

# **Test Definition: TNFA**

Tumor Necrosis Factor, Plasma

### Overview

#### **Useful For**

Evaluation of patients with suspected systemic infection, in particular infection caused by gram-negative bacteria

Evaluation of patients with suspected chronic inflammatory disorders, such as rheumatoid arthritis, inflammatory bowel disease, ankylosing spondylitis, or cancers.

Method Name Electrochemiluminescence

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



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## **Specimen Stability Information**

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen (preferred)	21 days	
	Refrigerated	24 hours	

# **Clinical & Interpretive**

# **Clinical Information**

Tumor necrosis factor-alpha (TNF-alpha) is a highly pleiotropic cytokine involved in a spectrum of physiological processes that control inflammation, anti-tumor responses, and homeostasis.(1-3) The main sources of TNF-alpha are macrophages and T cells; however, many other cell types such as B cells, neutrophils, and endothelial cells have been described to produce TNF-alpha. It is expressed as a type II transmembrane protein (mbTNF-alpha) but can be cleaved to its soluble form (sTNF-alpha) with increased biological activity. Targets for TNF-alpha include 2 type I transmembrane receptors, TNF receptor I (TNFR-I or CD120a) and TNF receptor II (TNFR-II or CD120b).(2, 3) TFNR-I is expressed on every cell type except erythrocytes while TNFR-II is found only on endothelial and immune cells and can be activated by mbTNF-alpha.(1-3)

Following infection, TNF-alpha produced by macrophages enhances the proliferation of T cells after stimulation with interleukin-2 (IL-2).(1) In the absence of IL-2, TNF-alpha induces the proliferation and differentiation of B cells. Due to its antitumor property, TNF-alpha can cause cell death via a number mechanisms and is also capable of chemotactic attraction of neutrophils. Additionally, it is capable of stimulating macrophages to produce acid phosphatase and collagenase, and osteoblasts to produce prostaglandin E2 and collagenase. These chemical mediators have been known to lead to bone resorption.(1-3)

Due to the significant proinflammatory and immunoregulatory functions of TNF-alpha, and the wide distribution of TNFRs, the deregulation of TNF-alpha is associated with the development of several immunologic disorders and prediction of disease outcomes.(1-7) Indeed, elevated levels of TNF-alpha in serum or plasma levels have been able to predict severity in some infectious diseases such as sepsis in bacterial infections or poor outcomes in coronavirus 2019 infections.(6) In addition, TNF-alpha has been implicated in post-transplant reactions, pathological mechanisms in certain autoimmune diseases (eg, rheumatoid arthritis, inflammatory bowel disease, ankylosing spondylitis), and cancers.(1-5,7) With the FDA approval of biologic and biosimilar therapies targeting TNF-alpha in patients with these diseases, it is likely that measurement of TNF-alpha levels may be useful in management of treatment response.(4-9)

### **Reference Values**

< or =2.8 pg/mL

### **Clinical Reference**

1. Varfolomeev E, Vucic D. Intracellular regulation of TNF activity in health and disease. Cytokine. 2018;101:26-32

2. Atretkhany KN, Gogoleva VS, Drutskaya MS, Nedospasov SA. Distinct modes of TNF signaling through its two receptors in health and disease. J Leukoc Biol. 2020;107(6):893-905

3. Salomon BL, Leclerc M, Tosello J, Ronin E, Piaggio E, Cohen JL. Tumor necrosis factor alpha and regulatory T cells in oncoimmunology. Front Immunol. 2018;9:444

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4. Ridgley LA, Anderson AE, Pratt AG. What are the dominant cytokines in early rheumatoid arthritis? Curr Opin Rheumatol. 2018;30(2):207-214

5. Friedrich M, Pohin M, Powrie F. Cytokine networks in the pathophysiology of inflammatory bowel disease. Immunity. 2019;50(4):992-1006

6. Wilson JG, Simpson LJ, Ferreira AM, et al. Cytokine profile in plasma of severe COVID-19 does not differ from ARDS and sepsis. JCI Insight. 2020;5(17):e140289

7. Li Y, Yuan L, Yang J, et al. Changes in serum cytokines may predict therapeutic efficacy of tofacitinib in rheumatoid arthritis. Mediators Inflamm. 2019;2019:5617431

8. Salomon BL. Insights into the biology and therapeutic implications of TNF and regulatory T cells. Nat Rev Rheumatol. 2021;17(8):487-504

9. Willrich MAV, Murray DL, Snyder MR. Tumor necrosis factor inhibitors: clinical utility in autoimmune diseases. Trans Res 2015;165(2):270-282

# Performance

### **Method Description**

MAYO CLINIC

LABORATORIES

The tumor necrosis factor (TNF)-alpha cytokine assay measures human cytokines in a 96-well spotted plate. The assay employs a sandwich immunoassay format where capture antibodies are coated on a single spot on the bottom of each well. Diluted samples, calibrators, and controls are added and to the plate. If present, TNF-alpha will bind to the capture antibodies. After incubation, a solution containing detection antibodies conjugated with electrochemiluminescent labels is added. After a final incubation, a buffer is added that creates the appropriate chemical environment for electrochemiluminescence. The plate is then read on the MSD QuickPlex SQ120. The machine applies a voltage that causes bound labels to emit measurable light. The MSD QuickPlex SQ120 measures the intensity of emitted light and correlates it to a set of standards of known quantity via a 4-point logistics curve fitting method.(Unpublished Mayo method)

PDF Report No

Day(s) Performed Thursday

Report Available 2 to 8 days

**Specimen Retention Time** 14 days

Performing Laboratory Location Rochester

### Fees & Codes



Tumor Necrosis Factor, Plasma

#### Fees

- Authorized users can sign in to <u>Test Prices</u> for detailed fee information.
- Clients without access to Test Prices can contact <u>Customer Service</u> 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

# LOINC<sup>®</sup> Information

Test ID	Test Order Name	Order LOINC <sup>®</sup> Value
TNFA	Tumor Necrosis Factor, P	3074-2

Result ID	Test Result Name	Result LOINC <sup>®</sup> Value
63022	TNF, P	3074-2