Tissue factor (TF) plays a central role in haemostasis serving as protective envelope around vascularised organs. Whether TF expressed by intravascular cells and by circulating or de novo generated microvesicles serve haemostasis or primarily cause thrombosis remains an active area of research. Vessel wall TF contributes to arterial thrombosis and myeloid cell TF is important for both, arterial and venous, thrombus formation in mice. In contrast, the pathophysiological roles of TF expressed by platelets remain uncertain or have been disputed altogether.

Platelet TF mRNA and antigen expression was demonstrated in isolated platelets. Because TF was not only detected in platelets, but also on microvesicles, a passive transfer of leukocyte-derived TF (1) remained a possibility. Another important advance was the demonstration of incompletely spliced platelet TF pre-mRNA that is processed following agonist stimulation into functional TF (2). The delayed protein expression documented in several studies (3) indicated that platelet TF may primarily serve to stabilise thrombi, rather than initiate TF-dependent clot formation and haemostasis.

Brambilla and colleagues (4) now studied in detail the transfer of TF from megakaryocytes to platelets. By employing a myeloblastic cell line and non-transformed bone marrow progenitors differentiated into mature megakaryocytes, these experiments minimised the transfer of pre-mRNA or TF on microvesicles from other bone marrow cells during platelet production. While both fully processed as well as the previously demonstrated pre-mRNA was detected in megakaryocytes, unspliced TF mRNA was selectively transferred into newly generated platelets. Intriguingly, a subpopulation of platelets expressed TF protein, but low to undetectable unspliced TF mRNA. While the experimental setup of platelet release under static conditions in vitro likely fails to completely recapitulate shear induced homeostatic platelet production or megakaryocyte rupture under inflammatory stress conditions, the demonstrated heterogeneity of platelet TF cargo raises important new questions on pre-thrombotic states in humans. Future studies aiming to assess the inter-individual variability in platelet procoagulant potential should simultaneously evaluate TF mRNA and protein cargo in platelets.

Conflicts of interest
None declared.

References