

Beta 2 Glycoprotein 1 (B2GP1) Antibodies and Thrombotic Disease

Summary:

Detection of antibodies to B2GP1 is a highly specific indicator of Antiphospholipid Syndrome (APS), now known as Hughes Syndrome

Hughes Syndrome, also known as Antiphospholipid Syndrome (APS), is characterized by venous and arterial thrombosis, thrombocytopenia, and recurrent miscarriages. The condition occurs either secondarily in patients with autoimmune disease (notably systemic lupus erythematosus), or as a primary condition without underlying disease.

The original name for this syndrome, Antiphospholipid Syndrome (APS), came from the discovery that patient sera usually contain antibodies that recognize cardiolipin, an acidic phospholipid. Further research, however, showed that the term APS is in fact a misnomer. The cardiolipin antibodies associated with this syndrome actually recognize a serum protein which attaches to cardiolipin in vitro, rather than cardiolipin itself. Hughes- or APS associated cardiolipin antibodies thus differ from syphilis-associated cardiolipin antibodies, which truly recognize cardiolipin.

The cardiolipin-binding serum protein recognized by antibodies in Hughes is beta 2 glycoprotein 1 (B2GP1), a protein involved in the regulation of the coagulation system. Detection of B2GP1 antibodies in vitro requires that the B2GP1 be bound to the solid phase via high-density negative charges. In traditional assays, these negative charges are supplied by cardiolipin or other anionic phospholipids (eg, phosphatidylserine)

attached to plastic microtiter wells. However, recent reports have shown that plastic microtiter wells can be chemically altered by gamma irradiation to express high-density negative charges. Thus, B2GP1 can now be attached directly to irradiated plastic microtiter wells, and these wells used to detect Hughes (APS)-associated B2GP1 antibodies. This cardiolipin-free approach for identifying antibodies associated with APS is more specific than the traditional cardiolipin antibody assay, since it eliminates false positive results caused by true cardiolipin antibodies found in syphilis and other infectious diseases.

A strong association between B2GP1 antibodies and thrombotic disease has been demonstrated by many different investigators worldwide. The proportion of clinically-defined Hughes (APS) patients exhibiting B2GP1 antibodies ranged from 72% to 100% in various studies. Compared to the traditional cardiolipin antibody assay, the B2GP1 antibody assay showed a particularly strong association with thrombotic manifestations of the Hughes Syndrome.

Focus Diagnostics' Reference Laboratory is pleased to offer B2GP1 antibody testing; IgG, IgM, and IgA antibodies recognizing human B2GP1 are measured using separate FDA cleared ELISAs. These assays should prove valuable to clinicians in the identification of patients with thrombotic disease.

To send specimens or obtain additional information, please contact our Client Services Department at 800-445-4032. For technical assistance, contact Focus Diagnostics' Scientific Director of Immunology.

For complete specimen information and CPT codes, view our Reference Laboratory test listing on our Web site at www.focusdx.com

Code #	Test Description
21520	Beta 2 Glycoprotein 1 (B2GP1) Antibodies (IgA, IgG, IgM)

Beta 2 Glycoprotein 1 (B2GP1) Antibodies and Thrombotic Disease

REFERENCES:

1. Cabiedes J, AR Cabral, D Alarcon-Segovia. 1995. Clinical manifestations of the antiphospholipid syndrome in patients with systemic lupus erythematosus associate more strongly with anti-beta-2-glycoprotein-1 than with antiphospholipid antibodies. *J Rheumatol* 22:1899-1906.
2. Cabral AR, J Cabiedes, D Alarcon-Segovia. 1995. Antibodies to phospholipid-free beta-2-glycoprotein-1 in patients with primary antiphospholipid syndrome. *J Rheumatol* 22:1894-1898.
3. Cabral AR, MC Amigo, J Cabiedes, D Alarcon-Segovia. 1996. The antiphospholipid/ cofactor syndromes: a primary variant with antibodies to beta 2-glycoprotein-1 but not antibodies detectable in standard antiphospholipid assays. *Am J Med* 101:472-481.
4. El-Kadi HS, LB Keil, VA DeBari. 1995. Analytical and clinical relationships between human IgG autoantibodies to beta 2 glycoprotein 1 and anticardiolipin antibodies. *J Rheumatol* 22:2233-2237.
5. Forastiero RR, ME Martinuzzo, LC Kordich, LO Carreras. 1996. Reactivity to beta 2 glycoprotein I clearly differentiates anticardiolipin antibodies from antiphospholipid syndrome and syphilis. *Thromb Haemostas* 75:717-720.
6. Lopez LR, et al. 2004. Anti beta 2 glycoprotein 1 and antiphosphatidylserine antibodies are predictors of arterial thrombosis in patients with antiphospholipid syndrome. *Am J Clin Pathol* 121:142-149
7. Martinuzzo ME, RR Forastiero, LO Carreras. 1995. Anti beta 2 glycoprotein 1 antibodies: detection and association with thrombosis. *Br J Haematol* 89:397-402.
8. Matsuura E, Y Igarashi, T Yasuda, DA Triplett, T Koike. 1994. Anticardiolipin antibodies recognize beta 2-glycoprotein 1 structure altered by interacting with an oxygen modified solid phase surface. *J Exp Med* 179:457-462.
9. Najmey SS, LB Keil, D YR Adib, VA DeBari. 1997. The association of antibodies to beta 2 glycoprotein 1 with the antiphospholipid syndrome: a meta-analysis. *Ann Clin Lab Sci* 27:41-46.
10. Pengo V, A Biasiolo, T Brocco, S Tonetto, A Ruffatti. 1996. Autoantibodies to phospholipid-binding plasma proteins in patients with thrombosis and phospholipid-reactive antibodies. *Thromb Haemostas* 75:721-724.
11. Roubey RAS, RA Eisenberg, MF Harper, JB Winfield. 1995. "Anticardiolipin" autoantibodies recognize beta 2-glycoprotein 1 in the absence of phospholipid. Importance of antigen density and bivalent binding. *J Immunol* 154:954-960.
12. Roubey RAS, MA Maldonado, SN Byrd. 1996. Comparison of an enzymelinked immunosorbent assay for antibodies to Beta 2-glycoprotein 1 and a conventional anticardiolipin immunoassay. *Arth Rheum* 39:1606-1607.
13. Tsutsumi A, E Matsuura, K Ichikawa, A Fujisaku, M Mukai, S Kobayashi, T Koike. 1996. Antibodies to beta-2 glycoprotein 1 and clinical manifestations in patients with systemic lupus erythematosus. *Arth Rheum* 39:1466-1474.
14. Wilson WA, Gharavi AE. 1996. Hughes syndrome: Perspectives on thrombosis and antiphospholipid antibody. *Am J Med* 101:574-575.

To send specimens or obtain additional information, please contact our Client Services Department at **800 445 4032**.

For technical assistance, contact Focus Diagnostics' Scientific Director of Immunology.



800-445-0185 • 714-220-1900 • Fax: 714-220-9213
Cypress, California 90630 USA
www.focusdx.com

RLB2G10509