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Cytoskeletal regulation of platelet formation: Coordination of F-actin and microtubules

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Signalling Network Facts

- Blood platelets are released into the circulation from their progenitor cell, the megakaryocyte which resides in the bone marrow.
- The process of platelet production involves maturation of megakaryocytes via endomitosis and the release of platelets from proplatelet extensions. Disruption of these processes can give rise to thrombocytopenia and/ or platelet function disorders.
- The actin and microtubule cytoskeletons are essential for proper maturation and proplatelet formation.
- Recent evidence has highlighted new roles for several proteins (e.g. WASp, Profilin, Pak2) in coordinating actin and microtubules to regulate platelet production.

Abstract

Platelets are small, anucleate blood cells which play an important role in haemostasis. Thrombocytopenia is a condition where the platelet count falls below 150 x 10^9/litre and patients suffering from severe forms of this condition can experience life-threatening bleeds requiring platelet transfusions. Platelets are produced from large progenitor cells called megakaryocytes which are found in the bone marrow. The process of megakaryocyte maturation and the formation of proplatelets are essential steps in the production of mature platelets and both depend heavily on the actin and microtubule cytoskeletons. Understanding these processes is important for the development of *in vitro* platelet production which will help to treat thrombocytopenia as well as produce model systems for studying platelet-associated disorders. This review will highlight some of the recent advances in our understanding of the role of the cytoskeleton in platelet production, especially the key molecules and signalling pathways that regulate actin and microtubule crosstalk.

Key Words

Megakaryocyte, Platelets, Proplatelet formation, Actin, Microtubules

1. Introduction

Platelets are small, anucleate, circulating blood cells which play a critical role in the process of haemostasis (the prevention of blood loss following injury). The activation of platelets in response to vascular injury, along with vasoconstriction and the coagulation cascade, ensure that blood loss is restricted and promotes repair of damaged vessel walls. The normal platelet count of blood ranges between 150 – 400 x 10^9/litre and human platelets have a lifespan of 8–10 days (Giles, 1981; Leeksma and Cohen, 1955). The average healthy adult produces 10^{11} platelets/day to maintain this count. Thrombocytopenia is a condition where the platelet count falls below the 150 x 10^9/litre threshold. This can be caused by a variety of factors ranging from genetic causes to drug-induced