

Toll-Like Receptor (TLR) Function Assay

FOR EVALUATION OF PATIENTS WITH RECURRENT INFECTION WHO MAY HAVE GENETIC DEFECTS RELATED TO TLR FUNCTION

Test Highlights

- This assay can be used to evaluate a patient with recurrent infections who is suspected of having genetic defects of the innate immune system.
- Mononuclear cells are isolated from anticoagulated whole blood and incubated with toll-like receptor (TLR) ligands for TLR 1, 2, 3, 4, 5, 6, 7, and 8 as well as media alone, followed by measurement of TNF α , IL-1 β , and IL-6
- A lack of response to specific TLR ligands may suggest a possible molecular defect in the innate immune system related to TLR function or other components of the signaling pathway such as IRAK or MyD88.

Clinical Background

- Patients who may have an immunodeficiency resulting from a genetic impairment related to TLR signaling may be detected.
- Patients usually have normal serum antibody titers against protein and polysaccharide antigens, normal immunoglobulins, complement concentrations, neutrophil function, and normal T and B cells.

Disease Overview

Recently, several syndromes have been identified that are related to human susceptibility to recurrent infections associated with abnormalities of TLR function. Since many other tests of the innate and adaptive immune systems show normal results, the TLR assay presents a diagnostic tool to ascertain TLR function, thus indicating a possible molecular defect in the innate immune system that is related to TLR function.

Genetics

- Genetic abnormalities associated with increased susceptibility to infection that also impair—or would be expected to impair—TLR function may be detected.
- Some of the abnormalities include mutations of the genes encoding TLR2, TLR4, the NF- κ B essential modulator (NEMO), IRAK4, MyD88, and an NF- κ B inhibitor, I κ B α .

Indication for Ordering

Patients with recurrent infections with no detectable abnormality of antibody function, complement activity, neutrophil function, or cell-mediated immunity who are suspected of having genetic defects of the innate immune system.

Interpretation

- Cytokine production by patient cells incubated with TLR ligands will be compared to cells incubated with media alone, as well as

cytokine production by control cells, for each monokine tested. The medical director determines whether there is an abnormal response to each of the ligands, indicating a possible molecular defect in the innate immune system related to TLR function.

- An interpretation by the medical director, based on comparison with the simultaneously run client and in-house laboratory controls, will be included with the report, indicating any abnormality in TLR function.

Limitations

The clinician should take into consideration the clinical status of the patient when ordering and analyzing the results of this assay.

Methodology

Mononuclear cells are isolated from anticoagulated whole blood and stimulated with TLR ligands, followed by measurement of monokine production in supernatant by Luminex multi-analyte technology.

Related Test

Interleukin-1-Receptor-Associated Kinase-4 (IRAK-4) Deficiency Screen ([0051393](#))

References

1. Deering RP, Orange JS. Development of a clinical assay to evaluate toll-like-receptor function. *Clin Vaccine Immunol*. 2006;13:68–76.
2. Moresco EMY, et al. Toll-like receptors. *Current Biol*. 2011;21(13):R488–R493.
3. Picard C. et al. Clinical features and outcome of patients with IRAK-4 and MyD88 deficiency. *Medicine*. 2010;89(6):403–25.
4. Zhang SY et al. TLR3 deficiency in patients with herpes simplex encephalitis. *Science*. 2007;317(5844):1522–7.

Test Information

0051589

Toll-Like Receptor Function Assay

For specific collection, transport, and testing information, refer to the ARUP website at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.

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