



## COFACTOR DEPENDENCY OF ANTI-PHOSPHATIDYLSERINE ANTIBODIES CORRELATES WITH THROMBOSIS IN SLE PATIENTS

It is now widely recognized that most assays for anti-phospholipid antibodies detect many, if not all, subsets of this heterogeneous group of antibodies (i.e. true anti-cardiolipin, anti-cardiolipin/cofactor complex, and anti-cofactor antibodies). As discussed previously, not all subsets of anti-phospholipid antibodies are necessarily associated with thrombosis. Recent efforts have been directed towards improving the laboratory identification and measurement of those antibodies which serve as more specific markers for patients at risk for thrombosis (anti-phospholipid syndrome).

Earlier research suggested that "autoimmune" anti-phospholipid antibodies more often associated with thrombosis require a cofactor for optimal immunological binding, most likely of the anti-cardiolipin/cofactor complex and anti-cofactor subsets. In contrast, true anti-cardiolipin antibodies found in infections (i.e. syphilis) are not associated with thrombosis. These observations lead to the development of the concept of "cofactor dependency" which was not only used to explain the possible pathogenic role of these antibodies in thrombosis but also to develop better procedures to identify the most clinically relevant subset(s) of antibodies in the laboratory. In the last issue of THE READER, we summarized the results of our study on a group of anti-phospholipid positive serum samples from patients with various autoimmune diseases and syphilis. Our results showed that relative to cofactor dependency, anti-phosphatidylserine (aPS) antibodies are distinct and appeared more clinically relevant than anti-cardiolipin (aCL) antibodies. The association between cofactor dependency of aPS antibodies with thrombosis was further explored in a group of selected SLE patients.

To examine the correlation of cofactor (B2GPI) dependency with clinical history of thrombosis

(anti-phospholipid syndrome), we selected 28 female SLE patients. Twelve (12) of these patients had a history of thrombosis, 6 a history of thrombocytopenia, and 10 without a history of either were used as controls. No cofactor dependency was seen in any of the selected SLE patients when tested for aCL antibodies. In contrast, 50% of the patients with a history of thrombosis showed positive cofactor dependency when tested for aPS antibodies. None of the patients with a history of thrombocytopenia and only 1 in the control group showed cofactor dependency. Interestingly, most of the patients with a history of thrombosis and cofactor dependency also had a history of recurrent abortion and higher serum levels of aPS antibodies compared to those without cofactor dependency. In addition, the single patient with cofactor dependency in the control group was the only one that showed a history of abortion and a borderline level of aPS antibodies.

In summary, our results showed a diminished B2GPI cofactor dependency when this group of selected SLE patients were tested for aCL antibodies in spite of their high aCL serum levels as determined by our standard assay. These results are consistent with our previous study performed on a different group of autoimmune patients. (presented in the last issue of THE READER). Similarly, a stronger and more prevalent cofactor (B2GPI) dependency was observed only when these SLE patient samples were tested for aPS antibodies. The presence of aPS cofactor dependency for this group also correlated with the clinical history of thrombosis (anti-phospholipid syndrome). These results further support our conclusion that relative to cofactor (B2GPI) dependency, aCL and aPS antibodies are two distinct populations of antibodies

(cont. on p. 2)

## READER ANNOUNCEMENTS

- Congratulations to Brian D. Kaider, the winner of the framed color print of the Colorado Rockies, displayed at our booth at AACC! Brian works in the Reproductive Immunology Lab at the Center for Human Reproduction, in Chicago, IL. Thanks to all of you who stopped by to see us at AACC, and/or participated in our drawing.

- **Clinical Laboratory Management Association (CLMA) Annual Conference**, August 22-25, 1996, at the Denver Convention Center, in Denver, CO. REAADS Medical Products invites you to visit us at booth #1200-02. We look forward to meeting with you at CLMA.

- The **Seventh International Symposium on Antiphospholipid Antibodies** will convene in New Orleans, Louisiana, on October 9 - 13, 1996. This biennial symposium is held in the United States only every four years, and is an opportunity to learn of the recent advances in the field of Antiphospholipid Antibodies. REAADS will present the following abstracts at the scientific program prior to publication in a regular issue of *Lupus*:

**B<sub>2</sub>GPI Enhances IgG Anti-phosphatidylserine (aPS) Binding Better than Anticardiolipin (aCL) Antibodies.** Keedy KJ and Lopez LR.

**Association of B<sub>2</sub>GPI Cofactor Effect of IgG Anti-Phosphatidylserine (aPS) Antibodies with History of Thrombosis, Thrombocytopenia and Recurrent Abortion in SLE Patients.** Keedy KJ and Lopez LR.

- The **American College of Rheumatology** will hold their 60<sup>th</sup> National Scientific Meeting October 18 - 22, 1996, in Orlando, Florida. The following abstract has been accepted for presentation:

**B<sub>2</sub>GPI Enhances IgG Anti-phosphatidylserine (aPS) Binding Better than Anticardiolipin (aCL) and Correlates with Clinical Manifestations of Antiphospholipid Syndrome in SLE Patients.** Keedy KJ and Lopez LR.

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## READER PRODUCT FEATURE

### **REAADS Anti-Phosphatidylserine ELISA Test Kit**

For *in vitro* Diagnostic Use

Assay format -	96-well micro plate (8 x 12)
Antigen substrate -	Brain phosphatidylserine
Conjugate -	Horseradish peroxidase (HRP)/goat $\alpha$ human IgG/IgM
Chromogenic substrate -	TMB
Sample dilution -	1:50
Incubations	
Sample -	15 min @ room temp.
Conjugate -	15 min @ room temp.
Substrate -	10 min @ room temp.
Stopping solution -	2.5 N Sulfuric acid
Wavelength -	450 nm
Clinical specificity -	IgG: 96%, IgM: 96%
Clinical sensitivity -	SLE: 32% IgG; 7.5% IgM
	SLE with thrombosis: 54% IgG; 15% IgM

(cont. from p. 1)

and further confirms that aPS antibodies are more clinically relevant than aCL for the serologic diagnosis of the anti-phospholipid syndrome. The laboratory measurement of aPS antibodies with higher B<sub>2</sub>GPI dependency may be a better marker to assess the risk of thrombosis. REAADS aPS assay provides bovine serum in the sample diluent as a source of B<sub>2</sub>GPI, and measures both cofactor-dependent (anti-phosphatidylserine/cofactor complex subset) and independent antibodies (true anti-phosphatidylserine) which may be present only in patients with the anti-phospholipid syndrome.

- **REAADS has** moved to a new and larger facility in the same building complex. Our new mailing address is:

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Our phone and fax numbers remain the same.