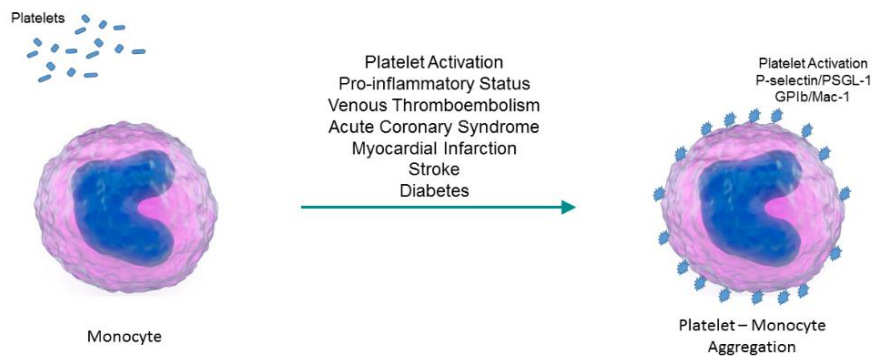




### Platelet – Leukocyte Aggregate Testing

Increasing evidence implicates platelets as key cellular mediators of inflammation and vascular disease. Platelets express and secrete a variety of molecules and inflammatory mediators, such as platelet factor 4, P-selectin, CD40L, vWF, CD63, thrombospondins, MMPs, polyphosphates, ADP, thromboxane, nitric oxide, IL-1 $\beta$  and GPIb. Many of these mediators promote recruitment of leukocytes to sites of endothelial damage or tissue inflammation and this pathway likely contributes to pathogenesis of inflammatory and cardiovascular diseases, such as atherosclerosis, diabetes, and rheumatoid arthritis.

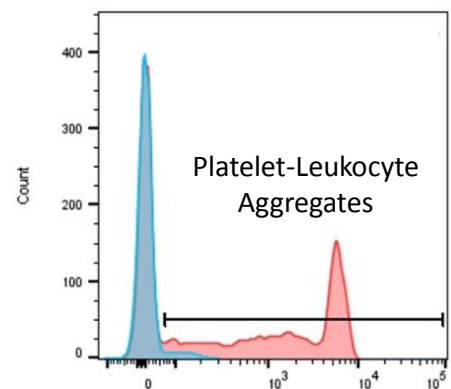
Targeting these pathways represents a potentially important therapeutic opportunity to ameliorate cardiovascular and inflammatory associated diseases. Thus, evaluating platelet-leukocyte aggregates in circulating blood can provide an early, non-invasive marker for potential therapeutic benefit, or to rule out the onset of cardiovascular and inflammatory disease.



**Platelet – Leukocyte Aggregation (PLA) is a sensitive marker for *in vivo* inflammation and platelet activation, and can be elevated in a variety of disease states.**

PLA testing is performed using multi-color flow cytometry. Anticoagulated whole blood, collected from study subjects or healthy donors, is incubated with or without relevant agonists to promote PLA formation. This approach indicates basal levels of *in vivo* inflammation or platelet activation, as well as the potential for PLA formation following *in vitro* stimulation. Following stimulation, the blood sample is labeled with an antibody cocktail specific for platelets and the leukocyte of interest, such as monocytes. The red blood cells are then lysed, and the final sample is analyzed by flow cytometry to determine the percent of leukocytes that have platelets bound to them.

At CirQuest, our expertise in specialty hematology testing will complement your drug discovery, pre-clinical, and clinical pursuits. Our highly trained research and project management team will work with you to identify your needs, outline testing, and customize methodology, if necessary, to meet your needs. Previous custom method development has included stabilizing patient samples at clinical sites for shipment and in-house testing.



Whole blood treated with saline (blue) or agonist (red), labeled with fluorescent antibodies, and analyzed by flow cytometry to generate histograms indicating platelet-leukocyte aggregates.