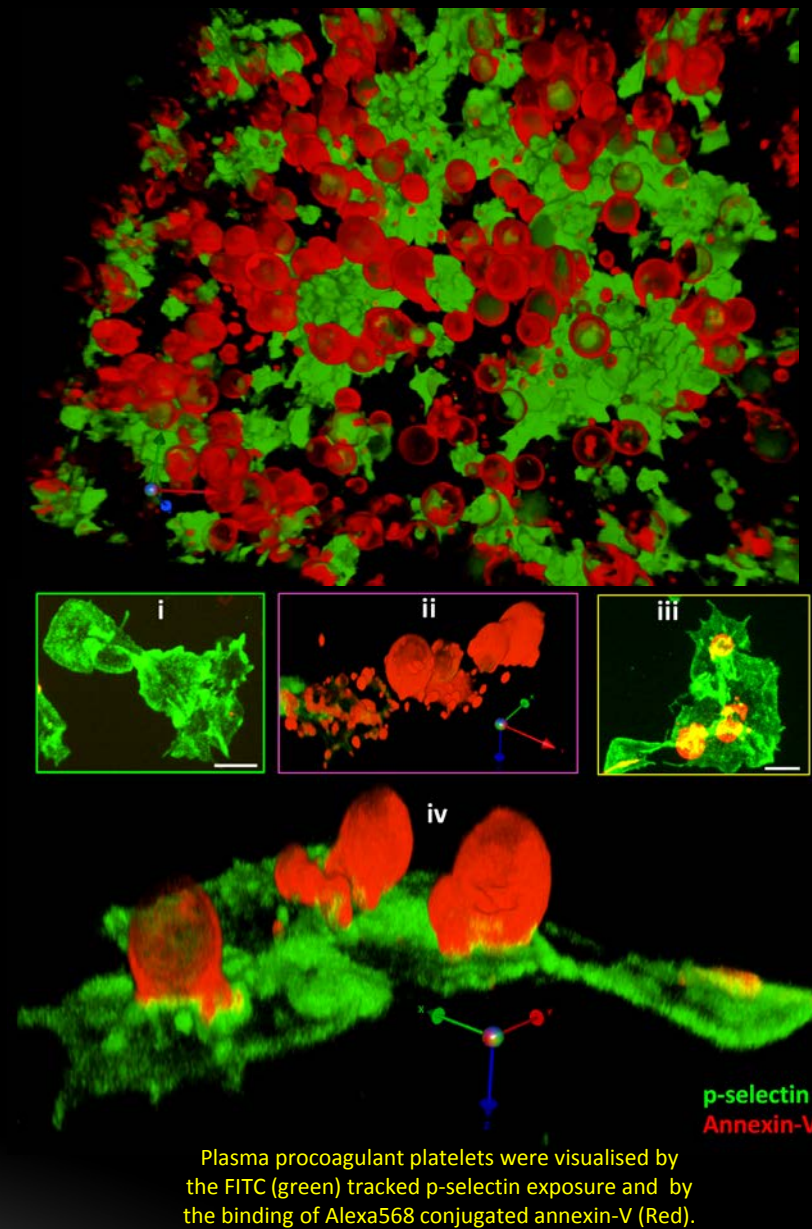


Predicting Perioperative Haemostasis through Procoagulant Membrane Dynamics

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Synopsis

Screening to assess patients' perioperative bleeding or thrombosis risks remain an unmet clinical need for precision medicine; largely because conventional in-vitro tests fail to capture pivotal in-vivo procoagulation mechanisms. Critical to thrombus formation and the haemostatic response is the surface exposure of inner aminophospholipids, particularly phosphatidylserine (PS), which promotes the assembly of the tenase and prothrombinase complexes on the platelet surface to facilitate the generation of thrombin and the localisation of coagulation. We have shown that platelets adhering to subendothelial procoagulant agonists undergo retractable membrane blebbing, membrane evagination and PS externalization, irreversible membrane ballooning, focal-membrane adhesion, procoagulant membrane-spreading, membrane thrombin formation, aggregation as well as membrane shedding/ microvesiculation. Together, we refer to these events as procoagulant membrane dynamics (PMD); and we have demonstrated that PMD is a critical amplifier of blood clotting. Furthermore, we have characterised aspects of the spatiotemporal dynamics and drivers of these dramatic morphological transformations. By using an advanced image-based approach, we are now selectively quantifying elements of PMD and correlating these with patients' perioperative coagulopathies to develop an individualised predictive model of the haemostatic response. We are also pooling these outcomes to innovatively compute numerical indexes (Prog-Index) that are both indicative of patients' status on the coagulation spectrum and amenable to machine learning. We aim to progress this study to develop a novel portable imaged-based device able to assess a patient's thrombosis or bleeding diathesis in 'pinprick' volumes of blood.



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