

## Overview

### Useful For

Measuring the concentration of soluble interleukin-2 receptor alpha (sIL-2r alpha) in plasma

Aids in the diagnosis and evaluation of patients for lymphoproliferative disorders, including autoimmune lymphoproliferative syndrome, hemophagocytic lymphohistiocytosis, and macrophage activation syndrome

May help monitor patients with sarcoidosis or hematologic malignancies with elevated sIL-2r alpha

### Highlights

This test aids the diagnosis and evaluation of lymphoproliferative disorders, including autoimmune lymphoproliferative syndrome, hemophagocytic lymphohistiocytosis, and macrophage activation syndrome.

### Method Name

Bead-Based Multiplex Immunoassay

### NY State Available

Yes

## Specimen

### Specimen Type

Plasma EDTA

### Ordering Guidance

If this test is ordered with CYPAN / Cytokine Panel, Plasma, this test will be canceled as duplicate and CYPAN performed as ordered.

If this test is ordered with CYTH1 / T-Helper Cell Type 1 Cytokine Panel, Plasma, this test will be canceled as duplicate and CYTH1 performed as ordered.

### 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 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.

**Additional Information:**

If a refrigerated centrifuge is not available, it is acceptable to use a room temperature centrifuge, provided the sample is kept on ice before centrifugation and is frozen immediately afterward.

**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**

The interleukin-2 (IL-2) receptor (CD25) is a membrane protein that is upregulated on activated T cells. Its soluble form, IL-2 receptor alpha soluble (sIL-2r alpha, soluble CD25) is notably elevated in lymphoproliferative disorders, such as hemophagocytic lymphohistiocytosis (HLH), autoimmune lymphoproliferative syndrome (ALPS), T-cell related leukemia-lymphoma and other conditions associated with T-cell activation.(1) Based on the HLH-2004 trial, the diagnosis of HLH syndrome should be based on compatible clinical presentation in the context of significantly elevated inflammatory markers, including ferritin, sIL-2r alpha, and CXCL9 (C-X-C motif chemokine ligand 9). sIL-2r alpha elevation at a significant level (2SD above age-adjusted laboratory-specific reference range) is a crucial diagnostic criterion.(2)

In addition to activated T cells, IL-2 receptor is also expressed on a certain subset of B cells, Regulatory T cells, granulocytes and natural killer (NK) cells.(3) Elevation of sIL-2r alpha can be observed in other chronic inflammatory conditions and malignancies.(4,5) In sarcoidosis patients with cardiac involvement, higher levels of sIL-2r alpha are associated with worse long-term clinical outcomes and increase systemic inflammatory activities.(6) In patients with hematological malignancies that express IL-2 receptors, sIL-2r alpha elevations are associated with poor prognosis or disease relapse.(4,7)

**Reference Values**

<18 years: Not established  
> or =18 years: <959 pg/mL

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**Interpretation**

A significant elevation in soluble interleukin-2 receptor alpha (sIL-2r alpha) concentration (2SD above age-adjusted laboratory-specific reference range) is one of the diagnostic criteria for hemophagocytic lymphohistiocytosis (HLH) syndrome. The diagnosis of HLH syndrome should be based on compatible clinical presentation in the context of significantly elevated inflammatory markers, including ferritin, sIL-2r alpha, and CXCL9 (C-X-C motif chemokine ligand 9).

**Cautions**

Soluble interleukin-2 receptor alpha (sIL-2r alpha) testing should only be used in conjunction with clinical presentation and other laboratory testing as part of a patient's overall assessment. Elevations in sIL-2r alpha can be seen in several inflammatory, malignancy, or infectious conditions involving activation of T-cells, B-cells, granulocytes or natural killer cells. Non-elevated concentration of sIL-2r alpha does not exclude the possibility of infection or other inflammatory condition.

There is substantial overlap in elevated sIL-2r alpha in patients with other chronic inflammatory conditions or infections

Soluble interleukin-2 receptor alpha is marker for lymphocyte activation and proliferation; a comprehensive cytokine evaluation, such as CYPAN / Cytokine Panel, Plasma may be more useful in overall disease assessment or pathophysiology.

**Clinical Reference**

1. Hayden A, Lin M, Park S, et al. Soluble interleukin-2 receptor is a sensitive diagnostic test in adult HLH. *Blood Adv.* 2017;1(26):2529-2534
2. Henter JI, Horne A, Arico M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer.* 2007;48(2):124-131
3. Riley, R.S., R. Mageau, and J. Ben-Ezra, Laboratory Evaluation of the Cellular Immune System, in *Henry's Clinical Diagnosis and Management by Laboratory Methods.* 2011. p. 877-898
4. Yang ZZ, Grote DM, Ziesmer SC, et al. Soluble IL-2Ra facilitates IL-2-mediated immune responses and predicts reduced survival in follicular B-cell non-Hodgkin lymphoma. *Blood.* 2011;118(10):2809-2820
5. Seidler S, Zimmermann HW, Weiskirchen R, Trautwein C, Tacke F. Elevated circulating soluble interleukin-2 receptor in patients with chronic liver diseases is associated with non-classical monocytes. *BMC Gastroenterol.* 2012;12:38
6. Kobayashi Y, Sato T, Nagai T, et al. Association of high serum soluble interleukin 2 receptor levels with risk of adverse events in cardiac sarcoidosis. *ESC Heart Fail.* 2021;8(6):5282-5292
7. Zoref-Lorenz A, Murakami J, Hofstetter L, et al. An improved index for diagnosis and mortality prediction in malignancy-associated hemophagocytic lymphohistiocytosis. *Blood.* 2022;139(7):1098-1110

**Performance****Method Description**

Testing for soluble IL-2 receptor alpha (sIL-2r alpha) in plasma is performed using a laboratory-developed immunoassay.(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****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

**LOINC® Information**

Test ID	Test Order Name	Order LOINC® Value
SIL2R	IL-2 receptor alpha soluble, P	76039-7

Result ID	Test Result Name	Result LOINC® Value
622328	IL-2 receptor alpha soluble	76039-7