Platelets on the move - key players in innate immunity

Platelets not only play an essential role in the formation of blood clots and sealing of wounds - they actively migrate and support our body’s innate immune response during bacterial infections.

Vertebrates possess a closed circulatory system pumping blood through a network of vessels carpeted by an endothelial cell barrier that covers a surface area of about seven square meters in adult humans. Vascular leakage is a threat to life and maintenance of vascular integrity is thus crucial for survival. Hemostasis is the physiological response to vascular injury that prevents excessive bleeding and maintains vascular integrity. In the human body two major mechanism are involved in hemostasis - the initiation of blood coagulation and the activation of platelets.

Billions of platelets constantly circulate in our bloodstream. They are the smallest blood cells of our body and do not even have a nucleus. Yet they are equipped with a toolbox of highly sensitive surface receptors that allows effective scanning of the vasculature for potential breaches. Having detected an injury platelets adhere and spread on proteins of the sub-endothelial cell layer. Many platelets then interact with each other to form a tight network that seals the leak like a sticking plaster.

In a Darwinian world, organisms live under a constant threat of pathogenic invaders, and vascular damage not only causes blood loss, but also presents a port of entry that has to be guarded instantaneously. Linked to the urgency of the hemostatic response platelets are among the first cells that encounter these sites of injury and establish the first line of host defense. Indeed, an ancient link between hemostasis and host defense was suggested by comparative studies analyzing more primitive blood of invertebrates. The Atlantic horseshoe is a marine anthropod whose origin can be traced back over 400 million years. Living in ocean waters horseshoe crabs face an environment colonized by huge numbers of potentially pathogenic microorganisms and any injury to their outer shell increases the risk of infection. 400 million years of survival however have certainly proven that these animals have developed highly efficient strategies to deal with these constant threads. In contrast to the complexity of human blood, horseshoe crabs possess only a single blood cell, the amebocyte. Following injury amebocytes migrate to the wound, aggregate and retract to seal the lesion while at the same time encapsulating and phagocytosing invading pathogens.

During the last decades researchers collected striking evidence supporting the idea that platelets, similar to amoebocytes, do not only form clumps to prevent bleeding, but indeed bind to and fight blood-borne pathogens. However, it remained largely unknown how sticking platelets do get in close contact with the invaders. An essential feature of immune cells is their ability to actively migrate within the body in order to detect and eliminate their prey. New insights from live cell microscopy now show that platelets are not only passively sticking to the vessel wall but are also capable of active locomotion. When adhering to sites of injury and inflammation they start to migrate and actively explore their immediate environment. When they encounter foreign particles, such as invasive bacteria, they use the traction associated with locomotion to collect them into bundles, rather like street-sweepers piling up debris. Platelets themselves cannot eat and digest these bundles but secure and present them on their surface. They get support from neutrophils, a blood cell specialized in phagocytosis, which in turn is activated by those platelet-bacteria bundles and finally engulfs the trapped microbes.

In summary, these findings support the concept that evolution provided circulating blood platelets to not only prevent blood loss after injury, but also as an efficient defense line to constantly scan the vascular system for potential invaders. The ability to migrate enables platelets to do their job as full-fledged immune cells.