Client: Example Client ABC123
123 Test Drive
Salt Lake City, UT 84108
UNITED STATES

Physician: Doctor, Example

Patient: Patient, Example

DOB	Unknown
Gender:	Unknown
Patient Identifiers:	01234567890ABCD, 012345
Visit Number (FIN):	01234567890ABCD
Collection Date:	00/00/0000 00:00

Envoplakin Antibody, IgG by ELISA

ARUP test code 3016533

EER Envoplakin Antibody, IgG by ELISA

See Note

Authorized individuals can access the ARUP Enhanced Report using the following link:

[redacted]

Envoplakin Antibody, IgG by ELISA

See Note

CLINICAL INFORMATION
Mucosal erosions and urticarial skin lesions. Presumptive diagnosis is drug reaction versus pemphigoid versus pemphigus, including paraneoplastic pemphigus.

Specimen Details
[redacted] - ; Collected: 11/20/2024; Received: 11/22/2024

DIAGNOSTIC INTERPRETATION

Normal IgG envoplakin antibody level by ELISA

(See Results and Comments including recommendations for correlating with other testing)

RESULTS

Enzyme-Linked Immunosorbent Assay (ELISA)

Envoplakin IgG Antibodies

IgG envoplakin antibody level: 0.35 ratio U/mL

Reference Range:
Normal (negative) = Less than 1.00 ratio U/mL
Increased (H) (positive) = 1.00 ratio U/mL and greater

(H) = high/positive
U = antibody level in ELISA units

COMMENTS

Specific

The normal IgG envoplakin antibody level in this ELISA testing

H=High, L=Low, *=Abnormal, C=Critical

does not provide support for, but does not rule out, the diagnosis of paraneoplastic pemphigus (PNP)/paraneoplastic autoimmune multiorgan syndrome (PAMS), or another malignancy-associated disorder. Clinical correlation is needed, including with direct immunofluorescence test findings on a biopsy specimen, histopathological examination of formalin-fixed tissue, and other serum epithelial antibodies.

Notably, various serum epithelial antibodies may be found in PNP/PAMS and other paraneoplastic presentations by various tests with differing sensitivities. Testing for IgG paraneoplastic pemphigus antibodies with rat bladder, mouse bladder, mouse heart, and mouse liver substrates by indirect immunofluorescence may provide more broad-based screening for paraneoplastic pemphigus antibodies, and testing for epithelial cell surface/intercellular substance and basement membrane zone antibodies can be helpful to expand the epithelial antibody profile and assess for other immunobullous diseases.

To further evaluate the immunopathological profile, additional indicated testing may be performed on this serum specimen by contacting ARUP Client Services at 1-800-242-2787, option 2, with add-on test request(s) for:
- Paraneoplastic Pemphigus (Paraneoplastic Autoimmune Multiorgan Syndrome) Screening Antibodies by IIF (rodent substrates including rat bladder) (ARUP test number 0092107), and
- Immunobullous Disease Antibody Panel (ARUP test number 3001409);

Or specific antibodies that may develop to other epithelial antigens in PNP/PAMS,
- Desmoglein 1 and Desmoglein 3 (Pemphigus) Antibodies, IgG by ELISA (ARUP test number 0090649, and
- Bullous Pemphigoid (BP180 and BP230) Antibodies, IgG by ELISA (ARUP test number 0092566);

with supporting indirect immunofluorescence,
- Basement Membrane Zone and Cell Surface (Epithelial) Antibodies, IgG and IgA by IIF (ARUP test number 0090299).

Detection, levels, and patterns of diagnostic antibodies may fluctuate with disease manifestations. Monitoring serum antibody profiles by indirect immunofluorescence testing and antibody levels by ELISAs may aid in assessing disease expression and activity, particularly with persistent, progressive, or changing disease, and in response to therapy.

If it would be helpful to discuss the patient case with this report, including request for additional testing on this serum specimen, contact ARUP Client Services at 1-800-242-2787, option 2, and ask to speak with the Immunodermatology Laboratory at the University of Utah regarding patient results.

General

IgG envoplakin antibodies develop in many patients with paraneoplastic pemphigus (PNP), also known as paraneoplastic autoimmune multiorgan syndrome (PAMS), and rarely in patients with other immunobullous diseases. This ELISA identifies IgG antibodies to the N-terminal recombinant fragment of envoplakin. Specificity of the test has been reported to be high at 96-99 percent and sensitivity of the test more variably reported at 55-86 percent. Patients with PNP/PAMS develop serum antibodies to multiple epithelia (simple, columnar, transitional) with several possible epithelial targets, including plakins (envoplakin, periplakin, desmoplakin I, desmoplakin II, epiplakin, plectin, BP230), also cadherins (desmoglein 1, desmoglein 3; desmocollin 1, desmocollin 2, desmocollin 3), alpha-2-macroglobulin-like-1 (A2ML1), laminin 332, and/or BP180. Envoplakin and periplakin are principal antigenic targets in the disease, and, based on the high specificity, an increased

envoplakin antibody level is a diagnostic marker for PNP/PAMS. ELISA may be more sensitive than indirect immunofluorescence testing for detecting antibodies, especially low levels, but indirect immunofluorescence testing with rodent substrates demonstrates antibodies to a broader range of epithelial targets than the envoplakin epitopes displayed in this tested ELISA.

Paraneoplastic pemphigus/paraneoplastic autoimmune multiorgan syndrome may affect all ages and develops as a severe mucocutaneous blistering and erosive disease in association with malignancies, most often hematologic (lymphoma, leukemia) and sarcoma. It also may develop in association with benign neoplasia, especially Castleman disease, which is the most frequent association in children and adolescents. Antibodies targeting the various types of epithelia can lead to involvement of various organs and tissues, for example, eyes, lungs, gastrointestinal tract, kidney, and thyroid and is the basis of the name, paraneoplastic autoimmune multiorgan syndrome. IgG envoplakin antibody levels correlate with extent of mucocutaneous paraneoplastic pemphigus disease expression. After successful tumor therapy, envoplakin antibody levels decrease significantly.

For positive/increased ELISA results without known malignancy, perform aggressive evaluation and monitoring for malignancy. For negative results, correlate with histopathological examination of formalin-fixed tissue in addition to direct immunofluorescence testing on a biopsy specimen and epithelial antibodies in serum characteristic of other immunobullous diseases with further clinical evaluation as indicated. Negative IgG envoplakin ELISA testing results do not rule out paraneoplastic/malignancy-associated disease. Other known paraneoplastic epithelial autoantibody associations include nonclassical, intercellular IgG/IgA dermatosis and anti-laminin 332 pemphigoid.

TESTING METHODS
Enzyme-Linked Immunosorbent Assay (ELISA)

IgG envoplakin serum antibody level determined by ELISA (Euroimmun US, Inc.). The performance characteristics of this test have been validated by the University of Utah Immunodermatology Laboratory and meet specifications required by the Clinical Laboratory Improvement Amendment of 1988 (CLIA). The test has CE Mark certification as an in vitro diagnostic in the European Union. The testing has not been cleared or approved by the US Food and Drug Administration (FDA). The testing was performed in a CLIA-certified laboratory and is intended for clinical purposes. The results are not intended to be used as the sole means for clinical diagnosis or patient management decisions. [One ELISA]

Electronically signed by [redacted], on 11/22/24 at 7:39 PM.
Performed At: IMMUNODERMATOLOGY LABORATORY
417 S. WAKARA WAY, SUITE 2151
SALT LAKE CITY, UT 84108
Medical Director: KRISTIN M. LEIFERMAN, MD
CLIA Number: 46D0681916

H=High, L=Low, *=Abnormal, C=Critical

VERIFIED/REPORTED DATES

Procedure	Accession	Collected	Received	Verified/Reported
EER Envoplakin Antibody, IgG by ELISA	24-325-116715	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00
Envoplakin Antibody, IgG by ELISA	24-325-116715	00/00/0000 00:00	00/00/0000 00:00	00/00/0000 00:00

END OF CHART

H=High, L=Low, *=Abnormal, C=Critical