blood® Editorial

Introduction to a review series on platelets and cancer

To the casual biologist, platelets may appear to be quite simple. Small and lacking nuclei, they are rather unassuming, but their small size and seemingly simple structure belie a potency that gives these cells important roles in many physiological and pathological processes beyond hemostasis and thrombosis. These processes include atherosclerosis and its thrombotic consequences,[1,2] inflammation,[3,4] wound healing,[5] angiogenesis,[6] lymphangiogenesis,[7,8] and even Alzheimer disease and other neurodegenerative diseases.[9,10]

Many factors account for the versatility of platelets. For example, the platelet surface is densely coated with adhesive proteins and agonist receptors that allow the platelets to physically interact with many substrates and other cells and to respond to a wide variety of stimuli.[11] Platelets are also endowed with an extensive repertoire of biologically active proteins that they carry in their α granules, which they can release when activated by any of a plethora of signals.[12] These proteins include adhesive proteins; clotting proteins, such as factor V, fibrinogen, and von Willebrand factor; chemokines, such as platelet factor 4 and β-thromboglobulin; growth factors, such as vascular endothelial growth factor, transforming growth factor-β, and platelet-derived growth factor; and other proangiogenic and antiangiogenic proteins. The other major platelet secretory granule, the dense granule, contains other molecules with potent biological effects, including adenosine 5′-diphosphate, serotonin, and polyphosphate.[13] Platelets also possess extensive and redundant internal membranes, which they can extrude to increase their membrane surface area severalfold.[14] Finally, when activated, platelets can externalize the anionic phospholipid phosphatidylserine (PS) from the inner leaflet of the plasma membrane and bud off extracellular vesicles from the plasma membrane rich in externalized PS.[15] The outward-facing PS serves many functions, including providing a platform for the enzymatic reactions of blood coagulation and signaling to other cells with receptors for PS. The PS may also enable the membrane vesicles, and possibly the activated platelets, to fuse with target cells, not only changing the composition of the target membrane but delivering cytosolic contents including messenger RNA and microRNAs.

All of these capabilities of the platelets are in play in another important and emerging role for platelets that is the topic of the current review series: their interface with cancer cells. This interface is bidirectional. The platelets influence several aspects of cancer biology, including cancer growth and metastasis, immune evasion, tumor angiogenesis, and sometimes the slowing of tumor growth. The platelets exert their influence in a variety of ways, which are discussed extensively in the reviews. Tumors, in turn, can also affect the number, behavior, and even phenotype of the platelets through a process called platelet "education." Finally, the evidence for and against the possibility that antiplatelet therapies may in some cases also serve as anticancer therapies is also explored. The 4 reviews in the series are:

- Harvey G. Roweth and Elisabeth M. Battinelli, "Lessons to learn from tumor-educated platelets"
- Silvia D'Ambrosi, R. Jonas Nilsson, and Thomas Wurdinger, "Platelets and tumor-associated RNA transfer"
- Sophia Lazar and Lawrence E. Goldfinger, "Platelets and extracellular vesicles and their cross talk with cancer"
- Derrick L. Tao, Samuel Tassi Yunga, Craig D. Williams, and Owen J. T. McCarty, "Aspirin and antiplatelet treatments in cancer"

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