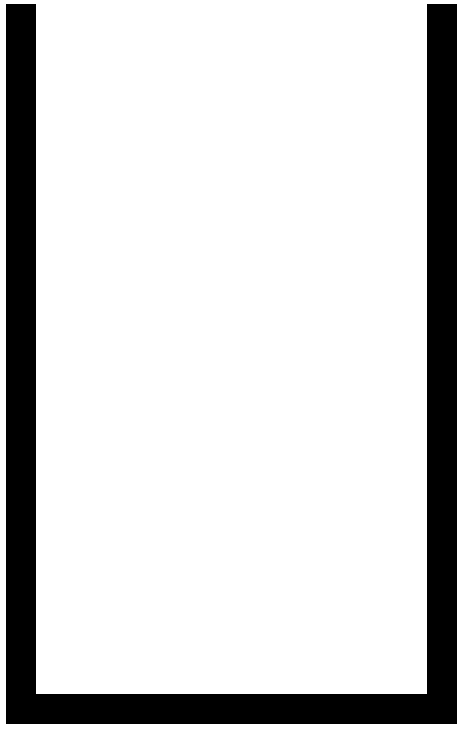
Platelet binding to leukocytes is a normal response to vascular damage and inflammation, however excessive platelet/leukocyte interactions have significant pathologic potential due to the ability of platelets to directly stimulat e leukocytes. Formation of stable platelet/granulocyte aggregates (PGAs) induces neutrophils to releas e inflammatory cytokine/chemokines and damaging proteases, produce reactive oxygen species, and upregulate adhesion molecule and tissue factor expression. High levels of circulating PGAs are found in patients with diverse inflammatory vascular diseases, and animal models of vascular injury have shown benefits to limiting PGA formation in vivo . The complement system enhances PGA formation in human blood stimulated with thrombin receptor-a ctivating peptide (TRAP), however precise mechanisms for the effects of complement are unknown. Here, we utilized ex vivo and in vitro flow cytometry assays to show that properdin, a positive regulator, and Factor H (FH), a negative regulator, of the alternative complement pathway (AP) have key roles in controlling the extent of TRAP-mediated PGA formation in human whole blood. Physiological properdin oligomers added exogenously to TRAP-stimulated whole blood enhance



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