

# Lipoprotein-Associated Phospholipase A<sub>2</sub> (PLAC™)

## *RISK MARKER FOR CORONARY HEART DISEASE AND ISCHEMIC STROKE ASSOCIATED WITH ATHEROSCLEROSIS*

### Introduction

Lipoprotein-associated phospholipase A<sub>2</sub> (Lp-PLA<sub>2</sub>) is a calcium independent enzyme that is associated with low-density lipoprotein (LDL) in human plasma. It is produced by macrophages and is specific for cardiovascular disease. Research has suggested that Lp-PLA<sub>2</sub> is involved in the oxidative modification of LDL that can lead to plaque formation and the generation of pro-inflammatory molecules. These molecules can recruit macrophages and contribute to the formation of atherosclerotic plaques.

### Methodology

The diaDexus PLAC™ test is a non-competitive (sandwich) microtiter enzyme-linked immunosorbent assay (ELISA) that employs two monoclonal antibodies to quantitatively measure the concentration of Lp-PLA<sub>2</sub> in human serum or plasma, and is calibrated to a recombinant protein standard.

### Clinical Background

Lp-PLA<sub>2</sub> has been shown to be an independent risk factor for coronary heart disease (CHD) and ischemic stroke in several studies. A meta-analysis of 14 studies demonstrated a twofold increase in CVD risk with elevated concentrations of Lp-PLA<sub>2</sub>, indicated that it may be useful in risk stratification, and can be useful as a novel CVD marker. In a retrospective case-control study using specimens from hypercholesterolemic men (WOSCOPS), a nearly threefold greater risk of CHD was seen for subjects in the upper quintile of Lp-PLA<sub>2</sub> concentrations. In a case-cohort study (ARIC), Lp-PLA<sub>2</sub> was a significant predictor of CHD risk, particularly in individuals with LDL <130 mg/dL. A significant interaction between Lp-PLA<sub>2</sub> and LDL was found and for individuals in the high LDL group, Lp-PLA<sub>2</sub> was predictive when higher Lp-PLA<sub>2</sub> cutpoints were used. Both studies (WOSCOPS and ARIC) found that Lp-PLA<sub>2</sub> was independent of the inflammatory CHD marker, C-reactive protein. The ARIC study also showed that Lp-PLA<sub>2</sub> is additive to hs-CRP in risk prediction. In addition, preliminary analyses from the MONICA Augsburg cohort have shown that Lp-PLA<sub>2</sub> concentrations predict a 14 year risk of events in men with moderately elevated cholesterol concentrations. In the ARIC cohort, Lp-PLA<sub>2</sub> concentrations were significantly higher in stroke cases than non-stroke subjects. Elevated Lp-PLA<sub>2</sub> concentrations presented an almost twofold increase in stroke risk, regardless of other risk factors. Further analyses showed that individuals with the highest concentrations of Lp-PLA<sub>2</sub> and systolic blood pressure were at the greatest risk of suffering an

ischemic stroke, conferring an over sixfold increase in stroke risk. Lp-PLA<sub>2</sub> is related to vascular inflammation and is not elevated in systemic inflammatory conditions, providing consistent and reliable results regardless of a patient's other clinical conditions.

### Laboratory Diagnosis

Lp-PLA<sub>2</sub> can be used to determine cardiovascular risk, both of coronary heart disease and cerebrovascular disease. A cutpoint of 235 ng/mL, which is the median of a healthy population, is recommended. Lp-PLA<sub>2</sub> concentrations <235 ng/mL are associated with a low risk of CVD, while concentrations >235 ng/mL are associated with a high risk of CVD.

### Indications for Ordering

The determination of Lp-PLA<sub>2</sub> should be used in conjunction with clinical evaluation and patient risk assessment to assist in predicting patient risk of cardiovascular disease. This test does not replace blood cholesterol tests or the use of other traditional risk factors for CHD. It does provide additional risk information when used in conjunction with other traditional markers. The following patients are candidates for Lp-PLA<sub>2</sub> testing:

1. Intermediate-risk persons with one to two traditional risk factors.
2. High-risk coronary risk equivalent patients, even if treated, to see if their plaque is still unstable.
3. Borderline lipid patients, to see how aggressive to be with an LDL-C of 131 mg/dL or an HDL-C of 39 mg/dL.
4. Borderline hypertension in apparently healthy patients. The risk of stroke may be 3.5 to 6.8 times higher than those with low blood pressure and low Lp-PLA<sub>2</sub>.

### Test Highlights

- Features:
  - Dual monoclonal ELISA methodology for high analytic specificity
  - Calibrated to a recombinant protein standard for consistency of results
- Benefits:
  - Independent of other inflammatory markers
  - Specific for inflamed plaque and not elevated by common inflammatory conditions, in contrast to systemic inflammatory markers
  - Can improve risk assessment for both CHD and ischemic stroke

## References

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## Test Information

**0081055**

### **Lipoprotein-Associated Phospholipase A<sub>2</sub> (PLAC™ Test)**

For specific collection, transport, and testing information, refer to the ARUP Web site at [www.aruplab.com](http://www.aruplab.com).

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at [www.arupconsult.com](http://www.arupconsult.com).