youngster than 65 years of age), with no co-morbidities such as history of DVT or arterial thromboembolic events, recent orthopedic surgery or vertebroplasty, immobilization, inherited thrombophilic abnormalities, history of coronary ischemic disease, atrial fibrillation. Nevertheless, the dose of dexamethasone is also a major risk factor and should be considered when deciding on the type of VTE prophylaxis. Thus, based on this study by Larocca et al, in newly diagnosed MM patients treated with lenalidomide and low–dose dexamethasone who are at low risk for VTE, aspirin reduces the risk of VTE to < 3% and may be considered an appropriate form of thromboprophylaxis.

According to the design of the study, the expected incidence of VTE in the aspirin group will be 12% to 67%. However, we must acknowledge that we do not know the real incidence of VTE in young MM patients with no risk factors for VTE who receive lenalidomide with low–dose dexamethasone without any type of prophylaxis. If one had to provide an estimate, one could anticipate that this risk would be well below 10%.

While this study by Larocca et al addresses the issue of prophylaxis in low–risk patients, we still need data from prospective studies to define the optimal thromboprophylaxis regimen for patients treated with lenalidomide–based induction regimens at intermediate or high risk for VTEs or those treated with lenalidomide and high–dose dexamethasone. Based on currently available data, it seems that aspirin may not be adequate for patients at intermediate or high risk and these patients should receive LMWH for at least the initial phase of induction. New antithrombotic agents (thrombin and factor Xa inhibitors) may also be evaluated in this context. Finally, genetic polymorphisms that have been shown to play a role in the development of VTE in patients treated with thalidomide–based regimens may also prove to be of value.

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REFERENCES


Comment on Ubukawa et al, page 1036

Exit strategy: one that works

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Enucleation is the culmination of terminal erythroid differentiation. It results in the release of 2 million new enucleate reticulocytes into your circulation and mine each second. In this issue of Blood, Ubukawa and colleagues shed new light on the mechanism, showing that non–muscle myosin IIb is intimately involved.1

Mammalian red cells and their immediate precursors, reticulocytes, are, unlike their counterparts in some other vertebrates, devoid of nuclei as a result of an “asymmetric” cell division at the final step of terminal erythroid differentiation. Fission of the erythroblast generates the enucleate reticulocyte and a larger moiety in which an extruded nucleus is encased in a plasma membrane (pyrenocyte).2 There has over many years been keen interest in defining the molecular machinery responsible for enucleation and in the similarities and differences between this process and classic cytokinesis, which produces 2 identical daughter cells. By studying and comparing both processes, Ubukawa and colleagues offer new insights into the roles of various cytoskeletal proteins in the 2 cases.

Inhibition of non–muscle myosin II ATPase by blebbistatin blocked both cell division and enucleation, implying its participation in both processes and establishing a previously undefined role for myosin in enucleation. Non–muscle myosin IIa and myosin IIb are both

Photomicrographs illustrating the different steps during the enucleation process. The nucleus is first displaced to one side of the erythroblast (left panel). A contractile actin ring is then formed to begin to pinch off the nascent reticulocyte from the nucleus (middle panel). Subsequent redistribution of membrane between the 2 lobes of the dividing cell by vesicle shuttling further restricts the area of contact between the 2 emerging cells (right panel). Images courtesy of Dr Marcel Bessis.
expressed during terminal erythroid differentiation and while both seem to be involved in cell division, a specific requirement for myosin IIb in enucleation was documented. Moreover, because inhibition of actin polymerization by cytochalasin D blocks both cell division and enucleation, an actomyosin-driven step in enucleation of erythroblasts during terminal erythroid differentiation may be inferred.

Enucleation is a multistep process (see figure) that requires displacement of the nucleus in the erythroblast to one side during the preparatory stage. This is followed by formation of a contractile actin ring, pinching off the nascent reticulocyte from the nucleus, and subsequent redistribution of membrane between the 2 lobes of the dividing cell by vesicle shuttling to restrict the area of contact between the 2 emerging cells. The coordinated execution of these diverse events during a period of 8 to 10 minutes requires complex machinery involving a number of distinct cytoskeletal components, and we hope that future work using genetic tools and state-of-the-art imaging techniques will provide more comprehensive insights into this fascinating biologic process.

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REFERENCES

THROMBOSIS & HEMOSTASIS

Comment on Pleines et al, page 1054

Inside platelets...

Robert K. Andrews and Elizabeth E. Gardiner

In this issue of Blood, Pleines and colleagues show how deletion of the GTPase family member RhoA in murine megakaryocytes/platelets induces macrothrombocytopenia but also protects against occlusive thrombosis or cerebral infarction, providing new insights into both RhoA function as well as platelet-related diseases.1

This multifaceted study of RhoA function in mouse platelets—by conditional gene knockout in megakaryocytes—is pertinent to the production of platelets in the marrow, their survival in the circulation, the hemostatic quality of the platelets in response to prothrombotic stimuli, and their effectiveness in thrombus formation in vivo. These experiments are topical in clinical hematology, because in certain congenital disorders, immune thrombocytopenia,
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