Figure S1. Testing for autoantibodies that mediate cancer-associated retinopathy.

CASEY EYE Institute
OHSU
Oregon Health & Science University
OCULAR IMMUNOLOGY LABORATORY
LBRB-Room 253
3181 SW Sam Jackson Park Road, Portland, Oregon 97239
Ph: 503-418-2543 Fax: 503-418-2541

Patient Name:
Medical Record #:
Account #:
Date of Birth:
Sex: Female
Referral Source: Casey Eye Institute Pathology

Accession #:
Reference Lab no.:
Physician(s):

Ocular Immunology (Final result)

Authorizing Provider:
Ordering Location:

Ordering Provider:
Collected:

Pathologist:

Received:

Specimens

A Blood, Serum 6ml frozen

Clinical History

History of progressive loss of night vision (nyctalopia) and subsequent deterioration of colour vision; electroretinographic evidence of severe loss of rod and cone function in an adult age (aquired disease); systemic malignancies under systemic chemotherapy.

Anti Retinal Result

Test results must be interpreted in the context of clinical presentation

Test Name	Result
Autoimmune Retinopathy Panel (ARP)	
Marker	
Carbonic anhydrase II	negative
HSP27	negative
Aldolase	negative
Enolase	**positive**
Arrestin	negative
Tubulin	negative
PKM2 (pyruvate kinase M2)	negative
GAPDH (glyceraldehyde 3-phosphate dehydrogenase)	negative

[Adequacy: Satisfactory for evaluation]
This test was developed and its performance characteristics determined by Ocular Immunology Laboratory OHSU. It has not been approved by the U.S. Food and Drug Administration.

Test Name	Result
Cancer-Associated Retinopathy Panel (CARP)	
Marker	

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Recoverin	negative
Carbonic anhydrase II	negative
Rab6	negative
Aldolase	negative
Enolase	**positive**
HSP60	negative
TULP1	negative
GAPDH (glyceraldehyde 3-phosphate dehydrogenase)	negative
Immunohistochemistry of human retina	POSITIVE - mild staining of the photoreceptor cell layer and nerve fiber layer

[Adequacy: Satisfactory for evaluation]
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Interpretation

A positive result indicates that anti-retinal autoantibodies (AAbs) are present, which may indicate Autoimmune Retinopathy. The disease is highly heterogeneous - patients differ in their clinical presentation and antibody profiles. Different anti-retinal antibodies frequently co-exist in a single patient, creating antibody-profiles related to the syndrome. Antibody profile can change with the progression of disease, with each disease stage having its own unique autoantibody signature.

The antigenic biomarkers have been selected based on their frequencies in CAR and AR. Autoantibodies against Recoverin (23-kDa) and Enolase (46-kDa) have been associated with AR and CAR. The presence of anti-recoverin AAbs indicates a high likelihood of associated neoplasm, especially small cell carcinoma of the lung, breast, and gynecological cancer in women [BMC Ophthalmol 4(1):5, 2004][IOVS, 2015;56:1680-8[Clin Immunol 2020, 210, 108317]. CAR symptoms and the presence of anti-retinal AAbs can manifest prior to the onset of cancer and the underlying cancer can remain undetectable for months or even years. Regular follow-up and tumor surveillance is essential in suspected paraneoplastic syndrome.

Of all patients with anti-retinal AAbs, more than 40% patients have anti-alpha-Enolase antibodies [Clin Immunol 2020, 210, 108317].These antibodies are less predictive of associated neoplasm than are anti-Recoverin antibodies. CAR associated with anti-Enolase AAbs occurs predominately in patients with breast and gynecological cancers, and usually develops years after discovery of the malignancy. Anti-Enolase antibodies have also been found in patients with skin cancer and hematological cancers and in patients without cancer [Autoimmun Rev 8(5):410, 2009][Clin Immunol 2020, 210, 108317].

Protocols:

OFF-HILL SUBMITTER