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Platelets Unplugged

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Platelets are small anucleate cellular fragments that are actively extruded into circulation at a rate of approximately 85 million per day from megakaryocytes residing in the bone marrow. The bleeding tendency in individuals with inherited or acquired defects in platelet number and/or function demonstrated the importance of these cells in hemostasis. In the last half of the 20th century, seminal work uniting basic and clinical efforts established the crucial role of platelets in arterial thrombosis. Certain unique features of platelets make them very amenable to drug targeting, and anti-platelet therapy is now among the most commonly prescribed and used class of medications. In this *Arteriosclerosis, Thrombosis, and Vascular Biology* review series, we present articles that highlight recent advances in several facets of platelet biology by leaders in the field.

Platelets have evolved to circulate in an inactive or resting state with the capacity to rapidly respond to disruption in vascular integrity and form a primary platelet plug that prevents bleeding. Because of the ability to isolate them relatively unperturbed from blood, platelets have historically served as a model system in which to study cellular signal transduction. Indeed, many of the fundamental aspects of G-protein coupled receptor and integrin signaling were first elucidated in platelets. In their article “Signaling during platelet adhesion and activation”, Li et al. discuss the latest concepts in G-protein coupled receptor, ITAM-, integrin-, and GPIb-mediated adhesive signaling in platelets. The extension in life expectancy that has occurred as a result of societal and medical advances has been accompanied by the development of age-related atherosclerotic vascular disease. As we live longer, the robust responses of platelets have the unwanted effect of contributing to arterial thrombosis. This is compounded by modern lifestyle and dietary behavior that escalates atherosclerosis and influences the propensity of platelets to activate and aggregate. Zimman and Podrez detail the current understanding of the impact of plasma lipid components on platelet function in their article, “Regulation of platelet function by class B scavenger receptors in hyperlipidemia”.

Growing evidence indicates that platelets factor into homeostatic mechanisms other than hemostasis. In lower organisms, thrombocytes participate in both hemostatic and immune responses. Thus, it is not surprising that mammalian platelets may retain residual capacity to influence inflammation, which is the topic of the article, “Platelet-leukocyte interactions in atherothrombosis and beyond” by Totani and Evangelista. They describe how platelets may link thrombosis and inflammation and discuss the evidence in support of a role for platelets in inflammatory disorders, including atherosclerosis. Cardiovascular disease and cancer, the leading causes of death in the United States and other developed countries, share common risk factors, including age and diet, and both are associated with a propensity for thrombosis.

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Jain et al. discuss the evidence that platelets may play a specific role in cancer progression and metastasis in their article entitled “Platelets in angiogenesis and cancer”. The ability of platelets to influence angiogenesis suggests the possibility that they may participate in vascular development. Exciting new findings supporting a role for platelets in the formation of lymphatic vessels during development are the topic of the article by Bertozzi et al. “Platelets: covert regulators of lymphatic development”.

Finally, bringing the series back to clinical application, Williams et al. summarize the approaches being used to associate genetic variants with platelet hypo- and hyperresponsive phenotypes and the ramifications of these associations in the clinical use of anti-platelet therapies.

In summary, this series of review articles illustrates the contribution of platelets to an assortment of processes, beginning soon after conception and extending to the proximate causes of most deaths in Western countries. The implications for health and disease may be profound in terms of the possibility of developing new anti-platelet therapies and the prospect that existing medications may have novel applications and untoward side effects. The articles are intended to enlighten individuals unfamiliar with the diverse aspects of platelet biology and serve as a useful resource for those already working in the field.

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