

## TLR2- cluster of differentiation 282

Toll-like receptor 2 (TLR2), often designated as CD282 (cluster of differentiation 282) is a type I transmembrane protein belonging to the large homologous family of Toll like receptors. TLR2 acts as functional receptor for both Gram-positive and Gram-negative bacteria. Like all other members of the TLR family, TLR2 is composed of an extracellular domain containing multiple leucine-rich repeats (LRRs), a transmembrane region, and a cytoplasmic tail containing the conserved TIR domain. TLR2 maps to chromosome 4q31-32 and encodes a putative 784 amino acid protein with 19 N-terminal LRRs and a calculated molecular weight of 84 kDa (1, 2, 3). Comparison of the amino acid sequence reveals that TLR2, TLR1, and TLR6 form a TLR subfamily, which presumably diverged from one common ancestral gene. In humans, TLR10 is also a member of this TLR2 subfamily. Among all TLR, TLR1 and TLR6 have the highest identity of overall amino acid sequence, which is 66%, and a similar genomic structure and thus it is assumed that they are the evolutionary products of gene duplication. &nbsp; In vivo transcripts for TLR2 are observed suggesting that the mRNA is alternatively spliced. TLR2 mRNA expression is observed in brain, heart, lung, and spleen tissues and is highest in PBLs, specifically those of myelomonocytic origin. In vitro PMA-differentiated THP-1, TLR2 is most significantly upregulated by autocrine IL-6 and TNF- $\alpha$ , IL-1 $\beta$ , and IL-10. Further, TLR2 mRNA expression is elevated after exposure to both Gram-positive and Gram-negative bacteria. The increase in TLR2 expression in monocytes and granulocytes on exposure to Gram-negative bacteria is only very modest. Furthermore, TLR2 appears to be up-regulated on mononuclear cells during disorders such as chronic obstructive pulmonary disease, influenza virus infections, and sepsis &nbsp; TLR2 act as signal transducers for various bacterial components which include lipoproteins derived from *M. tuberculosis*, *Borrelia burgdorferi*, *Treponema pallidum* and *Mycoplasma fermentans*. In addition, TLR2 mediates cellular responses to a wide variety of infectious pathogens and their products which include yeast cell walls, whole mycobacteria, mycobacterial ara-lipoarabinomannan, whole Gram-positive bacteria, peptidoglycan (PGN), *Treponema* glycolipid and *Trypanosoma cruzi* glycosphatidylinositol anchor. TLR2 forms heterodimers with TLR1, TLR6 and possibly TLR10, where each complex is particularly sensitive to subsets of TLR2-associated pathogen-associated molecular patterns (PAMPs).&nbsp; It has been studied that TLR6 and TLR2 function together to detect Gram-positive bacteria, PGN and zymosan, whereas TLR2 functions either alone or with TLRs other than TLR6 to detect bacterial lipopeptides. More recent studies have suggested that, like TLR4, TLR2 complexes require CD14 and MD-2 for detection of PAMPs and signaling. (4, 5)&nbsp; Upon ligand recognition, TLR2 recruits both the TIR domain-containing sorting adaptor TIRAP and the signaling adaptor MyD88, and initiates the MyD88-dependent pathway. The MyD88-dependent pathway activates nuclear factor (NF)- $\kappa$ B, activator protein-1 (AP-1) and interferon regulatory factor 5 (IRF5), which induce inflammatory cytokine expression such as IL-6, IL-12, and TNF $\alpha$ . (6) &nbsp; Aside from detection of non-self patterns, TLR2 complexes are also capable of detecting altered self patterns, such as those displayed by necrotic cells. Further, recent evidence indicates that TLR2 is recruited to phagosomes and may be directly involved in the internalization of microbial products by cells. &nbsp; Reference: 1. Rock, F.L. et al. (1998) Proc. Natl. Acad. Sci. USA 95:588. 2. Chaudhary, P.M. et al. (1998) Blood 91:4020. 3. Dunne, A. & L.A.J. O'Neill (2003) Sci. STKE 2003:re3. 4. Modlin, R.L. (2002) Ann. Allergy Asthma Immunol. 88:543. 5. J Endotoxin Res. 2000;6(5):401-5 6. Annual Review of Biochemistry Vol. 76: 447-480 (Publication date July 2007)

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