Blood platelets are an essential component of the hemostatic response that curbs bleeding from a cut or severed blood vessel. As platelets participate in hemostasis, they present a procoagulant surface to enhance the formation of thrombin via the coagulation pathway; this involves ‘flip-flop’ of phospholipids between the bilayers of the plasma membrane leading to surface exposure of the anionic aminophospholipid phosphatidylserine (PS). Rapid movement of phospholipids between membrane leaflets by scramblase is considered to be the major mechanism involved in PS exposure. An aminophospholipid translocase (APLT) rapidly and specifically transports aminophospholipids from the outer to the inner membrane leaflet, and would be expected to restore asymmetry.

There is heterogeneity in platelets in their ability to form a procoagulant surface, e.g., PS exposure occurs on the smallest platelets, and old platelets in the circulation expose PS, indicating that PS may be a marker for platelet clearance. PS is a hallmark of apoptosis in nucleated cells; platelets contain the cytoplasmic machinery for apoptosis and a proportion of PS-exposing platelets have other apoptotic markers as well, indicating roles for platelet activation and apoptosis in PS exposure.

Although APLT would be expected to restore PPL asymmetry, it becomes inactivated in the subpopulation of PS-exposing platelets such that the procoagulant surface persists. The persistence may have important implications in thrombosis, but the mechanisms involved remain unknown.

Blocking exposed PS on activated platelets, then, may be a target for reduction of platelet procoagulant activity. This has the effect of inhibiting thrombin generation as well as platelet-fibrin clot formation in vitro. In vivo, blocking PS reduces platelet activation and accumulation in a thrombosis model.