

Overview

Useful For

Understanding the etiology of infectious or chronic inflammatory diseases, when used in conjunction with clinical information and other laboratory testing

Research studies in which an assessment of cytokine responses is needed

Method Name

Bead-Based Multiplex Immunoassay

NY State Available

Yes

Specimen

Specimen Type

Plasma EDTA

Specimen Required

- Supplies:** Sarstedt Aliquot Tube, 5 mL (T914)
- Collection Container/Tube:** Lavender-top (EDTA)
- Submission Container/Tube:** Plastic vial
- Specimen Volume:** 0.5 mL

Collection Instructions:

1. Immediately after specimen collection, place the tube on wet ice.
2. Centrifuge at 4 degrees C, 1500 x *g* for 10 minutes.
3. Aliquot plasma into plastic vial.
4. Freeze specimen within 2 hours of collection.

Specimen Minimum Volume

0.3 mL

Reject Due To

Gross hemolysis	Reject
Gross lipemia	Reject
Gross icterus	Reject
Heat-treated specimen	Reject

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen	21 days	

Clinical & Interpretive

Clinical Information

Cytokines are important mediators of cell-to-cell communication within the innate and adaptive immune systems. The expression of most cytokines is highly regulated and generally occurs in response to foreign or self-antigenic stimulation. The functions of cytokines are extremely varied, with many cytokines also displaying pleiotropic effects, depending on their cellular target. Some cytokines, such as tumor necrosis factor (TNF), interleukin (IL)-1 beta, IL-6, interferon (IFN)-alpha and beta, IL-10, and IL-18 are particularly important in the innate immune response. For example, TNF, IL-1 beta, and IL-6 induce expression of acute phase proteins in the liver. TNF and IL-1 beta also lead to endothelial activation and are critical regulators of the hypothalamus, which can result in elevated body temperature. IL-6, in comparison, is a bridge to the adaptive immune response, by acting on B cells to induce proliferation. In contrast, IFN-alpha and IFN-beta (members of the type I IFN family) are key components of the innate immune response to viral infections. IFN-gamma, which is a type II IFN, has roles in both the innate and adaptive immune responses, including macrophage activation, induction of B-cell isotype switching, and T helper type 1 cell differentiation. Other cytokines, such as monocyte chemoattractant protein-1 and macrophage inflammatory protein-1 alpha, are categorized as chemokines because they function primarily to attract leukocytes to the site of inflammation. Further, some cytokines act on hematopoietic stem cells to induce differentiation of various leukocytes. For example, granulocyte-monocyte colony stimulating factor induces myeloid progenitor cells to differentiate into neutrophils and monocytes. Lastly, for some cytokines, soluble forms of the receptor can be found in the peripheral circulation. The IL-2 soluble receptor is produced from proteolytic cleavage of the membrane-bound receptor, which occurs during T-cell activation. As a group, cytokines and their receptors represent a highly complex and critical regulator of a normal immune response.

Reference Values

- Tumor necrosis factor: <10.0 pg/mL
- Interleukin (IL)-6: <5.0 pg/mL
- Interferon (IFN)-beta: <20.0 pg/mL
- IL-10: <7.0 pg/mL
- Monocyte chemoattractant protein-1: < or =198 pg/mL
- IL-1 beta: <20.0 pg/mL
- IFN-gamma: <60.0 pg/mL
- Macrophage inflammatory protein-1 alpha: <220 pg/mL
- Granulocyte-monocyte colony stimulating factor: <15.0 pg/mL
- IL-2 receptor alpha soluble: < or =959 pg/mL
- IFN-alpha: <20.0 pg/mL
- IL-18: < or =468 pg/mL

Interpretation

Elevated cytokine concentrations could be consistent with the presence of infection or other inflammatory process.

Cautions

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Results from cytokine testing should not be used to establish or exclude a specific diagnosis.

Cytokine testing should only be used in conjunction with clinical information and other laboratory testing as part of a patient's overall assessment.

Normal concentrations of cytokines do not exclude the possibility of infection or other inflammatory condition.

Cytokine concentrations could be affected by immunomodulatory agents.

Interleukin-6 (IL-6) concentrations may be elevated in patients receiving IL-6 receptor inhibitors, such as tocilizumab, due to receptor blockade and reduced clearance of IL-6. As a result, IL-6 concentrations are not reflective of adequate tocilizumab response. Additionally, patients receiving anti-IL-6 monoclonal antibodies such as siltuximab may also exhibit interference in IL-6 measurements. For both patient cohorts, a more reliable assessment of IL-6-mediated inflammation can be obtained by measuring downstream acute-phase reactants, such as C-reactive protein.

### Clinical Reference

1. Bozza FA, Salluh JJ, Japiassu AM, et al. Cytokine profiles as markers of disease severity in sepsis: a multiplex analysis. *Crit Care*. 2007;11(2):R49. doi:10.1186/cc5783
2. Milman N, Karsh J, Booth RA. Correlation of a multi-cytokine panel with clinical disease activity in patients with rheumatoid arthritis. *Clin Biochem*. 2010;43(16-17):1309-1314. doi:10.1016/j.clinbiochem.2010.07.012
3. Teijara JR. Type I interferons in viral control and immune regulation. *Curr Opin Virol*. 2016;16:31-40. doi:10.1016/j.coviro.2016.01.001
4. Tisoncki JR, Korth MJ, Simmons CP, Farrar J, Martin TR, Katze MG. Into the eye of the cytokine storm. *Microbiol Mol Biol Rev*. 2010;76(1):16-32. doi:10.1128/MMBR.05015-11
5. Garcia Borrega J, Godel P, Ruger MA, et al. In the eye of the storm: Immune-mediated toxicities associated with CAR-T cell therapy. *Hemasphere*. 2019;3(2):e191. doi:10.1097/HS9.0000000000000191

## Performance

### Method Description

Analyte-specific antibodies are pre-coated onto color-coded magnetic microparticles. Samples are diluted 1:2 in a mixing plate and then standards, samples, and microparticles are pipetted into wells and the immobilized antibodies capture the analytes of interest. Unbound substances are washed away while the magnetic microparticles are immobilized. Next, a biotinylated analyte specific antibody cocktail is added to each well. Following a wash to remove any unbound biotinylated antibody, streptavidin-phycoerythrin conjugate (Streptavidin-PE), is added to each well. After removal of unbound Streptavidin-PE and resuspension of the microparticles in buffer, the plate is analyzed using a Luminex FLEXMAP 3D analyzer. A charged-coupled device camera captures an image of each well and data reduction is performed using the XPONENT software.(Unpublished Mayo method)

### PDF Report

No

### Day(s) Performed

Wednesday

Report Available

2 to 8 days

Specimen Retention Time

14 days

Performing Laboratory Location

Mayo Clinic Laboratories - Rochester Superior Drive

Fees & Codes

- Fees
- Authorized users can sign in to [Test Prices](#) for detailed fee information.
  - Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
  - Prospective clients should contact their account representative. For assistance, contact [Customer Service](#).

Test Classification

This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. It has not been cleared or approved by the US Food and Drug Administration.

CPT Code Information

83520 x 10

83529

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
CYPAN	Cytokine Panel, P	82335-1

Result ID	Test Result Name	Result LOINC® Value
610307	TNF	3074-2
610308	IL-6	26881-3
610309	IFN-beta	97051-7
610310	IL-10	26848-2
610311	MCP-1	97052-5
610312	IL-1 beta	13629-1
610313	IFN-gamma	27415-9
610314	MIP-1 alpha	97053-3
610315	GM-CSF	97054-1
610316	IL-2 receptor alpha soluble	76039-7
610317	IFN-alpha	33820-2
610318	IL-18	33823-6