INTRODUCTION

Platelets play a major physiological role in control of vascular integrity at the site of vascular lesions. However, the pathophysiological role of platelets is much broader than regulation of hemostasis and thrombosis. Platelets are critical elements in linking and modulating thrombosis, inflammation, and tissue repair. Platelets are stimulated by a variety of agonists including thrombin or ADP and also by inflammatory agents such as antibodies, complement, bacteria, and others. Platelets contribute to inflammation by interacting with inflammatory cells via adhesion and secretion of prestored proinflammatory mediators. Thus, platelets are critical elements in the pathophysiology of inflammation and modulate significantly a variety of inflammatory diseases. A profound understanding of the molecular mechanisms underlying the role of platelet in
inflammation may result in new therapeutic strategies in acute and chronic inflammatory diseases.

THE PLATELET, THE INFLAMMATORY CELL

The fundamental role of platelets is to maintain the vascular integrity and to prevent loss of blood at sites of vascular injury. Under physiological conditions platelets circulate in the artery branch without interacting with each other or with structures of the intact vessel wall (1). At the location of an endothelial disruption, subendothelial matrix proteins including collagen and von Willebrand factor (vWF) are exposed to circulating platelets that are recognized by specific platelet membrane receptors such as glycoprotein (GP)VI (2) or the plasma membrane complex GPIb-IX-V (3-5). Once adherent to the subendothelium, platelets spread on the surface and release granule-stored components that recruit additional platelets to the arterial lesion. In addition, adhering platelets express the activated form of the fibrinogen receptor GPIIb-IIIa that mediates platelet aggregation through formation of fibrinogen bridges between two adjacent platelets (6,7) (Fig. 1).

Despite regulation of hemostasis, platelets are involved in thrombosis and inflammation. Hemostasis, thrombosis, and inflammation are complex mechanisms with overlapping steps and connecting pathways. Interactions between platelets and inflammatory cells (e.g., endothelium, leukocytes) take place at various stages of the inflammatory process (8). They occur in the circulation as well as in extravascular inflammatory sites and are regulated through adhesion receptors and proinflammatory mediators that are released from internal stores of activated platelets. Platelets have been shown to be involved in inflammatory diseases caused by pathogens including bacteria, viruses, or parasites, leading to infectious endocarditis, sepsis, or the acquired thrombocytopenia that occurs during retroviral infections caused by the human immunodeficiency virus (HIV) and T-cell lymphotropic virus (9) (Table 1). In these diseases platelets participate in nonspecific immunodefense mechanisms caused by exogenous pathogens. Furthermore, platelets are involved in acute and chronic inflammation that is not directly related to infectious pathogens including diseases such as acute respiratory distress syndrome (ARDS), systemic inflammatory response syndrome, immune complex disease, allergic asthma, inflammatory bowel disease (10), multiple organ failure in septic shock (11,12), organ dysfunction associated with cardiopulmonary bypass (13), or acute coronary syndromes (14) including acute myocardial infarction and reperfusion (15,16) (Table 1). Moreover, platelets are fundamentally involved in chronic inflammatory