Abstract
Dengue infection causes thousands of death every year around the globe. Although the pathophysiology of dengue infection is well studied, my PhD work focused specifically towards investigating the role of platelet activation in dengue infection pathogenesis. Our data describe a direct correlation between genome copies of Dengue virus (DV) in infected-platelets and the platelet activation in vitro and in patients. Our data also show the direct correlation between DV-mediated activation of platelets with platelet clearance mechanisms such as complement/antibody-mediated lysis of platelets, monocyte-mediated engulfment of platelets, and platelet agglutination and thrombus formation in vitro. Since we observed the phagocytosis of DV-activated platelets by monocytes, we further investigated the mechanism of DV replication in monocytes in presence/absence of platelet proteins to determine whether platelet activation influences viral propagation in patients. We identified the platelet chemokine, platelet factor-4 (PF4) as the potent enhancer of DV replication in monocytes. Data from patients also show the direct correlation between elevated plasma PF4 and DV replication in monocytes. Therefore, our works together provide new insight into the role of platelet activation in Dengue pathogenesis, specifically showing that platelet activation determines the outcome of the disease. Our study suggests that a careful strategy of inactivation of platelets may rescue platelets from rapid destruction. Further, the inhibition of PF4 or CXCR3 (PF4-receptor) may rescue from acute infection of DV.