

THE DYNAMIC CYTOSKELETON OF THE MEGAKARYTOCYTE

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Platelet production is a remarkable and elegant process. Platelets circulate in blood as small discs that are subcellular fragments released by megakaryocytes. Each platelet disc has a rigid trilaminar cytoskeleton formed from layers of a spectrin-based membrane skeleton, a microtubule coil, and a cytoplasmic actin network. Actin filaments connect to the membrane skeleton both directly and indirectly. The barbed ends of actin filaments serve as the joints between spectrin molecules. Targeting of these ends to the membrane skeleton is conferred by adducin, which is bound to the barbed actin filament ends of the resting cell and forms a tight complex between filament ends and spectrin. The sides of actin filaments are connected to the plasma membrane by linkages between the vWf receptor and filamin (FLN). These links align the vWf receptor into linear arrays on the platelet surface and restrict the lateral movement of the spectrin strands. This elaborate cytoskeleton must be assembled when platelets release from megakaryocytes. As megakaryocytes mature they both amplify their DNA content (2N to 64N) and compile huge reserves of plasma membrane that is folded within the cytoplasm. Suddenly, signals are generated that cause the cytoplasm to erode and become protruded in long, thin proplatelet processes. The mechanical forces for proplatelet elaboration derive from microtubule assembly/sliding. Platelets release only from the ends of proplatelet processes and these ends are increased at bifurcations formed by actin filament assembly. However, where and how the spectrin lattice assembles and becomes connected to underlying actin filaments and when the FLN-vWf receptor linkages are imposed on the spectrin lattice are not established. High-resolution structural studies have revealed that the spectrin lattice assembles early in the megakaryocyte and lines the plasma membrane of the proplatelet processes. Surprisingly, proplatelet processes, despite their spectrin coatings, are highly dynamic, converting reversibly from tubes to spread motile lamellae as well as bending and fusing at sites of bifurcations. FLN is also expressed early but vWfR is not linearized on the surface of the proplatelet tube. The implications of these events will be discussed.