Overview

Useful For

Screening for common variable immunodeficiency (CVID)

Identifying defects in TACI and BAFF-R in patients presenting with clinical symptoms and other laboratory features consistent with CVID

Evaluating B cell immune competence by assessing expression of BAFF-R and TACI proteins

Useful for assessing BAFF-R and TACI protein expression and frequency of B cells bearing these receptors. \textit{TNFRSF13C} (BAFF-R) and \textit{TNFRSF13B} (TACI) gene mutations have been described in a small subset of patients with humoral immunodeficiencies classified as CVID. The majority of \textit{TNFRSF13B} mutations preserve TACI protein expression and require genetic testing to identify pathogenic or potentially pathogenic mutations/variants.

Method Name
Fluorescent Flow Cytometry

NY State Available
Yes

Specimen

Specimen Type
Whole Blood EDTA

Shipping Instructions
Specimens are required to be received in the laboratory weekdays and by 4 p.m. on Friday. Draw and package specimen as close to shipping time as possible.

It is recommended that specimens arrive within 24 hours of draw.

Samples arriving on the weekend and observed holidays may be canceled.

Necessary Information
Ordering physician name and phone number are required.

Specimen Required
Container/Tube: Lavender top (EDTA)

Specimen Volume:
< or =14 years: 4 mL
>14 years: 10 mL

Collection Instructions: Send specimen in original tube. Do not aliquot.

Specimen Minimum Volume
Test Definition: CVID
CVID Confirmation Flow Panel

< or =14 years: 3 mL
>14 years: 5 mL

Reject Due To

<table>
<thead>
<tr>
<th>Gross hemolysis</th>
<th>Reject</th>
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<tbody>
<tr>
<td>Gross lipemia</td>
<td>Reject</td>
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Specimen Stability Information

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<th>Time</th>
<th>Special Container</th>
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<td>Whole Blood EDTA</td>
<td>Refrigerated</td>
<td>48 hours</td>
<td>PURPLE OR PINK TOP/EDTA</td>
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Clinical and Interpretive

Clinical Information

Common variable immunodeficiency (CVID) is the most prevalent primary immunodeficiency with a prevalence of CVID of 1:25,000 to 1:50,000.\(^1\) It has a bimodal presentation with a subset presenting in early childhood and a second set presenting between 15 and 40 years of age or even later. CVID is characterized by hypogammaglobulinemia usually involving most or all of the immunoglobulin (Ig) classes (IgG, IgA, IgM, and IgE), impaired functional antibody responses, and recurrent sinopulmonary infections.\(^1\) B cell numbers are usually normal, although a minority of patients (5%-10%) have very low B cell counts (<1% of peripheral blood leukocytes). It is reasonable to suspect a transmembrane activator and calcium modulator and cyclophilin ligand interactor (TACI) defect in patients with low to absent IgA, low IgG, and low or normal IgM, along with splenomegaly, autoimmune cytopenias, autoimmune thyroiditis, and tonsillar hypertrophy. In TACI-deficient patients, there may be an increased risk for developing neoplasias such as non-Hodgkin lymphoma or other solid tumors. CD19 defects result in absence of B cells expressing CD19. When an alternative B-cell marker such as CD20 is used, however, B cells can be detected in the blood of these patients. Inducible T-cell costimulator (ICOS)-deficiency results in reduced class-switched memory B-cells.

Of all patients with CVID, 25% to 30% have increased numbers of CD8 T cells and a reduced CD4/CD8 ratio (<1).\(^1\) A subset (5%-10%) exhibit noncaseating, sarcoid-like granulomas in different organs and also tend to develop a progressive T cell deficiency.\(^1\) Patients with mutations in the TACI gene (see below) are particularly prone to developing autoimmune disease, including cytopenias as well as lymphoproliferative disease.

The etiology of CVID is heterogeneous, but recently 4 genetic defects were described that are associated with the CVID phenotype. Specific mutations, all of which are expressed on B cells, have been implicated in the pathogenesis of CVID. These mutations encode for:

- ICOS: inducible costimulator expressed on activated T cells\(^2\)

- TACI: transmembrane activator and calcium modulator and cyclophilin ligand (CAML) interactor\(^3\)

- CD19\(^4\)

- BAFF-R: B-cell activating factor belonging to the tumor necrosis factor (TNF) receptor family\(^5\)
Of these, mutations of the gene that encodes TACI, \textit{TNFRSF13B} (tumor necrosis factor receptor superfamily, member 13B), probably account for about 10\% to 15\% of all CVID cases.\(^{(3)}\) Patients with mutations in the \textit{TACI} gene are particularly prone to developing autoimmune disease, including cytopenias, as well as lymphoproliferative disease. The other mutations each have been reported in only a handful of patients. The etiopathogenesis is still undefined in more than 75\% to 80\% of CVID patients.

A BAFF-R defect should be suspected in patients with low to very low class switched and nonswitched memory B cells and very high numbers of transitional B cells (see IABC / B-Cell Phenotyping Screen for Immunodeficiency and Immune Competence Assessment, Blood). Class switching is the process that allows B cells, which possess IgD and IgM on their cell surface as a part of the antigen-binding complex, to produce IgA, IgE, or IgG antibodies. A TACI defect is suspected in patients with low IgA and low IgG with normal to low switched B cells, with autoimmune or lymphoproliferative manifestations or both, and normal B cell responses to mitogens.

**Reference Values**

\%CD19+TACI+: >3.4\%

\%CD19+BAFF-R+: >90.2\%

Reference values apply to all ages.

**Interpretation**

BAFF-R is normally expressed on over 95\% of B cells, while TACI is expressed on a smaller subset of B cells (3\%-70\%) and some activated T cells. Expression on B cells increases with B cell activation.

The lack of TACI or BAFF-R surface expression on B cells is suggestive of a potential common variable immunodeficiency (CVID)-associated defect, if other features of CVID are present. The majority of \textit{TACI} mutations (>95\%) preserve protein expression but abrogate protein function, hence the only way to conclusively establish a \textit{TACI} mutational defect is to perform genetic testing (TACIF / Transmembrane Activator and CAML Interactor [\textit{TACI}] Gene, Full Gene Analysis).

**Cautions**

This test should not be ordered serially.

This test should not be ordered for general evaluation of immune competence.

This test is preferable to order ONLY when there is clear evidence for common variable immunodeficiency and/or evidence of dysregulated B cell subsets (which can be obtained through IABCS / B-Cell Phenotyping Profile for Immunodeficiency and Immune Competence Assessment, Blood).

**Clinical Reference**


### Performance

### Method Description

Peripheral blood mononuclear cells are isolated and stained with CD19, TACI, and BAFF-R, each conjugated to a fluorochrome. After the staining with specific antibody, the cells are washed, fixed with paraformaldehyde, and then analyzed by flow cytometry on a BD FACSCanto instrument. The cell-surface expression is denoted as the percent of CD19+ B cells expressing TACI and BAFF-R. (Unpublished Mayo method)

### PDF Report

No

### Day(s) and Time(s) Test Performed

Specimens are required to be received in the lab weekdays and by 4 pm on Friday. **No weekend processing.**

### Analytic Time

3 days

### Maximum Laboratory Time

4 days

### Specimen Retention Time

PBMC's are stored for 7 days at -70 degrees C

### Performing Laboratory Location

Rochester

### Fees and 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 Regional Manager. For assistance, contact [Customer Service](#).

### Test Classification

This test was developed using an analyte specific reagent. Its performance characteristics were determined by Mayo Clinic in a manner consistent with GLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

### CPT Code Information

88184

88185 x 2

### LOINC® Information
## Test Definition: CVID

### CVID Confirmation Flow Panel

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