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## **Platelets and their Role in Innate Immunity**

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Although platelets are best known as primary mediators of hemostasis, this function intimately acquaints them with inflammatory processes and it has been increasingly recognized that platelets play an active role in both innate and adaptive immunity. For example, when aggregated on damaged vessel walls, activated platelets capture circulating leukocytes and attract them to the inflamed tissue. This aggregation response was considered the ultimate platelet function, but in the 1990's reports began to emerge that suggested that platelets may in fact play an active role in the stimulation of innate immunity. Platelets can secrete several pro-inflammatory cytokines that can affect local inflammatory responses and may regulate classical humoral immune responses via CD40/CD40L interactions. They may thus represent an important linkage between inflammation and thrombosis, which is important in disease processes such as atherogenesis. Platelets are also known to bind and phagocytose microorganisms and several viruses have been shown to have cross-reactivity with platelet antigens, potentially important in the development of autoimmune thrombocytopenia. Perhaps more surprisingly, platelets have recently been shown by many laboratories to express several different Toll-like receptors perhaps allowing them act as primary circulating sentinel cells that first encounter bacterial products (e.g. LPS) for presentation and activation of innate immunity. Recent work on platelet TLR4 in particular, has elucidated the role of platelets in sepsis and a better understanding of this central role of platelets as defensive cells may be important for the potential development of efficient therapeutic modalities against infectious agents. It appears that not only is the thrombocytopenia of sepsis dependent on platelet TLR expression, but platelets can also present bacterial products to mononuclear cells modulating their inflammatory cytokine secretion patterns and phagocytosis which has implications for both autoimmune and alloimmune platelet disorders. This talk will discuss the central role that platelets play in inflammation linking them with varied pathological conditions such as atherosclerosis, sepsis and immune thrombocytopenic purpura and will argue that platelets can act as primary mediators of innate immune defenses.

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