Test Definition: C5B9

SC5b-9 Level Terminal Complement Complex, Plasma

Overview

Useful For
Detecting increased complement activation

Method Name
Enzyme-Linked Immunosorbent Assay (ELISA)

NY State Available
Yes

Specimen

Specimen Type
Plasma EDTA

Ordering Guidance
If testing to evaluate C5b-9 in the context of atypical hemolytic uremic syndrome is desired, see AHUSD / Atypical Hemolytic Uremic Syndrome Complement Panel, Serum and Plasma.

Specimen Required
Patient Preparation:
1. Fasting: 8 hours, preferred but not required
2. **Do not** collect specimens for at least 48 hours following plasma exchange.

Supplies: Sarstedt Aliquot Tube, 5 mL (T914)
Collection Container/Tube:
Preferred: Lavender top (K2 EDTA)
Acceptable: Lavender top (K3 EDTA), light-blue top (sodium citrate)
Submission Container/Tube: Plastic vial
Specimen Volume: 1.5 mL Plasma
Collection Instructions:
1. Immediately after specimen collection, place the tube on wet ice.
2. Centrifuge between 1000 and 2000 x *g* for 10 minutes at 4 degrees C.
3. Aliquot plasma into a plastic vial.
4. Within 30 minutes of centrifugation, freeze specimen. Specimen must be placed on dry ice if not frozen immediately.

Note: 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 immediately afterward, the plasma is aliquoted and frozen.

Forms
If not ordering electronically, complete, print, and send a Renal Diagnostics Test Request (T830) with the specimen.

Specimen Minimum Volume

Plasma: 0.75 mL

Reject Due To

Gross hemolysis	OK
Gross lipemia	OK
Gross icterus	OK

Specimen Stability Information

Specimen Type	Temperature	Time	Special Container
Plasma EDTA	Frozen	14 days	

Clinical & Interpretive

Clinical Information

The complement system membrane attack complex (MAC) is formed by the C5b fragment along with C6, C7, C8 and several C9 molecules. This complex is recognized by multiple names, including MAC, terminal complement complex, and C5b-9. Laboratory tests measure the amount of soluble C5b-9 (sC5b-9) complex. The formation of C5b-9 and sC5b-9 is a consequence of activation of the complement system by either the classical, lectin, or alternative pathways. Therefore, measurement of the sC5b-9 complex can be used as a surrogate marker of terminal complement activation via all complement pathways.

Elevated concentrations of C5b-9 are associated with the development of transplant-associated thrombotic microangiopathy (TA-TMA), a complication of hematopoietic stem cell transplant.(1-3) Patients with higher sC5b-9 concentrations at baseline may require the use of higher doses of eculizumab to treat TA-TMA,(4) especially in children. Because of this association, measurement of sC5b-9 before transplant as part of a diagnostic evaluation and then repeat measurements during therapy have been proposed as tools to follow-up patients.(5) Importantly, while the elevation of sC5b-9 has shown very high sensitivity for TA-TMA, it has shown only a modest specificity, ranging from 40% to 50%, and the increased sC5b-9 may be found in other transplant complications as well as several other conditions where complement activation may occur: immune-complex disease, infection, atypical hemolytic uremic syndrome, C3 glomerulopathies, etc.

A panel of complement tests, such as AHUSD / Atypical Hemolytic Uremic Syndrome Complement Panel, Serum and Plasma, may provide additional information on the extent of the complement activation, along with the information of which pathway is most dysregulated.

Reference Values

< or =250 ng/mL

Interpretation

Elevated concentrations of soluble C5b-9 suggest recent or ongoing activation of the complement system, while normal and low concentrations suggest that the complement system has not been excessively activated.

A panel of complement tests may be clinically indicated to further identify the extent of the complement activation, along with the information of which pathway is most dysregulated.

Cautions

As with all complement assays, proper specimen handling is of utmost importance to ensure that the complement system is not activated before clinical testing.

Measurement of soluble C5b-9 should be ideally performed prior to treatment initiation and in the absence of therapy with complement inhibitors, such as eculizumab and ravulizumab. Complement inhibitors, such as eculizumab and ravulizumab, may affect performance of this assay.

Clinical Reference

1. Qi J, Wang J, Chen J, Su J, et al. Plasma levels of complement activation fragments C3b and sC5b-9 significantly increased in patients with thrombotic microangiopathy after allogeneic stem cell transplantation. Ann Hematol. 2017;96(11):1849-1855
2. Horvath O, Kallay K, Csuka D, et al. Early increase in complement terminal pathway activation marker sC5b-9 Is predictive for the development of thrombotic microangiopathy after stem cell transplantation. Biol Blood Marrow Transplant. 2018;24(5):989-996
3. Mezo B, Horvath O, Sinkovits G, Veszeli N, Krivan G, Prohaszka Z. Validation of early increase in complement activation marker sC5b-9 as a predictive biomarker for the development of thrombotic microangiopathy after stem cell transplantation. Front Med (Lausanne). 2020;7:569291
4. Jodele S, Dandoy CE, Lane A, et al. Complement blockade for TA-TMA: lessons learned from a large pediatric cohort treated with eculizumab. Blood. 2020;135(13):1049-1057
5. Young JA, Pallas CR, Knovich MA. Transplant-associated thrombotic microangiopathy: theoretical considerations and a practical approach to an unrefined diagnosis. Bone Marrow Transplant. 2021;56(8):1805-1817

Performance

Method Description

Standards, controls, and test specimens are added to microassay wells coated with mouse monoclonal antibody that binds specifically to the C9 ring of SC5b-9 activation complex. A wash cycle removes unbound material following incubation. Horseradish peroxidase (HRP)-conjugated goat antibodies to antigens of SC5b-9 are added to each well and will bind to SC5b-9 that was captured on the surface of the microassay wells. A wash cycle removes unbound, excess conjugate. A chromogenic enzyme substrate is added to each microassay well. The bound HRP-conjugate reacts with the substrate forming a blue color. After incubation, the enzyme reaction is stopped chemically, and the color intensity is measured spectrophotometrically at 450 nm. The color intensity of the reaction mixture is proportional to the concentration of SC5b-9 complex present.(Package insert: MicroVue SC5b-9 Plus EIA Kit. Quidel Corporation; PIA020004EN00, 06/2022)

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PDF Report
No

Day(s) Performed
Varies

Report Available
3 to 5 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
86160

LOINC® Information

Test ID	Test Order Name	Order LOINC® Value
C5B9	SC5b-9 Complement, P	93244-2

Result ID	Test Result Name	Result LOINC® Value
616921	SC5b-9 Complement, P	93244-2