PLA2R Autoantibodies
Diagnostic Marker for Membranous Nephropathy

EXPERT INSIGHTS Bradley P. Dixon, MD, *Nephrologist, Cincinnati Children's*

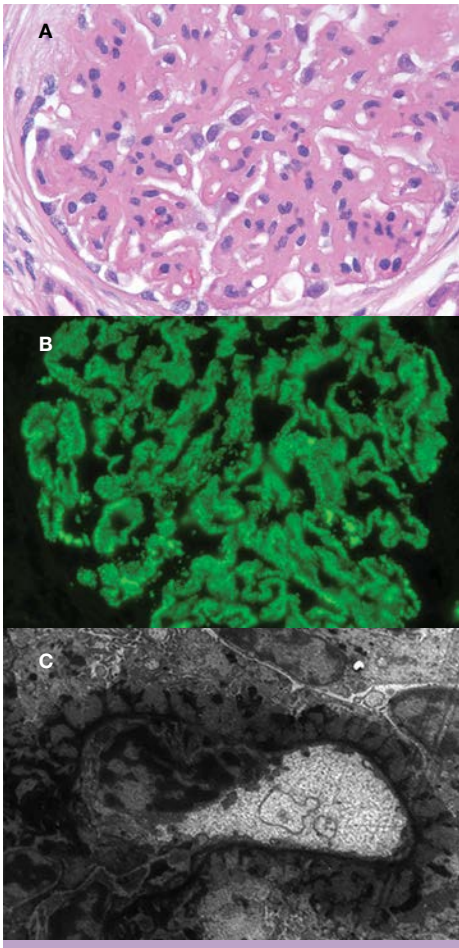
Cincinnati Children's Nephrology Clinical Lab is pleased to announce that we now offer testing for PLA2R autoantibodies. This FDA-cleared ELISA is a quantitative assay used for the detection of IgG antibodies directed against M-type Phospholipase A2 receptors (PLA2R) in human serum or plasma. Autoantibodies against PLA2R are highly specific for the diagnosis of idiopathic membranous nephropathy and can be detected in 70%-75% of patients with the disease, but are largely absent in patients with secondary forms of membranous nephropathy, other causes of glomerulonephritis, and in healthy individuals.[1]

BACKGROUND

Idiopathic membranous nephropathy (IMN) is one of the most common causes of nephrotic syndrome in adults, and occasionally causes nephrotic syndrome in children.[2] It affects men slightly more than women, with a peak incidence in the fourth to fifth decades of life and progresses to end stage renal disease in up to 40% of cases. Secondary forms due to autoimmune diseases such as systemic lupus erythematosus, infections such as hepatitis B and C, certain medications, and malignancies account for approximately one third of cases of membranous nephropathy in adults, and a larger percentage in children, and therefore the diagnosis of IMN can be made only after ruling out secondary forms of membranous nephropathy.[2] The identification of the phospholipase A2 receptor as the major target antigen in IMN and the detection of circulating autoantibodies against PLA2R in patients with IMN represent major advances in understanding this disease.

INDICATIONS

Identifying and quantitating the level of anti-PLA2R antibodies facilitates a rapid diagnosis of IMN and helps to distinguish IMN from other forms of glomerular disease including secondary membranous nephropathy. The level of autoantibody appears to correspond to disease activity, in that an increase, decrease or disappearance of the antibody titer often precedes a change in the clinical status of the disease.[3-5] In conjunction with other laboratory tests and clinical assessment, the PLA2R autoantibody titer may therefore have a predictive value with respect to clinical remission, relapse, or recurrence after kidney transplantation. Measuring the PLA2R autoantibody titer over time may also aid in establishing the course of therapy, in that reducing or eliminating the antibody may herald reduction of proteinuria and improvement of the disease.[4,5]



Biopsy of Idiopathic Membranous Nephropathy

A. Hematoxylin & eosin, illustrating thickened capillary loops. **B.** Immunofluorescence to IgG, demonstrating extensive deposits along the capillary loop. **C.** Electron microscopy, with subepithelial deposits and basement membrane "spikes." *Images courtesy of Dr. David Witte.*

SPECIMEN REQUIREMENTS

Testing for the PLA2R autoantibody (CPT 86021) requires less than 0.5 mL of serum or plasma. Specimens should be shipped refrigerated or frozen to:

Cincinnati Children's Hospital Medical Center
Attention: Lab Processing (B4)
3333 Burnet Avenue
Cincinnati, Ohio 45229

You may also visit our website www.cincinnatichildrens.org/nephrology-labtests to download a test requisition and learn more about our specialized diagnostic testing services.

INTERPRETATION OF TEST RESULTS

A positive result for the PLA2R autoantibody is > 20 Units/mL. A PLA2R autoantibody level between 14 and 20 Units/mL is a borderline result, and may require retesting depending on the clinical status of the patient. Results below 14 Units/mL are negative. If a patient is seronegative for the PLA2R autoantibody, testing for colocalization of PLA2R and IgG4 on kidney biopsy tissue may assist in confirming or excluding a diagnosis of PLA2R antibody-mediated IMN.

THE NEPHROLOGY CLINICAL LABORATORY AT CINCINNATI CHILDREN'S

Founded by a pioneer in complement biology Dr. Clark West, the Nephrology Clinical Laboratory in the Division of Nephrology and Hypertension at Cincinnati Children's Hospital Medical Center provides specialized diagnostic testing for children and adults throughout the world, and offers interpretation of test results by clinical experts. We provide a robust test menu (Table 1.1) to aid in the diagnosis and management of many forms of glomerulonephritis, thrombotic microangiopathies such as atypical hemolytic uremic syndrome and thrombotic thrombocytopenic purpura, systemic lupus erythematosus, hereditary angioedema, and a wide variety of immune system disorders including complement deficiencies, dysgammaglobulinemias, and immunoglobulin subclass deficiencies.

Table 1.1

Additionally Available Diagnostic Tests
Glomerulonephritis and Nephrotic Syndrome
Complement Profile (C1q, C2, C3, C4, C5, C6, C7, C8, C9, Factor B, Factor H, Factor I, Properdin, C1 Inhibitor, C4BP)
C3 Nephritic Factor
Complement Activation
Complement Bb
sC5b-9 (available through collaborating lab at Cincinnati Children's)
CH50 (Total Hemolytic Complement)
Thrombotic Microangiopathy
Factor H Autoantibody
Factor B, Factor I, Factor H levels
C3, C4
ADAMTS13 Activity and Antibody
Autoimmune Diseases and Immunodeficiency
HANE/Active SLE Profile (C1q, C2, C3, C4, C1 Inhibitor)
Rheumatoid Factor
IgG Subclasses (IgG1, IgG2, IgG3, IgG4, total IgG)
Immunoglobulin Profile (IgA, IgM, IgG)
Chronic Kidney Disease
Cystatin C

1. Beck LH Jr, Bonegio RG, Lambeau G, Beck DM, Powell DW, Cummins TD, Klein JB, Salant DJ. M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy. *N Engl J Med* 361: 11-21, 2009. 2. Fervenza FC, Sethi S, Specks U. Idiopathic Membranous Nephropathy: Diagnosis and Treatment. *Clin J Am Soc Nephrol* 3: 905-919, 2008. 3. Hoxha E, Thiele I, Zahner G, Panzer U, Harendza S, Stahl RA. Phospholipase A2 receptor autoantibodies and clinical outcome in patients with primary membranous nephropathy. *J Am Soc Nephrol* 25(6):1357-66. 2014 Jun. 4. Beck LH Jr, Fervenza FC, Beck DM, Bonegio RG, Malik FA, Erickson SB, Cosio FG, Cattran DC, Salant DJ. Rituximab-induced depletion of anti-PLA2R autoantibodies predicts response in membranous nephropathy. *J Am Soc Nephrol* 22(8):1543-50. 2011 Aug. 5. Hoxha E, Harendza S, Pinnschmidt H, Panzer U, Stahl RAK. M-type Phospholipase A2 Receptor Autoantibodies and Renal Function in Patients with Primary Membranous Nephropathy. *Clin J Am Soc Nephrol* 9, 2014 Sep 29 [Epub ahead of print].

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT NEPHROLOGY 2014–15

Cincinnati Children's is ranked #2 in Nephrology and third among all Honor Roll hospitals in the 2014-15 *U.S. News & World Report* listing of Best Children's Hospitals.

For questions regarding specimen requirements, test results, or other inquiries, contact the Nephrology Clinical Laboratory at **1-513-636-4530**.

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