MAYO CLINIC LABORATORIES

# Test Definition: GLYCS

Glycine Alpha1 LCBA, S

## Overview

### Useful For

Evaluating patients with suspected autoimmune stiff-person spectrum disorders (stiff-person syndrome, stiff-limb, stiff trunk or progressive encephalomyelitis with rigidity and myoclonus [PERM]) using serum specimens

### Method Name

Live Cell-Binding Assay (LCBA)

### NY State Available

Yes

## Specimen

### Specimen Type

Serum

### Specimen Required

**Container/Tube:**

**Preferred:** Red top

**Acceptable:** Serum gel

**Specimen Volume:** 1 mL

### Forms

If not ordering electronically, complete, print, and send a Neurology Specialty Testing Client Test Request (T732) with the specimen.

### Reject Due To

| | |
|---|---|
| Gross hemolysis | Reject |
| Gross lipemia | Reject |
| Gross icterus | Reject |

### Specimen Minimum Volume

See Specimen Required

### Specimen Stability Information

| Specimen Type | Temperature | Time | Special Container |
|---|---|---|---|
| Serum | Refrigerated (preferred) | 28 days | |
| | Frozen | 28 days | |
| | Ambient | | |

## Clinical & Interpretive

### Clinical Information

Inhibitory synaptic transmission is mediated by gamma-aminobutyric acid-ergic (GABA-ergic) and glycinergic spinal interneurons, which regulate motor neuron excitability in the brainstem and spinal cord. Autoimmune central nervous system disorders include classic stiff-man syndrome (also known as stiff-person syndrome), limited stiff-man forms (eg, stiff-limb syndrome) and a severe (and sometimes fatal) encephalomyelitic variant known as progressive encephalomyelitis with rigidity and myoclonus (PERM). These disorders are unified clinically by exaggerated startle, stiffness, and spasms of the axis and/or limbs. Characteristic electrophysiologic findings include continuous motor unit activity by unipolar electromyographic (EMG) recording, and exaggerated and non-habituating acoustic startle responses. Eighty percent of patients are seropositive for antibody targeting the 65 kDa isoform of glutamic acid decarboxylase (GAD65).

The alpha-1-subunit of the glycine receptor (GlyRa1), which is enriched in brainstem and spinal cord, has emerged as an antigenic target with specificity for the autoimmune stiff-person spectrum, and is particularly useful for diagnostics among patients seronegative for GAD65-IgG. GlyRa1-IgG has been described among patients with PERM (33%), classic stiff-man syndrome (9%), and limited stiff-man forms (17%). Seropositivity for GlyRa1-IgG is detected in 19% of patients from the stiff-man spectrum who are GAD65-IgG seronegative. The clinical context is usually non-paraneoplastic, though thymoma and lymphomas have been occasionally described. Disease-specific antibodies may be detected in serum only, CSF only, or both. Improvements with immunotherapy (steroids, plasma exchange or intravenous immune globulin) occur more commonly in GlyRa1-IgG seropositive patients than among patients seropositive for GAD65 antibody only. In one series, improvement was noted in 6/7 GlyRa1-IgG antibody positive patients compared with only 7/25 without these antibodies.

### Reference Values

Negative

### Interpretation

In the appropriate clinical context, this profile is consistent with a stiff-person syndrome spectrum disorder (classical stiff-person, stiff-limb, or progressive encephalomyelitis with rigidity and myoclonus [PERM]). A paraneoplastic cause should be considered.

### Cautions

Negative results do not exclude autoimmune stiff-person spectrum or cancer.

### Clinical Reference

1. Hutchinson M, Waters P, McHugh J, et al: Progressive encephalomyelitis, rigidity, and myoclonus: a novel glycine receptor antibody. Neurology. 2008;71:1291-1292

2. McKeon A, Martinez-Hernandez E, Lancaster E, et al: Glycine receptor autoimmune spectrum with stiff-man syndrome phenotype. JAMA Neurol. 2013;70:44-50

3. Carvajal-Gonzalez A, Leite MI, Waters P, et al: Glycine receptor antibodies in PERM and related syndromes: characteristics, clinical features and outcomes. Brain. 2014;137:2178-2192

4. Martinez-Hernandez E, Arino H, McKeon A, et al: Clinical and immunologic investigations in patients with stiff-person spectrum disorder. JAMA Neurol. 2016;73:714-720

5. Hinson SR, Lopez-Chiriboga AS, Bower JH, et al: Glycine receptor modulating antibody predicting treatable stiff-person spectrum disorders. Neurol Neuroimmunol Neuroinflamm. 2018; 5:e438

## Performance

### Method Description

This assay utilizes the T-REx System (Thermo Fisher). Expression of the glycine receptor alpha-1-subunit is repressed in the absence of tetracycline or doxycycline and induced in the presence of tetracycline or doxycycline.(Yao F, Svensjo T, Winkler T, Eriksson C, Eriksson E: Tetracycline repressor, tetR, rather than the tetR-mammalian cell transcription factor fusion derivatives, regulates inducible gene expression in mammalian cells. Hum Gene Ther. 1998 Sep;9[13]:1939-1950)

HEK293 cells stably expressing the tetracycline repressor and stably transfected with a plasmid encoding the alpha-1-subunit of the glycine receptor, under control of doxycycline, are grown in wells of a chamber slide. Twenty four hours prior to the assay, the wells on the bottom half of the slide are treated with culture media including doxycycline. After 24 hours, patient CSF and/or serum will be added to the living HEK293 cells held on ice. Bound IgG will be detected using a fluorophore conjugated anti-human IgG secondary antibody. Patient samples with IgG specific for the glycine receptor will be positive on doxycycline-treated cells and negative on cells not treated with doxycycline.(Unpublished Mayo method)

### PDF Report

No

### Specimen Retention Time

28 days

# Test Definition: GLYCS

Glycine Alpha1 LCBA, S

### Performing Laboratory Location

Rochester

## Fees & Codes

### Test Classification

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

### CPT Code Information

86255

### LOINC® Information

| Test ID | Test Order Name | Order LOINC Value |
|---|---|---|
| GLYCS | Glycine Alpha1 LCBA, S | 96496-5 |

| Result ID | Reporting Name | LOINC® |
|---|---|---|
| 606972 | Glycine Alpha1 LCBA, S | 96496-5 |