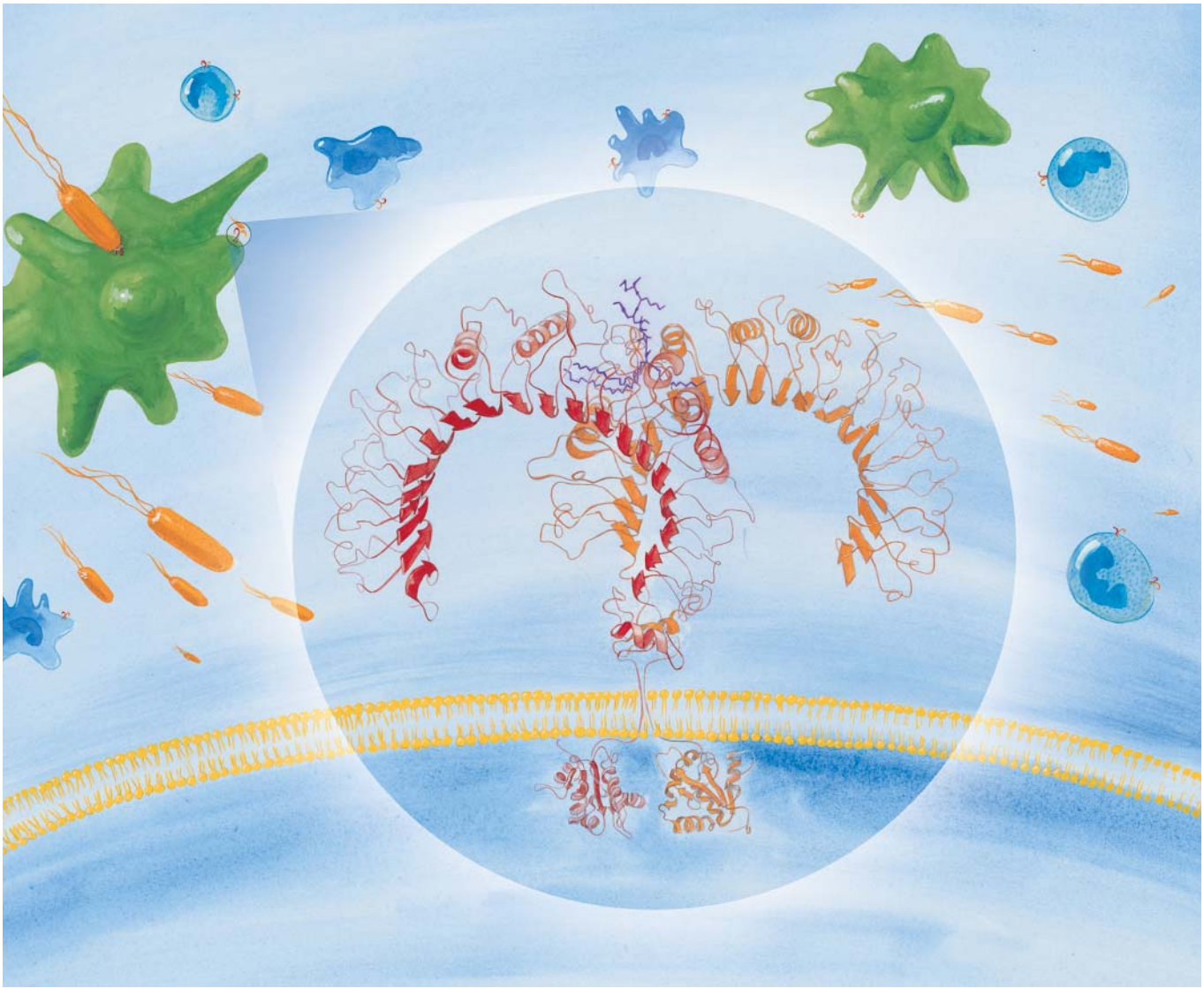
# Pattern Recognition Receptors



R&D SYSTEMS®

# Pattern Recognition Receptors

Pattern recognition receptors (PRRs) expressed by innate immune cells are essential for detecting invading pathogens and initiating the innate and adaptive immune response. There are multiple families of PRRs including the membrane-associated Toll-like receptors (TLRs) and C-type lectin receptors (CLRs), and the cytosolic NOD-like receptors (NLRs), RIG-I-like receptors (RLRs), and AIM2-like receptors (ALRs). PRRs are activated by specific pathogen-associated molecular patterns (PAMPs) present in microbial molecules or by damage-associated molecular patterns (DAMPs) exposed on the surface of, or released by, damaged cells. In most cases, ligand recognition by PRRs triggers intracellular signal transduction cascades that result in the expression of pro-inflammatory cytokines, chemokines, and antiviral molecules.[1] In contrast, activation of some ALRs and NLRs leads to the formation of multiprotein inflammasome complexes that serve as platforms for the cleavage and activation of Caspase-1.[2] Caspase-1 promotes the maturation and secretion of IL-1β and IL-18, which further amplifies the pro-inflammatory immune response. Since a single pathogen can simultaneously activate multiple PRRs, crosstalk between different receptors may also play a role in enhancing or inhibiting the immune response.[3] Therefore, tight regulation of PRR signaling is required in order to eliminate infectious pathogens and at the same time, prevent aberrant or excessive PRR activation, which can lead to the development of inflammatory and autoimmune disorders.[4]


**References**

1. Takeuchi, O. & S. Akira (2010) Cell **140**: 805.
2. Schroder, K. & J. Tschopp (2010) Cell **140**:821.
3. Kingeter, L.M. & X. Lin (2012) Cell. Mol. Immunol. **9**:105.
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## Select Pattern Recognition Receptor Agonists

### Toll-like Receptors (TLRs)

| TLRs | Agonist(s) | Source |
|---|---|---|
| **TLR1/TLR2** | Triacyl lipopeptides | Bacteria |
| **TLR2** | Lipoproteins | Multiple Pathogens |
| | Peptidoglycan (PGN) | Bacteria |
| | Porins | Bacteria |
| | Zymosan | Fungi |
| | β-Glycan | Fungi |
| | GPI-mucin | Protozoa |
| | Envelope glycoproteins | Viruses |
| **TLR2/TLR6** | Diacyl lipopeptides | Bacteria |
| | Lipoteichoic acid (LTA) | Bacteria |
| **TLR3** | Double-stranded RNA | Viruses |
| | Poly (I:C) | Synthetic analog of double-stranded RNA |
| **TLR4** | Lipopolysaccharide (LPS) | Bacteria |
| | Glycoinositolphospholipids | Protozoa |
| | Envelope glycoproteins | Viruses |
| | Host-derived HMGB1 and HSPs | Endogenous |
| **TLR5** | Flagellin | Bacteria |
| **TLR7** | Single-stranded RNA | Viruses |
| **TLR8** | Single-stranded RNA | Viruses |
| **TLR9** | Unmethylated CpG DNA | Bacteria |
| | | Protozoa |
| | | Viruses |
| | Mitochondrial DNA | Endogenous |
| **TLR10** | Unknown | Unknown |

### C-type Lectin Receptors (CLRs)

| CLRs | Agonist(s) | Source |
|---|---|---|
| **BDCA-2** | Mannose, fucose | Unknown |
| **CLEC-1** | Unknown | Unknown |
| **CLEC-2** | Unknown | Endogenous podoplanin (PDPN); HIV; Snake venom protein rhodocytin |
| **CLEC4D/CLECSF8** | Unknown | Unknown |
| **CLEC9a** | Filamentous form of actin | Necrotic cells |
| **CLEC12B** | Unknown | Unknown |
| **DCAR/CLEC4B** | Unknown | Unknown |
| **DCIR/CLEC4A** | Mannose, fucose | HIV |
| **DC-SIGN/CD209** | High mannose, fucose | *Candida albicans*, Cytomegalovirus, Dengue virus, filoviruses, HIV, *Leishmania* spp., measles virus, *Mycobacterium* spp., SARS, *Schistosoma mansoni egg antigen* |
| **Dectin-1/CLEC7A** | β-1,3 glucans | Fungi, mycobacteria |
| **Dectin-2/CLEC6A** | High mannose; α-mannans | *Aspergillus fumigatus*, *Candida albicans, Cryptococcus neoformans, Histoplasma capsulatum, Microsporum audouinii, Mycobacterium tuberculosis, Paracoccidioides brasiliensis, Saccharomyces cerevisiae, Trichophyton rubrum* |
| **Dectin-2α/CLEC6A** | High mannose; α-mannans | *Aspergillus fumigatus, Candida albicans, Cryptococcus neoformans, Histoplasma capsulatum, Microsporum audouinii, Mycobacterium tuberculosis, Paracoccidioides brasiliensis, Saccharomyces cerevisiae, Trichophyton rubrum* |
| **LOX-1/OLR1** | Oxidized low density lipoprotein (ox-LDL); modified lipoproteins | Endogenous; Bacteria; Also activated by aged cells, advanced glycation end products, and HSP70 |
| **MDL-1/CLEC5A** | Unknown | Dengue virus |
| **MICL/CLEC12A** | Unknown | Unknown |
| **Mincle/CLEC4E** | α-mannose, glycolipids, SAP130 (endogenous) | *Candida albicans*, *Malassezia* spp., *Mycobacterium tuberculosis*, dead cells |
| **SIGNR3/CD209d** | High mannose, fucose | *Mycobacterium tuberculosis* |

### NOD-like Receptors (NLRs)

| NLRs | Agonist(s) | Source |
|---|---|---|
| **NOD1 (NLRC1)** | Meso-diaminopimelic acid (Meso-DAP) | Bacteria |
| **NOD2 (NLRC2)** | Muramyl dipeptide (MDP) | Bacteria |
| **CIITA** | Unknown | |
| **NAIP** | *Legionella pneumophila*; Flagellin (Naip5) | |
| **NLRC3** | Unknown | |
| **NLRC4 (IPAF)** | *Legionella pneumophila; Pseudomonas aeruginosa; Salmonella typhimurium; Shigella flexneri* | |
| **NLRC5** | Unknown | |
| **NLRP1/NALP1** | *Bacillus anthracis* lethal toxin; Muramyl dipeptide (MDP) | |
| **NLRP2/NALP2** | Unknown | |
| **NLRP3/NALP3** | Adenoviral DNA; Bacterial RNA; *Candida albicans/Saccharomyces cerevisiae;* Danger signals: Extracellular ATP, $NAD^+$, β-amyloid, and particulates such as calcium pyrophosphate dihydrate and monosodium urate; Pore-forming toxins: Hemolysins, Listeriolysin O, Nigericin, Pneumolysin; Xenogenous compounds: Silica, asbestos, alum, and uric acid; Influenza and Sendai virus RNA; Lipopolysaccharide (LPS); *Klebsiella pneumoniae, Mycobacterium tuberculosis, Salmonella typhimurium, Schistosoma mansoni* | |
| **NLRP4-14/ NALP4-14** | Unknown | |
| **NLRX1** | Unknown | |

### RIG-I-like Receptors (RLRs)

| RLRs | Agonist(s) | Source |
|---|---|---|
| **RIG-I** | Short 5' triphosphate single-stranded RNA containing some double-stranded regions | Viruses |
| **MDA5** | Long double-stranded RNA | Viruses |
| **LGP2** | Unknown | RNA Viruses |

**Cover Illustration:** A model of the ligand-bound TLR1/TLR2 heterodimer based on the crystal structure [Adapted from Jin, M.S. *et al.* (2007) Cell **130**:1071.]

# Toll-like Receptors

Toll-like receptors (TLRs) are a family of type I transmembrane pattern recognition receptors (PRRs) that are expressed by a number of different immune and non-immune cell types including monocytes, macrophages, dendritic cells, neutrophils, B cells, T cells, fibroblasts, endothelial cells, and epithelial cells.[1] TLRs initiate the immune response following recognition of either conserved, pathogen-associated molecular patterns (PAMPs) present in microbial molecules or endogenous danger signals released by damaged cells. There are ten functional TLRs in humans and twelve in mice.[2] Of the human TLRs, TLR1, 2, 4, 5, 6, and 10 are expressed on the cell surface and primarily recognize microbial membrane and/or cell wall components, while TLR3, 7, 8, and 9 are expressed in the membranes of endolysosomal compartments and recognize nucleic acids.[3] TLRs have a variable number of ligand-sensing, leucine-rich repeats at their N-terminal ends and a cytoplasmic Toll/IL-1 R (TIR) domain. The TIR domain mediates interactions between TLRs and adaptor proteins involved in regulating TLR signaling including MyD88, TRIF, TRAM, and TIRAP/MAL. Signaling pathways activated downstream of these adaptor molecules promote the expression of pro-inflammatory cytokines, chemokines, and type I and type III interferons. As a result, additional immune cells are recruited to the infection site and pathogenic microbes and infected cells are eliminated. Although TLRs provide protection against a wide variety of pathogens, inappropriate or unregulated activation of TLR signaling can lead to chronic inflammatory and autoimmune disorders.[4]

## References


1. Iwasaki, A. & R. Medzhitov (2004) Nat. Immunol. **5**:987.
2. Kawai, T. & S. Akira (2011) Immunity **34**:637.
3. Blasius, A.L. & B. Beutler (2010) Immunity **32**:305.
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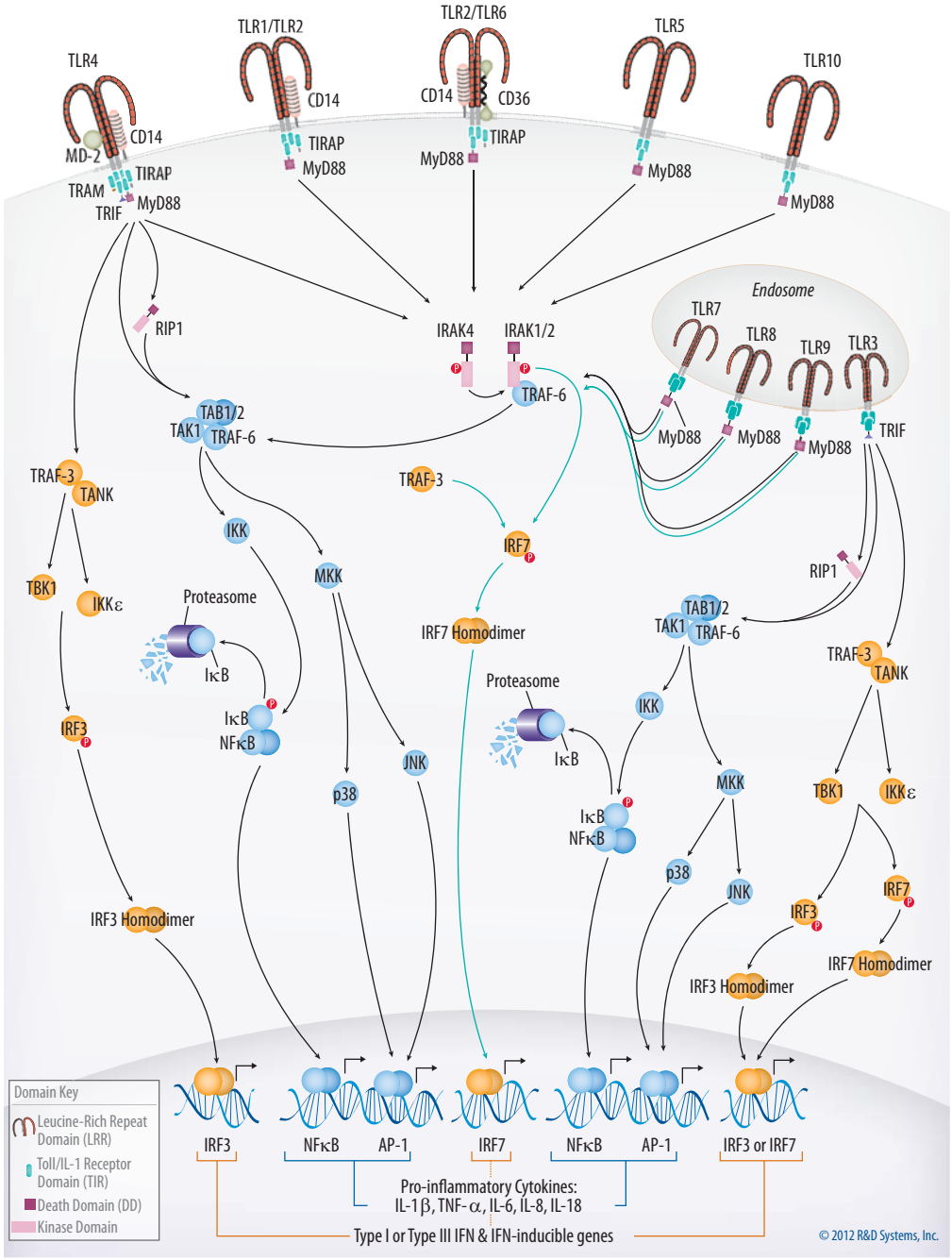
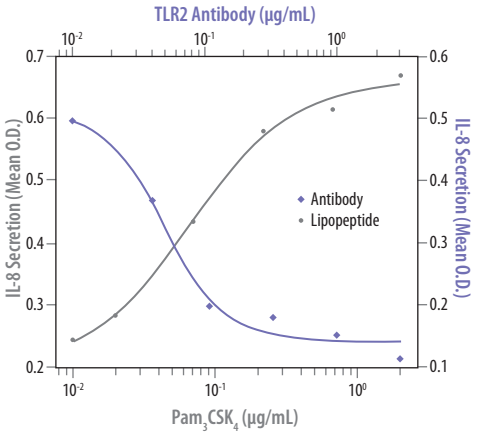
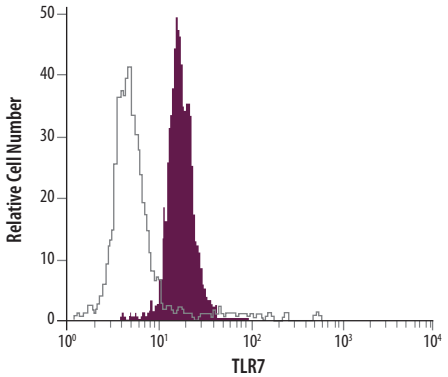



**TLR2 Ligand-induced IL-8 Secretion and Neutralization using an Anti-Human TLR2 Antibody.** The HEK293 human embryonic kidney cell line transfected with human TLR2 was treated with increasing concentrations of the synthetic tri-palmitoylated lipopeptide $Pam_3CSK_4$. IL-8 secretion was measured using the Human CXCL8/IL-8 Quantikine® ELISA Kit (Catalog # D8000C; gray line). The stimulatory effect induced by 0.5 µg/mL $Pam_3CSK_4$ was neutralized by treating the cells with increasing concentrations of a Mouse Anti-Human TLR2 Monoclonal Antibody (Catalog # MAB2616; purple line).




**Detection of TLR7 by Flow Cytometry.** The Ramos human Burkitt's lymphoma cell line was stained with a Fluorescein-conjugated Mouse Anti-Human TLR7 Monoclonal Antibody (Catalog # IC5875F; filled histogram) or a Fluorescein-conjugated Mouse $IgG_{2A}$ Isotype Control (Catalog # IC003F; open histogram).

# C-type Lectin Receptors (CLRs)

C-type lectin receptors (CLRs) are a diverse family of soluble and transmembrane proteins that contain one or more C-type lectin-like domain (CTLD). Multiple members of the CLR family are considered to be pattern recognition receptors (PRRs) due to their ability to recognize pathogen-associated molecules and induce intracellular signaling pathways that regulate the immune response. With the exception of DC-SIGN, most CLRs that function as PRRs belong to either the Dectin-1 (Dectin-1, CLEC-1, CLEC-2, CLEC9a, CLEC12B, LOX-1/OLR1, and MICL/CLEC12A) or Dectin-2 (Dectin-2, BDCA-2, CLEC4D/CLECSF8, DCAR, DCIR, and Mincle) subgroups.[1] Members of these subgroups are transmembrane proteins that are primarily expressed by monocytes, macrophages, and dendritic cells, and recognize fucose, mannose, or glucan carbohydrate structures. Signaling pathways activated by CLRs either directly regulate gene expression or modulate TLR signaling.[2] Dectin-1 and Dectin-2 are two well-characterized CLRs that function as PRRs. Both receptors have been shown to promote canonical NFκB signaling through activation of spleen tyrosine kinase (SYK) and a multiprotein complex consisting of CARD9, Bcl-10, and MALT1.[1-4] While Dectin-1 directly interacts with SYK through its cytoplasmic, immunoreceptor tyrosine-based activation motif (ITAM), Dectin-2 interacts with SYK through the ITAM-containing adaptor protein, FcRγ. Dectin-1 also regulates NFκB activity through the NIK-dependent, non-canonical NFκB signaling pathway, and through Raf-1-mediated phosphorylation and acetylation.[4] In addition, both Dectin-1 and Dectin-2 activate NFAT and AP-1.[2] As a result, signaling initiated by either receptor can precisely control the expression of numerous cytokines that direct the innate and adaptive immune response. Other CLRs do not directly regulate cytokine expression, but instead modulate TLR-induced signaling pathways. DCIR/CLEC4A, MICL/CLEC12A, and CLEC12B are CLRs that contain an immunoreceptor tyrosine-based inhibitory motif (ITIM) in their cytoplasmic domains. Upon activation, DCIR and MICL recruit the phosphatases, SHP-1 or SHP-2, and inhibit TLR8 or TLR9 signaling by an undefined mechanism.[2,4] In contrast, BDCA-2 and DC-SIGN/CD209 do not contain a cytoplasmic ITIM motif but have also been shown to modulate TLR signaling through alternate pathways.[2,4] CLRs are particularly important for antifungal immunity.[3] This is highlighted by the fact that targeted deletion of specific CLRs in mice, as well as polymorphisms or mutations in human Dectin-1 or CARD9, respectively, are associated with an increased susceptibility to a variety of fungal pathogens.[2,3,5]

## References


1. Kingeter, L.M. & X. Lin (2012) Cell. Mol. Immunol. **9**:105.
2. Osorio, F. & C. Reis e Sousa (2011) Immunity **34**:651.
3. Drummond, R.A. *et al.* (2011) Eur. J. Immunol. **41**:276.
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5. Hardison, S.E. & G.D. Brown (2012) Nat. Immunol. **13**:817.


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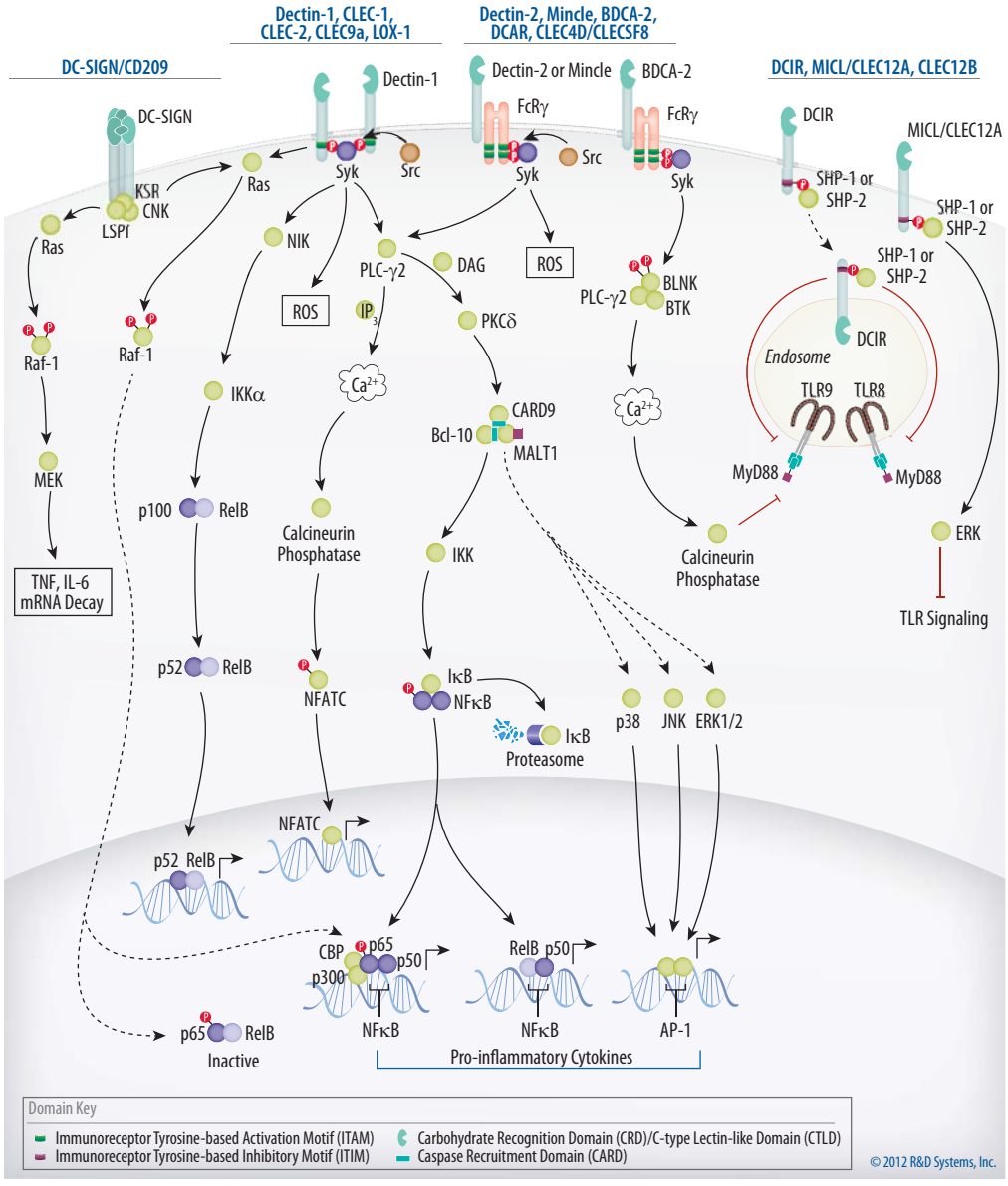
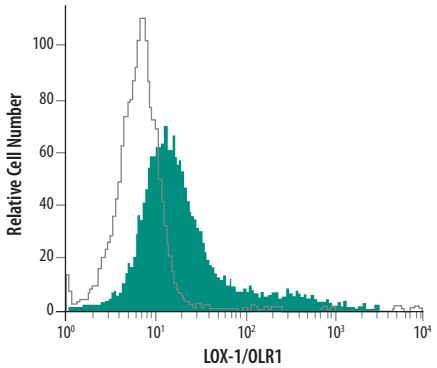
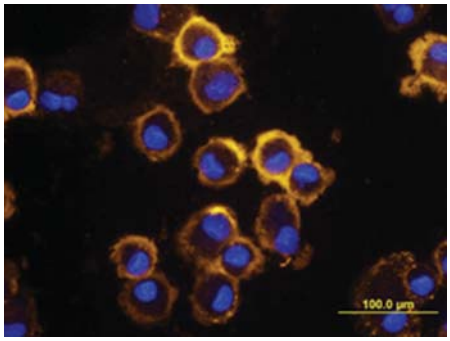





**Detection of LOX-1/OLR1 by Flow Cytometry.** The RAW264.7 mouse monocyte/macrophage cell line was stained with a PE-conjugated Rat Anti-Mouse LOX-1/OLR1 Monoclonal Antibody (Catalog # FAB1564P; filled histogram) or a PE-conjugated Rat $IgG_{2A}$ Isotype Control (Catalog # IC006P; open histogram).




**DC-SIGN in Human Dendritic Cells.** DC-SIGN was detected in immersion-fixed mature human dendritic cells using a Mouse Anti-Human DC-SIGN/CD209 Monoclonal Antibody (Catalog # MAB161). Cells were stained using the NorthernLights™ 557-conjugated Anti-Mouse IgG Secondary Antibody (Catalog # NL007; yellow) and counterstained with DAPI (blue).

# NOD-like Receptors & RIG-I-like Receptors

Nucleotide-binding, oligomerization domain (NOD)-like receptors (NLRs) and retinoic acid-inducible gene-I (RIG-I)-like receptors (RLRs) are cytosolic receptors that provide a second line of defense against invading pathogens. The NLR family consists of twenty-two human proteins and at least thirty-four mouse proteins that are divided into subfamilies (NLRA, NLRB, NLRC, NLRP, NLRX) based on their N-terminal protein-interacting domains.[1] In addition to this domain, all NLRs contain a central nucleotide-binding/oligomerization domain (NACHT) and a variable number of ligand-sensing, leucine-rich repeats at their C-terminal ends. NOD1 and NOD2 are two well-characterized NLRs belonging to the NLRC subfamily that recognize components of bacterial peptidoglycan (PGN). Upon activation, they homo-oligomerize and recruit signaling molecules that drive the NFκB-/AP-1-dependent expression of pro-inflammatory cytokines and the IRF3-/IRF7-dependent expression of type I interferons.[2] Other NLRs, including NLRP1, NLRP3, and NLRC4, are activated by a number of different pathogens or endogenous danger signals and oligomerize to form multiprotein inflammasome complexes.[3] Inflammasome oligomerization induces the cleavage and activation of Caspase-1, which promotes the processing and secretion of IL-1β and IL-18, and may induce an inflammatory form of cell death known as pyroptosis. Similar to TLR signaling, inflammasome activation is tightly regulated. Constitutive inflammasome activation and the overproduction of IL-1β and IL-18 have been linked to autoinflammatory and autoimmune disorders.[4]

RIG-I-like receptors (RLRs) are a subset of cytosolic pattern recognition receptors (PRRs) that detect viral RNA. The RLR family consists of three members: RIG-I, MDA5, and LGP2. RIG-I and MDA5 contain two N-terminal caspase recruitment domains (CARDs), an internal RNA helicase domain, and a C-terminal repressor/RNA-binding domain. Signaling through both receptors activates NFκB- and IRF3-/IRF7-dependent gene expression. In contrast, LGP2 has not been shown to bind to RNA and lacks the N-terminal CARD domains required for signaling. It is currently thought to serve as a regulator of viral RNA recognition by RIG-I and MDA5.[5]

**References**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2. Elinav. E. *et al.* (2011) Immunity **34**:665.
3. Franchi, L. *et al.* (2009) Nat. Immunol. **10**:241.
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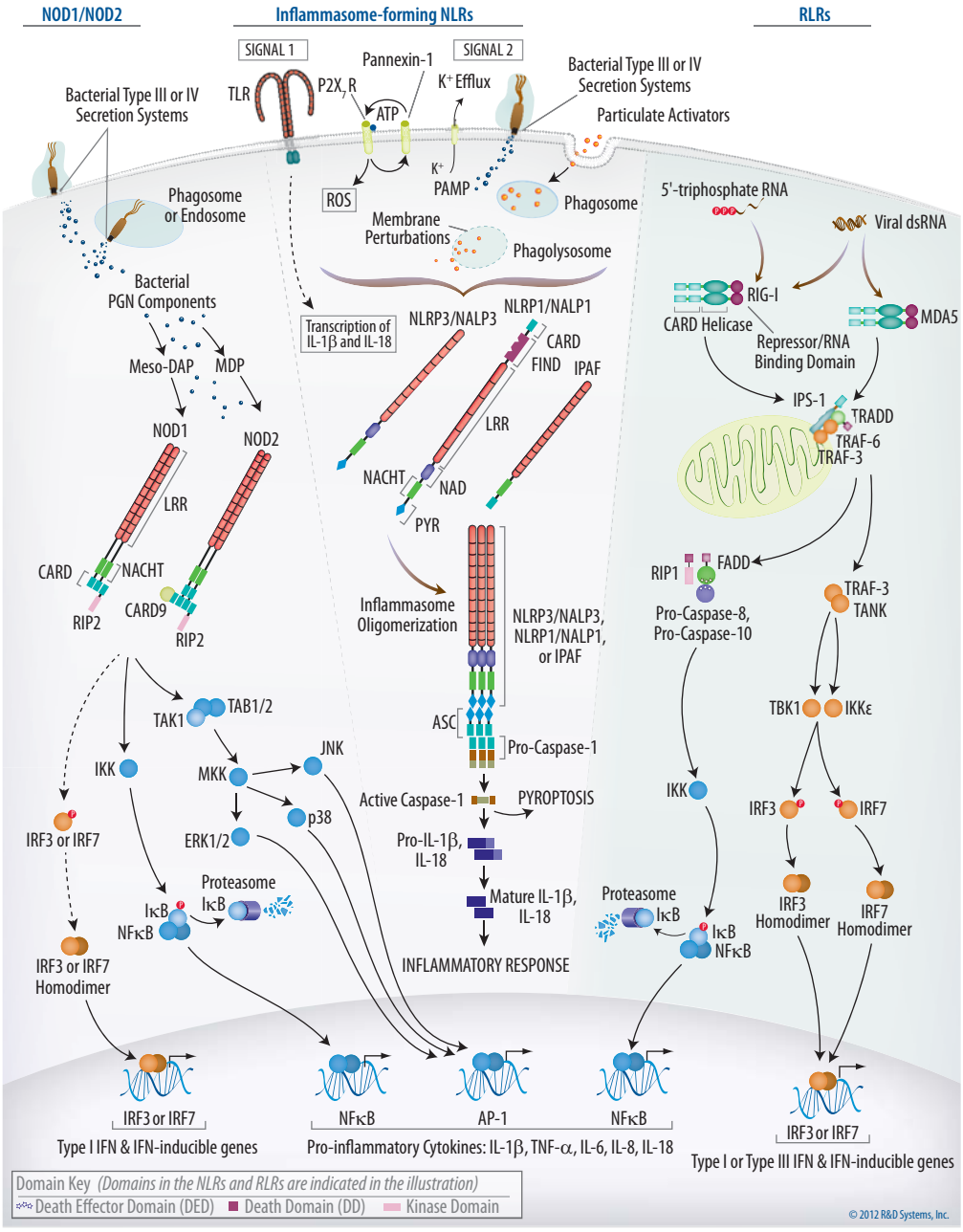
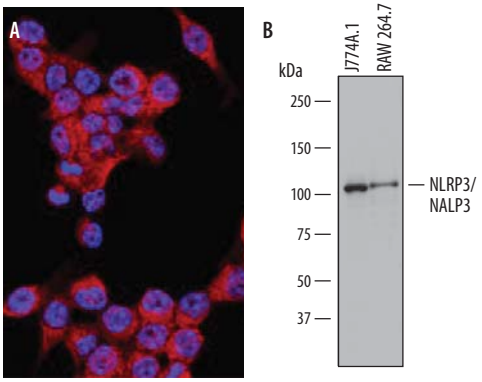
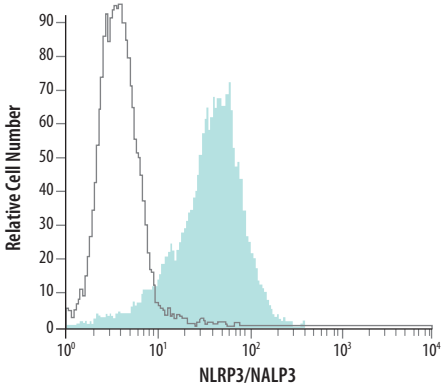



**NLRP3/NALP3 in RAW264.7 Cells. A.** NLRP3/NALP3 was detected in the immersion-fixed RAW264.7 mouse monocyte/macrophage cell line using a Rat Anti-Mouse NLRP3/NALP3 Monoclonal Antibody (Catalog # MAB7578). Cells were stained using the NorthernLights 557-conjugated Goat Anti-Rat IgG Secondary Antibody (Catalog # NL013; red) and counterstained with DAPI (blue). **B.** Lysates from the J774A.1 mouse reticulum cell sarcoma cell line and the RAW264.7 mouse monocyte/macrophage cell line were immunoblotted using the same Rat Anti-Mouse NLRP3/NALP3 Monoclonal Antibody (Catalog # MAB7578) followed by a HRP-conjugated Goat Anti-Rat Secondary Antibody (Catalog # HAF005). A specific band for NLRP3/NALP3 was detected at approximately 117 kDa under reducing conditions (as indicated).




**Detection of NLRP3/NALP3 by Flow Cytometry.** The RAW264.7 mouse monocyte/macrophage cell line was stained with a PE-conjugated Rat Anti-Mouse NLRP3/NALP3 Monoclonal Antibody (Catalog # IC7578P; filled histogram) or a PE-conjugated Rat $IgG_{2A}$ Isotype Control (Catalog # IC006P; open histogram).

# Products for Pattern Recognition Receptor Research from R&D Systems

## C-type Lectin Receptors (CLRs)

| Molecules | Proteins | Antibodies for Flow Cytometry* (Available Fluorochromes) | Antibodies for ICC/IHC, Neutralization, & Western blot | ELISAs | Multiplex Array Kits |
|---|---|---|---|---|---|
| CLEC-1 | H | H (Alexa Fluor® 488, PE) | H (WB) | | H |
| CLEC-2 | H | H (APC) | H (WB) | | H |
| CLEC4D/CLECSF8 | | H (APC, PE) | H (WB) | | |
| CLEC9a | H M | H (Alexa Fluor 488, APC, PE)<br>M (Alexa Fluor 700, Alexa Fluor 488, APC, PE, PerCP) | H (B/N, IHC, WB)<br>M (IHC, WB) | | |
| DCAR/CLEC4B | | M (Unlabeled) | M (WB) | | |
| DCIR/CLEC4A | | H (APC, Biotin, Fluorescein, PE) M (PE) | H (WB) M (WB) | | H |
| DC-SIGN/CD209 | H | H (Alexa Fluor 700, APC, Fluorescein, PE, PerCP) | H (B/N, ICC, IHC, WB) | | |
| Dectin-1/CLEC7A | H M | H (Alexa Fluor 700, APC, Fluorescein, PE, PerCP) M (Alexa Fluor 488, Alexa Fluor 700, APC, PE, PerCP) | H (B/N, ICC, WB)<br>M (B/N, WB) | | H |
| Dectin-2/CLEC6A | H | H (APC, Fluorescein, PE) | H (WB) | | |
| Dectin-2α/CLEC6A | M | M (APC) | M (WB) | | |
| LOX-1/OLR1 | H M | H (Alexa Fluor 488, APC, PE, PerCP)<br>M (PE) | H (B/N, E, WB)<br>M (B/N, E, WB) | H M | H |
| MDL-1/CLEC5A | | H (APC, PE) M (APC, PE) | H (WB) M (WB) | | H |
| MICL/CLEC12A | | H (APC, PE) M (Alexa Fluor 488, PE) | H (ICC, WB) M (ICC, WB) | | |
| MMR/CD206 | H M | H (Alexa Fluor 488, APC, PE)<br>M (Alexa Fluor 488, APC, PE) | H (ICC, IHC, WB)<br>M (WB) | | H |
| SIGNR3/CD209d | | | M (WB) R (WB) | | |

## NOD-like Receptors (NLRs) & RIG-I-like Receptors (RLRs)

| Molecules | Proteins | Antibodies for Flow Cytometry* (Available Fluorochromes) | Antibodies for ICC/IHC, Neutralization, & Western blot | ELISAs | Multiplex Array Kits |
|---|---|---|---|---|---|
| NAIP | | | H (IHC, WB) M (WB) | | |
| NLRP1/NLRP1/NALP1 | | | H (WB) | | |
| NLRP2/NALP2 | | | H (WB) | | |
| NLRP3/NALP3 | | M (Alexa Fluor 488, APC, PE) | H (ICC, WB) M (ICC, WB) | | |
| NLRP10/Pynod/NALP10 | | | H (WB) M (WB) R (WB) | | |
| NOD1** | | | H (IHC, WB) | | |
| RIG-I | | | H (WB) | | |

## Toll-like Receptors (TLRs)

| Molecules | Proteins | Antibodies for Flow Cytometry* (Available Fluorochromes) | Antibodies for ICC/IHC, Neutralization, & Western blot | ELISAs | Multiplex Array Kits |
|---|---|---|---|---|---|
| TLR1 | H M | H (APC, PE) M (Biotin, PE) | H (WB) M (WB) | | |
| TLR2** | H M | H (APC, Biotin, Fluorescein, PE, PerCP)<br>M (APC, Fluorescein) | H (B/N, E, WB)<br>M (WB) | H | H |
| TLR3** | H M | M (APC, PE) | H (WB) M (WB) | | |
| TLR4** | H | H (Alexa Fluor 488, APC, Biotin, Fluorescein, PE, PerCP) M (APC, PE) | H (B/N, ICC, IHC, WB) | | H |
| TLR4/MD-2 Complex | H | | | | |
| TLR6** | H M | M (APC, PE) | M (WB) | | |
| TLR7** | | H (Fluorescein, PE, PerCP) | M (WB) R (WB) | | |
| TLR9 | | H (Alexa Fluor 488) | | | |
| TLR10 | | | H (WB) | | |
| TLR11 | | M (APC, PE) | | | |

## Regulators of CLR, NLR, or TLR Signaling

| Molecules | Proteins | Antibodies for Flow Cytometry* (Available Fluorochromes) | Antibodies for ICC/IHC, Neutralization, & Western blot | ELISAs | Multiplex Array Kits |
|---|---|---|---|---|---|
| CD14 | H M | H (Alexa Fluor 700, APC, Fluorescein, PE, PerCP) M (Alexa Fluor 700, APC, PerCP) P (Unlabeled) | H (B/N, E, IHC, WB)<br>M (WB)<br>P (WB) | H M | H |
| CD36/SR-B3 | H M | H (APC, Fluorescein, PE)<br>M (APC) | H (WB)<br>M (E, IHC, WB) | M | H |
| CD37 | | H (APC, Fluorescein, PE) | | | |
| CL-P1/COLEC12 | H M | H (Unlabeled) M (Unlabeled) | H (B/N, ICC, WB) M (B/N, WB) | | |
| MARCO | H M | M (APC, Fluorescein, PE) | M (WB) | | |
| MD-1 | H M | H (Unlabeled) | H (IHC, WB) M (WB) | | H |
| MD-2 | H | | H (ICC, WB) | | |
| PRAT4A | H M | | M (WB) | | |
| PRAT4B | | R (Unlabeled) M (Unlabeled) | M (WB) R (WB) | | |
| Profilin-like Protein | | | Pz (WB) | | |
| RP105/CD180 | M | | | | |
| SR-AI/MSR | H M | H (Alexa Fluor 700, APC, PE)<br>M (APC, Fluorescein, PE) | H (B/N, WB)<br>M (B/N, WB) | | |
| SREC-I/SCARF1 | H | H (Biotin) | H (B/N, FC, WB) | | H |

*Most fluorochrome-conjugated antibodies for flow cytometry are also available in an unconjugated form. **We also offer small molecule inhibitors or receptor agonists for these molecules.

## Products for Select Cytokines Regulated by PRRs

| Molecules | Proteins | Antibodies | ELISAs/ELISpot-FluoroSpot Assays | Multiplex Array Kits | Activators/ Inhibitors |
|---|---|---|---|---|---|
| IFN | H | | | | |
| IFN-α (Multiple Isoforms) | H M R P CR F Pr | H (B/N, FC, IHC, IP, WB) M (B/N, FC, IHC)<br>P (B/N, IP, WB) CR (B/N, WB) | H M | | |
| IFN-β | H M R | H (B/N, FC, IHC, WB) M (B/N, FC, IHC)<br>R (B/N) | H M | | |
| IFN-γ | H M R P B Ca CR E F RM | H (B/N, E, FC, ICC, WB) M (B/N, E, FC, ICC, WB)<br>R (B/N, E, ICC, WB) P (B/N, FC, ICC, WB)<br>B (E, F, ICC, WB) Ca (B/N, E, ICC, WB)<br>CR (B/N, E, WB) E (B/N, E, ICC, WB)<br>F (B/N WB) RM (B/N, E, WB) | H M R B Ca CR E F P Pr | H M R | ✓ |
| IL-1β/IL-1F2 | H M R P Ca CR E F Rb RM | H (B/N, E, FC, ICC, IHC, WB) M (B/N, E, FC, ICC, IHC, IP, WB) R (B/N, E, ICC, WB) P (B/N, E, WB)<br>Ca (B/N, FC, WB) CR (B/N, WB) E (B/N, ICC, WB) F (B/N, E, ICC, WB) | H M R P F<br>H P | H M R | |
| IL-6 | H M R P Ca CR E F | H (B/N, E, FC, ICC, WB) M (B/N, E, FC, ICC, WB)<br>R (B/N, E, ICC, WB) P (B/N, E, FC, ICC, WB)<br>Ca (B/N, E, FC, ICC, WB) CR (B/N, WB)<br>E (B/N, ICC, WB) F (B/N, ICC, WB) | H M R P Ca CR F<br>H M R Ca F | H M R | |
| IL-8/CXCL8 | H P Ca F | H (B/N, E, FC, ICC, IHC, WB)<br>P (B/N, E, WB) Ca (B/N, E, ICC, WB)<br>F (B/N, E, ICC, WB) | H P Ca F<br>H Ca | H | |

| Molecules | Proteins | Antibodies | ELISAs/ELISpot-FluoroSpot Assays | Multiplex Array Kits | Activators/ Inhibitors |
|---|---|---|---|---|---|
| IL-18 | H M R P F RM | H (B/N, E, IP, WB) M (B/N, E, IP, WB)<br>R (B/N, WB) P (ICC, WB) Ca (ICC, WB)<br>F (B/N, WB) RM (B/N, ICC, WB) | H M | R | |
| IL-28A | H M | H (B/N, E, ICC, WB) M (B/N, WB) | H | H | |
| IL-28A/B | | M (B/N, E) | M | | |
| IL-28B | H M | H (WB) M (B/N, WB) | H M | | |
| IL-29 | H | H (B/N, E, WB) | H | | |
| IL-29/IL-28B | | H (B/N, E, WB) | H | | |
| TNF-α | H M R P B Ca CR E F GP Rb RM | H (B/N, E, FC, ICC, WB) M (B/N, E, FC, ICC, WB)<br>R (B/N, E, ICC, WB) P (B/N, E, ICC, WB) B (E, ICC, WB) Ca (B/N, E, ICC, WB) CR (B/N, WB) E (B/N, E, ICC, WB) GP (E) Rb (B/N, WB) RM (B/N, E, WB) | H M R P B Ca CR E F GP Pr Rb RM<br>H M P Ca E Pr | H M R | ✓ |

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**For research use only. Not for use in diagnostic procedures.**

## Products for Intracellular Signaling Molecules/Adaptor Proteins Required for PRR Signaling

| Molecules | Proteins | Antibodies | ELISAs/ Activity Assays | Multiplex Array Kits | Activators/ Inhibitors |
|---|---|---|---|---|---|
| ASC | | H (WB) | | | |
| Bcl-10 | | H (WB) M (WB) R (WB) | | | |
| BLNK | | H (IHC, WB) | | | |
| BTK | | H (ICC, WB) | | | ✓ |
| Phospho-BTK (Y223) | | H (ICC, WB) | | | |
| Phospho-BTK (Y551) | | H (WB) | | | |
| CARD9 | | H (WB) | | | |
| Caspase-1 | | H (ICC, WB) | H/Ms | | |
| IκB-α | | H (WB) M (WB) | H | | ✓ |
| Phospho-IκB-α (S32/S36) | | H (WB) | H M R | | |
| IκB-β | | H (WB) M (WB) R (WB) | | | |
| IκB-ε | | H (IHC, WB) M (WB) | | | |
| IKK-α | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| IKK-β | | H (WB) M (WB) | | | ✓ |
| IKK-γ | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| IKK-ε | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| IRAK1 | | H (WB) | | | |
| IRAK2 | | H (WB) | | | |
| IRAK3 | | H (WB) | | | |
| IRAK4 | | H (ICC, WB) | | | |
| JNK | | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M R | | ✓ |
| Phospho-JNK (T183/Y185) | | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M R | H | |
| JNK1 | M | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| Phospho-JNK1 (T183/Y185) | | | | H | |
| JNK1/2 | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| JNK2 | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | H M R | H | ✓ |
| Phospho-JNK2 (T183/Y185) | | | H M R | H | |
| MALT1 | | H (WB) | | | |
| MKK3 | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |
| Phospho-MKK3 (S218/T222) | | | H | H | |
| MKK3/MKK6 | | H (WB) M (WB) R (WB) | | | ✓ |
| Phospho-MKK3 (S218/T222)/ MKK6 (S207/T211) | | H (WB) | | | |
| MKK4 | | H (ICC) | | | ✓ |
| Phospho-MKK4 (S257/T261) | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | |
| MKK6 | | H (ICC, WB) M (ICC, WB) R (ICC, WB) | | | ✓ |

| Molecules | Proteins | Antibodies | ELISAs/ Activity Assays | Multiplex Array Kits | Activators/ Inhibitors |
|---|---|---|---|---|---|
| Phospho-MKK6 (S207/T211) | | | H | H | |
| MKK7 | | H (IHC, WB) | | | ✓ |
| MyD88 | | H (FC, ICC, WB) M (FC, ICC, WB) R (FC, ICC, WB) | H | | |
| Phospho-p38 (T180/Y182) | | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M | | |
| p38α | H | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M R | | ✓ |
| Phospho-p38α (T180/Y182) | | H (WB) | H M R | H | |
| p38β | | H (ICC, WB) M ( WB) R (WB) | | | ✓ |
| Phospho-p38β (T180/Y182) | | | | H | |
| p38γ | | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M R | | ✓ |
| Phospho-p38γ (T183/Y185) | | | H M | H | |
| p38δ | | H (IHC, WB) | | | ✓ |
| Phospho-p38δ (T180/Y182) | | | H | H | |
| PKCδ | H | H (WB) | | | ✓ |
| PLC-γ2 | | H (ICC, WB) M (ICC, WB) | | | ✓ |
| Phospho-PLC-γ2 (Y753) | | H (WB) | | | |
| Phospho-PLC-γ2 (Y759) | | H (ICC, WB) | | | |
| Raf-1 | H | H (IHC, WB) M (IHC, WB) R (IHC, WB) | | | ✓ |
| Phospho-Raf-1 (S301) | | H (WB) M (WB) R (WB) X (WB) | | | |
| Phospho-Raf-1 (S642) | | H (WB) M (WB) R (WB) | | | |
| RIP1 | | H (WB) M (WB) R (WB) | | | ✓ |
| SHP-1 | H | H (IHC, WB) M (IHC, WB) R (IHC, WB) | H M R | | ✓ |
| SHP-2 | H | H (WB) M (WB) R (WB) | H M R | | ✓ |
| Phospho-SHP-2 (Y542) | | H (ICC, WB) M (ICC, WB) | H M R | | |
| Src | H V | H (IHC, WB) M (IHC, WB) R (IHC, WB) | | | ✓ |
| Phospho-Src (Y419) | | H (IHC, WB) | H | H | |
| SYK | H | H (WB) | | | ✓ |
| Phospho-SYK (Y525/Y526) | | H (WB) | | | |
| TAB1 | | H (ICC, WB) M (ICC, WB) | | | |
| TAK1 | | H (WB) | | | ✓ |
| TANK | | H (WB) M (WB) | | | |
| TRAF-3 | | H (WB) M (WB) R (WB) | | | |
| TRAF-6 | | H (WB) | | | |
| TRAM/TICAM2 | | H (FC, ICC, WB) M (FC, ICC, WB) R (FC, ICC, WB) | | | |
| TRIF/TICAM1 | | H (ICC, WB) | | | |

| Transcription Factors | Antibodies | ELISAs/Transcription Factor Binding & IP Assays | Activators/ Inhibitors |
|---|---|---|---|
| c-Fos | H (WB) | | ✓ |
| FosB/G0S3 | H (IHC, WB) M (WB) | | ✓ |
| FRA-1 | H (IHC, WB) | | ✓ |
| IRF3 | H (FC, ICC, WB) M (WB) | | |
| c-Jun | H (ICC, WB) M (ICC, WB) | | ✓ |
| Phospho-c-Jun (S63) | | H M R | |
| JunB | H (WB) | | ✓ |
| JunD | H (WB) M (WB) | | ✓ |
| NFATC1 | H (WB) | | ✓ |
| Phospho-NFATC1 (S172) | H (WB) | | |

| Transcription Factors | Antibodies | ELISAs/Transcription Factor Binding & IP Assays | Activators/ Inhibitors |
|---|---|---|---|
| NFATC2 | H (WB) | | ✓ |
| NFATC3 | H (WB) M (WB) R (WB) | | ✓ |
| NFκB1*** | H (ChIP, WB) M (ChIP, WB) | H | ✓ |
| NFκB2 | H (ChIP, ICC, WB) | H | ✓ |
| c-Rel | H (ChIP, ICC, WB) M (ChIP, ICC, WB) | H | ✓ |
| RelA/NFκB p65 | H (ChIP, FC, ICC, WB) M (ChIP, FC, ICC, WB) | H | ✓ |
| Phospho-RelA/NFκB p65 (S529) | H (WB) | | |
| Phospho-RelA/NFκB p65 (S536) | H (WB) | H M R | |
| RelB | H (ICC, IHC, WB) | | ✓ |

***Also available in Human Multiplex Array kit.

SPECIES KEY:
H Human, M Mouse, R Rat, B Bovine, Ca Canine, CR Cotton Rat, E Equine, F Feline, GP Guinea Pig, Ms Multi-species P Porcine, Pr Primate, Pz Protozoa, Rb Rabbit, RM Rhesus Macaque, V Viral X *Xenopus*

APPLICATION KEY:
**B/N** Blocking/Neutralization, **ChIP** Chromatin Immunoprecipitation, **E** ELISA, **FC** Flow Cytometry, **ICC** Immunocytochemistry, **IHC** Immunohistochemistry, **IP** Immunoprecipitation, **WB** Western blot

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# Recent Publications Citing R&D Systems Products for Pattern Recognition Receptor Research

1. Andersson, M. *et al.* (2012) *Mycobacterium bovis* bacilli Calmette-Guerin regulates leukocyte recruitment by modulating alveolar inflammatory responses. Innate Immun. **18**:531.

   **Mouse Anti-Human TLR2 Monoclonal Antibody** (Catlaog # MAB2616)

   **Mouse Anti-Human TLR4 Monoclonal Antibody** (Catalog # MAB1478)

   **Sample**: Human umbilical vein endothelial cells and A549 human alveolar epithelial cell lysates
   **Application**: Flow cytometry, Immunocytochemistry, Neutralization, and Western blot

   **Human CCL2/MCP-1 Quantikine ELISA Kit** (Catalog # DCP00)

   **Human CXCL8/IL-8 Quantikine ELISA Kit** (Catalog # D8000C)

   **Human IL-6 Quantikine ELISA Kit** (Catalog # D6050)

   **Human TNF-α Quantikine ELISA Kit** (Catalog # DTA00C)

   **Sample**: *Mycobacterium bovis*-infected A549 human alveolar epithelial cell culture supernates
   **Application**: ELISA

2. Emara, M. *et al.* (2012) Retagging identifies dendritic cell-specific intercellular adhesion molecule-3 (ICAM3)-grabbing non-integrin (DC-SIGN) protein as a novel receptor for a major allergen from house dust mite. J. Biol. Chem. **287**:5756.

   **Recombinant Human DC-SIGN/CD209 Fc Chimera** (Catalog # 161-DC)

   **Sample**: House dust mite Der p1 allergen
   **Application**: ELISA-based binding assay

   **Recombinant Human IL-2** (Catalog # 202-IL)

   **Sample**: Human T cells
   **Application**: Bioassay – proliferation

   **Recombinant Human GM-CSF** (Catalog # 215-GM)

   **Sample**: Peripheral blood mononuclear cells
   **Application**: Bioassay – Dendritic cell generation

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   **Mouse Anti-Human DC-SIGN/CD209 Monoclonal Antibody** (Catalog # MAB161)

   **Sample**: Recombinant Human DC-SIGN
   **Application**: ELISA Development

3. Gringhuis, S.I. *et al.* (2012) Dectin-1 is an extracellular pathogen sensor for the induction and processing of IL-1β via a noncanonical caspase-8 inflammasome. Nat. Immunol. **13**:246.

   **Mouse Anti-Human Dectin-1/CLEC7A Monoclonal Antibody** (Catalog # MAB1859)

   **Sample**: Human Dendritic Cells
   **Application**: Neutralization

4. Elsori, D.H. *et al.* (2011) Protein kinase Cδ is a critical component of Dectin-1 signaling in primary human monocytes. J. Leukoc. Biol. **90**:599.

   **Mouse Anti-Human Dectin-1/CLEC7A Monoclonal Antibody** (Catalog # MAB1859)

   **Sample**: Monocyte cell lysates
   **Application**: Immunoprecipitation

   **Goat Anti-Human Dectin-1/CLEC7A Antigen Affinity-purified Polyclonal Antibody** (Catalog # AF1859)

   **Sample**: Zymosan-treated human monocytes
   **Application**: Western blot

5. Sakaguchi, M. *et al.* (2011) TIRAP, an adaptor protein for TLR2/4, transduces a signal from RAGE phosphorylated upon ligand binding. PLoS One **6**:e23132.

   **Recombinant Human TLR2** (Catalog # 2616-TR)

   **Recombinant Human TLR4/MD-2 Complex** (Catalog # 3146-TM)

   **Recombinant Human LBP** (Catalog # 870-LP)

   **Recombinant Human HMGB1** (Catalog # 1690-HM)

   **Sample**: HEK293 human embryonic kidney cell line
   **Application**: Bioassay - stimulation

6. Uciechowski, P. *et al.* (2011) Susceptibility to tuberculosis is associated with TLR1 polymorphisms resulting in a lack of TLR1 cell surface expression. J. Leukoc. Biol. **90**:377.

   **Recombinant Human TLR1 Fc Chimera** (Catalog # 1484-TR)

   **Application**: Western blot control

   **Biotinylated Goat Anti-Human TLR1 Antigen Affinity-purified Polyclonal Antibody** (Catalog # BAF1484)

   **Sample**: Polymorphonuclear neutrophil cell lysates
   **Application**: Western blot

7. Ma, C.J. *et al.* (2011) PD-1 negatively regulates IL-12 expression by limiting STAT1 phosphorylation in monocytes/macrophages during chronic hepatitis C virus infection. Immunology **132**:421.

   **PE-conjugated Mouse Anti-Human TLR7 Monoclonal Antibody** (Catalog # IC5875P)

   **Sample**: Human peripheral blood mononuclear cells
   **Application**: Flow cytometry

8. Wang, J. *et al.* (2011) Morphine inhibits murine dendritic cell IL-23 production by modulating TLR2 and Nod2 signaling. J. Biol. Chem. **286**:10225.

   **Fluorescein-conjugated Rat Anti-Mouse TLR2 Monoclonal Antibody** (Catalog # FAB1530F)

   **PE-conjugated Rat Anti-Mouse TLR4 Monoclonal Antibody** (Catalog # FAB2759P)

   **Sample**: *Streptococcus pneumoniae*-infected bone marrow-derived dendritic cells
   **Application**: Flow Cytometry

   **Mouse IL-23 Quantikine ELISA Kit** (Catalog # M2300)

   **Sample**: *Streptococcus pneumoniae*-infected bone marrow-derived dendritic cell culture supernates
   **Application**: ELISA