular viruses and bacteria including Listeria and triggers caspase-1-dependent maturation of IL-1β and IL-18 (Franchi et al., 2007a; Jin et al., 2013).

Malaria

Note

Malaria is characterized by cyclical fevers and associated with high levels of IL-1β and other cytokines. Mice infected with plasmodium demonstrate caspase-1 activation dependent on ASC, NLRP3 and other inflammasome components. Pro-IL-1β production depends on secondary stimulation with LPS, IFN-γ or TNF-R1. Uric acid release during malaria infection may further augment host response via NLRP3 inflammasome activation. As a result of caspase-1 activation in plasmodium-infected mice, microbial stimulus results in extremely high levels of IL-1β and sensitivity to septic shock. IL-1R antagonist prevents bacterial-induced lethality in rodents. Peripheral blood monocytes in febrile malaria patients display activated caspase-1 and produce large amounts of IL-1β after stimulation with LPS, suggesting that NLRP3/ASC-dependent activation of caspase-1 is crucial to production of systemic IL-1β and hypersensitivity to sepsis during malaria infection (Ataide et al., 2014).

Pseudomonas

Note

Pseudomonas aeruginosa increases expression of human pattern recognition receptors including TLR2 and TLR4, proinflammatory cytokines including IL-1 and IFN-γ, and inflammasome components NLRP3, NLRC4 and ASC compared with control donor corneas. Putative molecules triggering this response are the bacterial pilus protein type IV pilin, as well as several type III secretion apparatus proteins (Franchi et al., 2007b; Arlehamn and Evans, 2011; Karthikeyan et al., 2013).

Salmonella

Note

ASC forms a complex with NLRP3, NLRC4, caspase-1, caspase-8 and pro-IL-1 in S. typhimurium-infected THP-1 macrophages (Broz et al., 2010; Man et al., 2013; Man et al., 2014). The nuclear promyelocytic leukemia (PML) protein limits formation of cytosolic ASC dimers in S. typhimurium-infected bone marrow macrophages with subsequent decreases in IL-1β and IL-18 secretion but no effect on pyroptotic cell death (Dowling et al., 2014). Double-stranded RNA-dependent protein kinase (PKR, EIF2AK2) interacts with ASC and other inflammasome components including NLRP3, NLRP1, NLRC4 and AIM2 to trigger caspase-1-dependent IL-1β production and pryopoptosis in S. typhimurium-infected macrophages (Lu et al., 2012). Salmonella flagellin and type III secretion proteins promotes potassium-efflux independent ASC oligomerization and NLRC4 inflammasome-dependent caspase-1 activation (Franchi et al., 2007a; Hwang et al., 2012).

Schistosoma mansoni

Note

Schistosoma infection activates the Dectin-2 receptor, which triggers NLRP3/ASC-dependent IL-1β secretion as well with subsequent alteration of the adaptive immune reponse, increased granuloma formation and liver disease (Ritter et al., 2010).

Shigella

Note

Shigella type III secretion proteins induce NLRC4/ASC/caspase-1-dependent processing of IL-1β and pyroptosome formation in macrophages (Suzuki et al., 2007; Willingham et al., 2007; Suzuki et al., 2014).

Streptococcus pneumonia

Note

ASC is involved in controlling pneumococcus infection via several putative downstream intermediates including IL-17, GM-CSF and adaptive immune regulatory genes (van Lieshout et al., 2014). ASC regulates systemic inflammatory responses to pneumococcal meningitis infection via caspase-1, IL-1, IL-18 and IFN-γ (Fang et al., 2011; Geldhoff et al., 2013). Bacterial keratitis caused by S. pneumonia pneumolysin triggers increased expression of inflammasome components NLRP3, NLRC4 and ASC compared with control donor corneas (Karthikeyan et al., 2013).

Streptococcus pyogenes

Note

ASC and NLP3 is necessary for caspase-1-dependent IL-1β secretion (but not pro-IL-1β expression) in response to S. Pyogenes infection. Caspase-1 activation activation in response to streptolysin O pore-forming toxin also depdends on NF-κB but not on P2X7R or TLR signaling (Harder et al., 2009).

Tuberculosis

Note

Mycobacterium tuberculosis infection induces NLRP3/ASC-dependent IL-1β secretion and apoptosis in bone marrow derived dendritic cells (Abdalla et al., 2012).

West Nile virus

Note

ASC is critical for clearance of west nile virus infection via secretion of IL-1β, IL-6, IFN-γ, and IFN-α as well as increased levels of IgM, suggesting a role for ASC in coordinating innate as well as adaptive immune reponses to west nile virus infection (Kumar et al., 2013).

Vaccine adjuvent

Note

ASC has an NLRP3/caspase-1-independent role in mediating antigen-specific immunity to oil-in-water adjuvent H5N1 influenza vaccine via B-cell antigen-specific antibody production and dendritic cell inflammatory cytokine release (Ellebedy et al., 2011).

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