

Toll-like Receptor Modulators

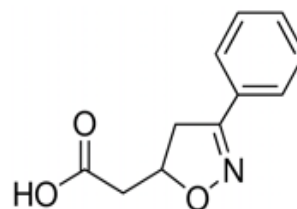
Toll-like receptors (TLRs) are pattern recognition receptors expressed in immune cells such as macrophages and dendritic cells; they play a significant role in the development of the innate immune response.

These receptors recognize structurally conserved molecules shared by classes of pathogens. These structures are pathogen-associated molecular patterns. Although associated with pathogens, some structures can also be found endogenously. There are 11 isoforms of TLRs, and each one recognizes distinct ligands, including single-stranded RNA, double-stranded RNA, CpG DNA, lipopolysaccharides, and bacterial peptidoglycans¹.

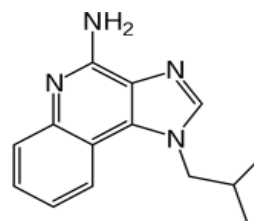
TLRs are heavily involved in propagation of signals for inflammation, phagocytosis, antigen presentation, and other immune responses, making them good targets for compounds that regulate allergic reactions, inflammation, and autoimmune diseases.

References:

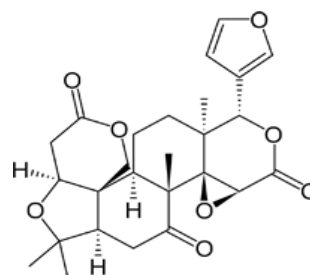
1. Roach JC, Glusman G, Rowen L, et al. Proc Natl Acad Sci U S A. 2005 Jul 5;102(27):9577-82.
2. Fagone P, Muthumani K, Mangano K, et al. Immunology. 2014 Aug;142(4):594-602.
3. Nazmi A, Mukherjee S, Kundu K, et al. 2014 Sep;69:235-47.
4. Mahmoud MF, Gamal S, El-Fayoumi HM. 2014 Oct 5;740:676-82.



VGX-1027 (V2792) is an inhibitor of TLR4, a receptor that recognizes many endogenous structures. This compound inhibits antigen presentation in models of systemic lupus erythematosus².



Imiquimod (I5034) is an agonist at TLR7 and TLR8 receptors. It recognizes viral RNA sequences, stimulating a Th1-based immune response against Japanese encephalitis virus³.



Limonin (L3550) is a product that can be isolated from citrus fruits that downregulates expression of TLR2 and TLR, suppressing proinflammatory cytokine release⁴.

