Toll-Like Receptor Function Testing

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Toll-like receptors (TLRs) enable innate immunity to prevent infection. Immunodeficiencies associated with impaired innate immunity (nuclear factor kappa B signaling) include disruptions to signaling pathways for interleukin-1 (IL-1) receptor-associated kinase 4 (IRAK4) and myeloid differentiation primary response protein 88 (MYD88) and may be associated with recurrent pyogenic bacterial infections. IRAK4 deficiency and MYD88 deficiency are rare so they should not be considered unless more common immunodeficiencies are ruled out. After screening for more common immunodeficiencies (eg, by assessing immunoglobulin levels, complement testing, cell-mediated immunity testing, and neutrophil function testing), consider TLR functional testing to determine TLR function and identify a possible molecular defect in the innate immune system that is related to TLR function.

Featured ARUP Testing

Toll-Like Receptor Function 0051589

Method: Cell Culture/Quantitative Multiplex Bead Assay

- Use to assist in diagnosis of innate immunodeficiencies when genetic defects of the innate immune system are suspected in individuals negative for other immunodeficiencies (eg, no detectable abnormality of antibody function, complement activity, neutrophil function, or cell-mediated immunity)
- This test does not measure the function of toll-like receptor 3 (TLR3); molecular testing is the preferred method for detection of defects in TLR3.

Test Information

TLRs are tested independently by stimulation with TLR-specific ligands in a peripheral blood mononuclear cell (PBMC) culture. Mononuclear cells isolated from anticoagulated whole blood are incubated with the TLR ligands described in the table below.

TLR Target	Ligand
TLR2-TLR1	Pam3CSK4 synthetic bacterial lipopeptide
TLR6-TLR2	Zymosan cell wall particles from *Saccharomyces cerevisiae*
TLR4	Lipopolysaccharide (LPS), ultrapure, from *Salmonella minnesota* variant R595
TLR5	Flagellin from *Salmonella typhimurium*
TLR7-TLR8	CL097 derivative of imidazoquinoline compound R848

PBMC production of tumor necrosis factor alpha (TNFα), interleukin 1 beta (IL-1β), and interleukin 6 (IL-6) are measured by multiplex bead assay for TLR1, 2, and 4-8.

Test Interpretation

Results

Interpretation that compares an individual's results to a client's normal control, as well as the laboratory control, will be provided.

Result	Finding	Clinical Significance
Decreased	Lack of or marginal response to specific TLR ligands	Suggests a possible molecular defect in the innate immune system related to TLR function or other components of the signaling pathway, such as IRAK4 or MYD88
Normal	Normal cytokine responses	Suggests normal TLR function

Limitations

- Results should be interpreted in conjunction with the individual’s clinical status
- Defects in IRAK4 and MYD88 result in compromised TLR signaling.
    - Exception is endosomal TLR4, which is IRAK4 and MYD88 independent

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