

Metalloproteinase-dependent TLR2 ectodomain shedding is involved in soluble toll-like receptor 2 (sTLR2) production

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© 2014 Langjahr et al. Toll-like receptor (TLR) 2, a type I membrane receptor that plays a key role in innate immunity, recognizes conserved molecules in pathogens, and triggering an inflammatory response. It has been associated with inflammatory and autoimmune diseases. Soluble TLR2 (sTLR2) variants have been identified in human body fluids, and the TLR2 ectodomain can negatively regulate TLR2 activation by behaving as a decoy receptor. sTLR2 generation does not involve alternative splicing mechanisms, indicating that this process might involve a post-translational modification of the full-length receptor; however, the specific mechanism has not been studied. Using CD14⁺ peripheral human monocytes and the THP-1 monocytic leukemia-derived cell line, we confirm that sTLR2 generation increases upon treatment with pro-inflammatory agents and requires a post-translational mechanism. We also find that the constitutive and ligand-induced release of sTLR2 is sensitive to pharmacological metall