Platelets Unplugged: An ATVB Special Series Focused on Platelet Biology

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Platelets are small anucleate cells 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 features of platelets make them amenable to drug targeting, and antiplatelet therapy is among the most commonly prescribed and used class of medications. In this issue of Arteriosclerosis, Thrombosis, and Vascular Biology, 6 review articles by leaders in the field and 7 original articles cover recent advances in several facets of platelet biology.

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 for studying 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 and ITAM-, integrin-, and platelet glycoprotein Ib–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; both are associated with a propensity for thrombosis. Jain et al discuss the evidence that platelets may play a specific role in cancer progression and metastasis in their article entitled "Platelets: Linking Hemostasis 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 hyporesponsive and hyperresponsive phenotypes and the ramifications of these associations in the clinical use of antiplatelet therapies.

In summary, this issue of ATVB 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 antiplatelet therapies and the prospect that existing medications may have novel applications and untoward adverse effects. The articles are intended to enlighten individuals unfamiliar with the diverse aspects of platelet biology and serve as a useful resource work for those already working in the field.

Sources of Funding
This work was supported by grants HL070304 and HL080166 from the National Institutes of Health and resources from the Lexington VA Medical Center.

Disclosures
Dr Smyth is the recipient of an investigator-initiated grant from the Medicines Company and AstraZeneca.

References

Key Words: platelets
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Arterioscler Thromb Vasc Biol. 2010;30:2339-2340
doi: 10.1161/ATVBAHA.110.217992
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2010 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/30/12/2339

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