THE PLATELET SOCIETY

Edition 4

Image Credit: Gagan D. Flora, University of Iowa

Hetty Walker, University of Bristol
Nathan Asquith, University of Oxford
Lauren Murphy, University of Oxford

The Platelet Society
Journal Club

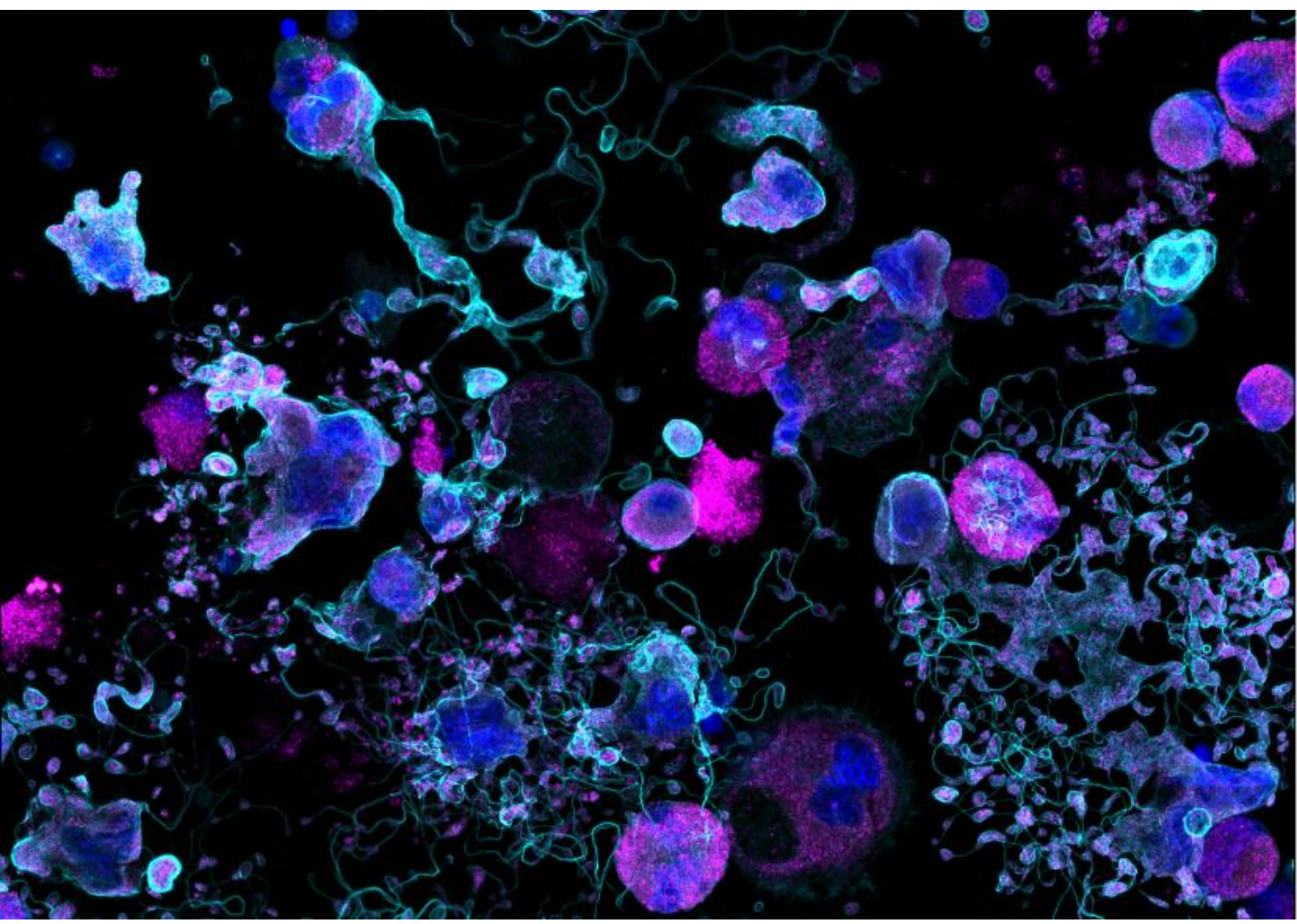


Image Credit: Nathan Asquith, University of Oxford

January 2026

Supporting Research and Education of Platelet Related Diseases

Papers

Interferon-α enhances NK cell function to counteract autologous platelet-mediated tumor immune evasion

L. Wang et al., Cancer Cell International *DOI:*10.1186/s12935-025-04118-w

Platelets suppress natural killer (NK) cell anti-tumour activity by lowering IFN-γ secretion and CD107a degranulation, leading to increased viability of K562 leukaemia cells. Wang et al. cultured NK cells and platelets from 34 healthy donors with K562 cells, observing a drop in NK IFN-γ from <0.45 % to 6.34 % and CD107a from 25.1 % to 20.1 %, while tumour cell survival rose to ~70 % ($p < 0.05$). This platform enables screening of adjunctive agents to counter platelet-mediated evasion and supports NK-cell immunotherapy advanced future clinical strategies.

Proprotein Convertase Subtilisin/Kexin Type 9 Induces Platelet-Derived Transforming Growth Factor-β to Promote Myocardial Fibrosis After Myocardial Infarction

Q. Wang et al., Human Mutation *DOI:*10.1155/humu/4574795

After myocardial infarction, plasma Proprotein Convertase Subtilisin/Kexin Type 9 (PCSK9) rises, activating platelets and releasing Transforming Growth Factor beta (TGF-β), which induces fibroblast-to-myofibroblast transition and collagen deposition, worsening fibrosis. PCSK9-KO mice show reduced platelet activation, 45 % less fibrosis, and improved left ventricular function, linked to down-regulation of Itga2b and immune-adhesion pathways, suggesting therapeutic potential of PCSK9 inhibition in post-MI remodelling strategies.

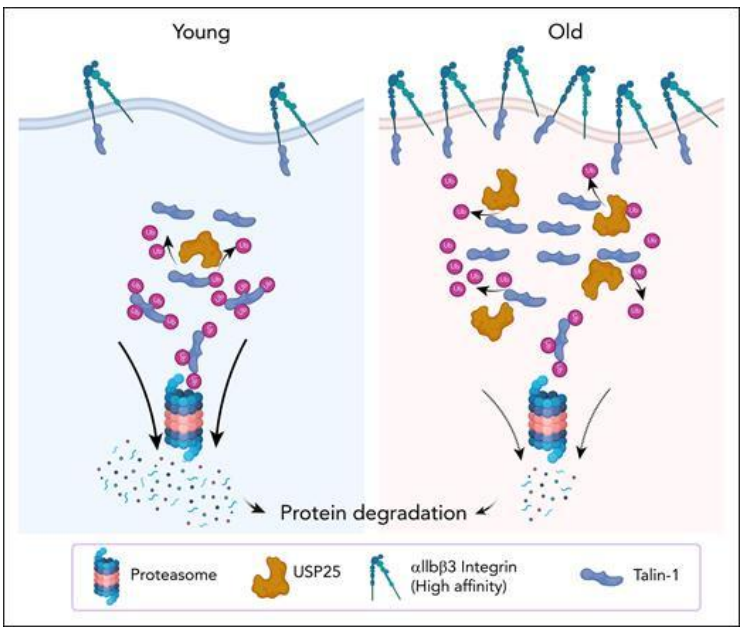
Tethered platelets in Severe Infection

G. Perrella and J. Rayes, Immunology, *DOI:*10.1126/science.aed1243

In severe infection, platelets form novel integrin-αIIbβ3- and CD9-rich tethers that remain anchored to VWF- and fibrin-laden endothelium while the platelet body detaches and re-enters circulation in a hyporesponsive state. Pore-Induced Intracellular Traps (PITTs) recruit neutrophils, promote NET formation, and amplify local inflammation and tissue damage. Depletion of αIIbβ3 from the parent platelet reduces its reactivity, contributing to bleeding complications observed in COVID-19 and sepsis. PITTs arise without classic platelet activation, depend on blood-flow-mediated adhesion, and represent a mechanistic link between thrombosis and inflammation, highlighting potential therapeutic targets to modulate platelet immune functions. Further studies are needed to define their frequency and molecular machinery.

USP25 and Platelet Hyperreactivity in Aging

P. Davizon-Castillo et al., Blood, *DOI:*10.1182/blood.2025031416



Platelet hyperreactivity increases with age, contributing to higher rates of myocardial infarction, stroke, and venous thromboembolism in older adults. Aging impairs proteostasis, altering protein synthesis, folding, and degradation, which sensitizes platelets to stressors such as hyperglycaemia and inflammatory cytokines. Jia et al. identified the deubiquitinase USP25 is up-regulated in aged platelets, where it stabilizes talin-1, enhancing αIIbβ3 integrin activation and collagen-induced aggregation. Genetic deletion or pharmacologic inhibition of USP25 with AZ1 reduces platelet reactivity and arterial thrombosis in mice, suggesting USP25 as a target and biomarker. Limitations include male-only mouse models and focus on stimuli, warranting further investigation in human studies.

Papers

Induction of moderate DNA damage enhances megakaryopoiesis and platelet production

Camacho V, Beckendam RH, Stone AP, et al., Blood Advances. DOI: 10.1101/2025.05.08.652525

This study shows that moderate DNA damage enhances megakaryocyte development and increases platelet production in mice. Using low-dose PARP inhibition and low-dose γ-irradiation, the authors induced DNA damage in haematopoietic stem and progenitor cells, leading to expansion of megakaryocyte progenitors, increased megakaryocyte ploidy and higher circulating platelet counts without impairing platelet function. These findings identify a DNA damage–responsive pathway that promotes thrombopoiesis, with potential implications for improving platelet yields in clinical or ex vivo settings.

MicroRNA-223-3p is a determinant of platelet procoagulant activity

Charlon-Gay J, Nolli S, Dunoyer-Geindre S, et al. Research and Practice in Thrombosis and Haemostasis. DOI: 10.1182/bloodadvances.2024015290

This paper identifies miR-223-3p as a key regulator of platelet procoagulant activity. Manipulation of miR-223-3p levels in human $CD34^{+}$-derived megakaryocytes and platelets demonstrated that increased miR-223-3p reduces the formation of procoagulant platelets and platelet-supported thrombin generation, whereas reduced expression has the opposite effect. Mechanistically, miR-223-3p directly targets TMEM16F, a phospholipid scramblase required for phosphatidylserine exposure. The study highlights post-transcriptional regulation as an important determinant of platelet functional heterogeneity.

Thrombocytosis in cancer patients: when more is not better- in fact, the opposite

Aleksandrowicz K, Polityńska B, Kruszewska J, et al. International Journal of Molecular Sciences. DOI: 10.1007/s10555-025-10309-8

This review examines the association between thrombocytosis and poor outcomes in cancer patients. It summarises clinical evidence linking elevated platelet counts with increased tumour progression, metastasis and reduced survival, and explores underlying mechanisms including platelet-mediated immune evasion, angiogenesis and protection of circulating tumour cells. Rather than platelet number alone, the authors emphasise platelet–tumour interactions as drivers of disease, supporting therapeutic strategies that target platelet function in cancer.

Extraterrestrial regolith is hemostatic and potentially suitable for hemorrhage control in space

Ali-Mohamad N, Wang T-H, Juang LJ, et al. Research and Practice in Thrombosis and Haemostasis. DOI: 10.1016/j.rpth.2025.103342

This proof-of-concept study investigates lunar and Martian regolith simulants as haemostatic agents for use in space. The authors show that regolith accelerates clot formation and reduces blood loss in in vitro assays and trauma models, primarily through activation of factor XII. Although not platelet-focused, the work highlights how non-biological surfaces can initiate haemostasis and promote platelet recruitment, with relevance for both space medicine and the design of novel terrestrial haemostatic materials.

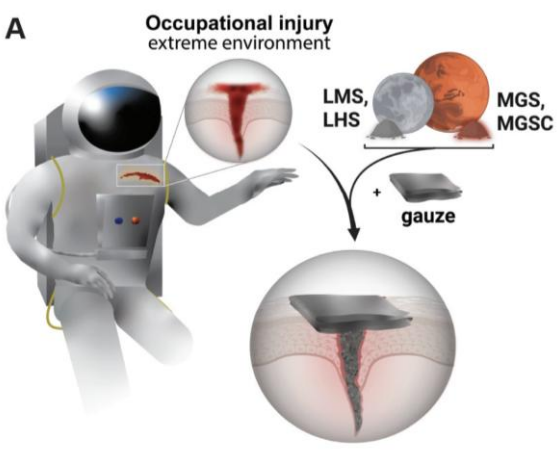


Fig. 1A (legend adapted from paper). Trauma-related haemorrhage is a potential cause of preventable death in astronauts. Lunar (LMS, LHS) and Martian (MGS, MGSC) regolith simulants act as effective haemostatic materials, accelerating plasma clotting in a factor XII-dependent manner.

Papers

Interleukin-1α alters megakaryocyte maturation, promotes emperipolesis, and induces a distinct proteomic profile

Kolman, R., et al J Thromb Haemostasis *DOI:*10.1016/j.jtha.2025.08.037

In this original research article, Kolman et al. demonstrate that interleukin-1α (IL-1α) modulates megakaryocyte (MK) maturation. Using bone marrow–derived MK cultures stimulated with thrombopoietin (TPO) and IL-1α, the authors show that MKs become larger and produce increased numbers of platelet-like particles despite reduced expression of canonical maturation markers such as von Willebrand factor (vWF) and the GPIb receptor complex. Additionally, IL-1α significantly increases the frequency of emperipolesis, predominantly involving $Ly6G^+$ neutrophils, which in turn skews the MK proteomic profile toward an immune-associated phenotype. Overall, this study identifies a role for IL-1α in altered platelet biogenesis and in shaping MK–neutrophil interactions during inflammatory conditions.

Structure and multiple functions of von Willebrand factor

S.L Haberichter et al. Hematologica. *DOI:*10.3324/haematol.2024.286029)

In this comprehensive review, Haberichter and O'Donnell summarize our current understanding of von Willebrand factor (VWF) and detail the major advances made over the past century. The authors discuss VWF structure, biosynthesis, and function, followed by its secretory pathways in platelets and endothelial cells. Importantly, the review also highlights the expanding roles of VWF in haemostasis and beyond, including inflammation, angiogenesis, and immune regulation.

Understanding how a highly prevalent GRK5 polymorphism affects platelets and enhances thrombotic risk

Yarman, Y. & Zhao, X., et al Blood *DOI 10.1182/blood.2025030223*

In this original research article, Yarman and Zhao identify the mechanistic consequences linking an intronic G protein–coupled receptor kinase 5 (GRK5) A→G variant (rs10886430), previously identified by GWAS, to increased thrombotic risk. Platelets from homozygous GG individuals exhibit a ~90% reduction in GRK5 protein expression, resulting in enhanced thrombin- and PAR1-mediated activation, calcium signalling, and aggregation, while PAR4 signalling remains unaffected. Using human platelets, GRK5-deficient iPSC-derived megakaryocytes, microfluidic flow assays, and in vivo mouse thrombosis models, the authors demonstrate increased venous and arterial thrombus formation associated with this variant.