Cleveland Clinic Innovations

PRODUCT
Diagnostic assay.

INDICATION
Antiphospholipid Syndrome (APS).

VALUE PROPOSITION
- Novel production method for scalable manufacturing/ increased yields for anti-ß2GPI assays.
- Increased standardization, avoiding use of human plasma, and more efficient ß2GPI production.

DEVELOPMENT STAGE
- rß2GPI production process established and validated.
- Additional resources needed for development of vitro diagnostic test kit/commercial assay manufacturing.

INTELLECTUAL PROPERTY
Issued US Patent 11,661,447.

RELATED PUBLICATIONS

- Chaturvedi S, McCrae KR. Curr Rheumatol Rep. 2017 Jul;19(7):43. PMID: 28711993.
- Chaturvedi S, McCrae KR. Blood Rev. 2017 Nov;31(6):406-417. PMID: 28784423.

CONTACT INFORMATION

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Novel Diagnostic Assay for Antiphospholipid Syndrome

Keith R. McCrae and colleagues – *Lerner Research Institute*

UNMET NEED

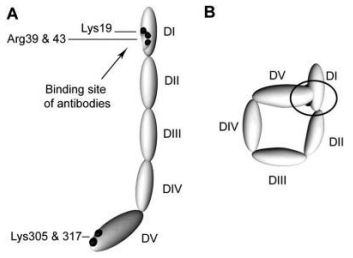
Antiphospholipid syndrome (APS) is the most common cause of acquired thrombophilia and a major cause of vascular morbidity and mortality. APS is defined by the development of arterial and venous thrombosis, or recurrent fetal loss, in patients with antiphospholipid antibodies (APLA). Beta2-glycoprotein I (ß2GPI) is the primary antigen for pathologic autoantibodies in patients with APS. A majority of diagnostic assays currently at market use native ß2GPI purified from plasma.

While there are several anti-β2GPI assays on the market, all of these use purified plasma β2GPI. Purification of β2GPI from plasma is difficult, and most procedures utilize a perchloric acid precipitation step which may oxidize and cause conformational alterations in β2GPI that affect its antigenicity. Moreover, while recombinant ß2GPI (rß2GPI) commercial kits are available, they are expensive to manufacture and only use a singular protein domain.

SOLUTION

Cleveland Clinic researchers have developed a novel alternative methodology through cloning ß2GPI into a lentiviral expression vector and substituting a kininogen leader peptide for the ß2GPI leader peptide in rß2GPI. Purification of rß2GPI is also simplified by using a heparin affinity column and high salt elution in comparison to harsh acidic, basic, or oxidizing solvent exposure. The result is a full sequence rß2GPI inclusive of protein domains 1-5. This novel expression system combined with high-efficiency purification results in an efficient method of rß2GPI production, generating high-quality protein that can be produced at scales suitable for the manufacturing of commercial products and diagnostic kits.

Our recombinant β2GPI will allow us to develop anti-β2GPI ELISAs that offer superior sensitivity, specificity and most importantly, reproducibility, than currently available assays



Proposed structures of the open and closed forms of β2GPI