THE PLATELET SOCIETY

Edition 4

Image Credit: Gagan D. Flora, University of Iowa

Hetty Walker, University of Bristol
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The Platelet Society
Journal Club

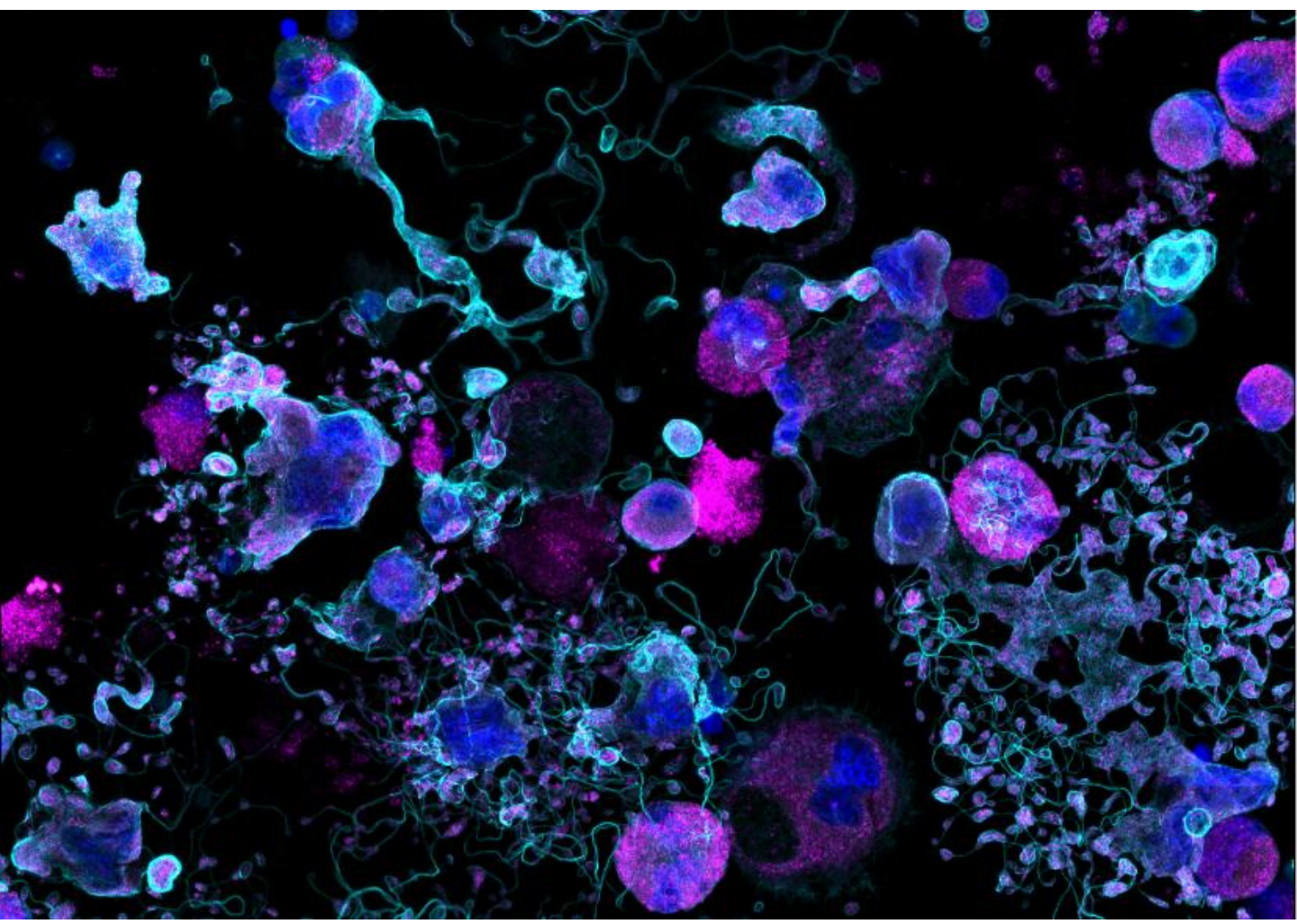


Image Credit: Nathan Asquith, University of Oxford

February 2026

Supporting Research and Education of Platelet Related Diseases

Papers

Biocompatible de novo indolylchalcones as platelet aggregation inhibition and diabetic wound healing agents

S. Kumar et al., *RSC Medicinal Chemistry*, DOI: 10.1039/d5md00984g

This study synthesized N-acylated indolylchalcones, identifying compounds 24 and 25 as potent dual-acting therapeutic agents for cardiovascular diseases and diabetic wound healing. They effectively inhibited ADP-induced platelet aggregation (compound 25 achieving 65.4% inhibition at 50 μM) and significantly activated endothelial nitric oxide synthase (eNOS), increasing the phospho-eNOS/total eNOS ratio to 0.78 and NO production to 38.5 μM with compound 25. In diabetic rats, compound 25 reduced inflammatory markers (IL-1β, cleaved caspase-3) and accelerated wound contraction and re-epithelialization. The compounds demonstrated excellent biocompatibility, with negligible cytotoxicity, hemolysis, or oxidative stress, making them promising candidates for further therapeutic development.

Polymeric anti-platelet carriers for the precision-targeting of age-related cardiovascular and cerebrovascular diseases

JingJing Fa et al., *Materials Today Bio*, DOI: 10.1016/j.mtbio.2026.102920

Polymeric anti-platelet carriers aim to deliver drugs directly to age-related thrombotic lesions, reducing systemic bleeding risk in patients over 75 years old. They target platelet biomarkers such as GPVI, PDGF-B/PDGFR-β, ROS, and high shear, using ligand-guided, biomimetic, or multivalent designs. Stimuli-responsive platforms- pH-sensitive uPA-Oxd-RGD micelles, enzyme-cleavable Fuco-UK nanoparticles, and shear-activated SA-NTs achieve over 70 % thrombus ablation in $FeCl_3$ rat models with only ~10 % bleeding increase versus aspirin. Meta-analysis shows dual antiplatelet therapy raises bleeding risk. Future work should integrate cloaking, ligand-density control, and thorough PK/PD evaluation for safe clinical translation. Additionally, these carriers improve drug loading, release control, and compatibility with vascular environments.

Regulation of platelet contractility by agonists present across a thrombus

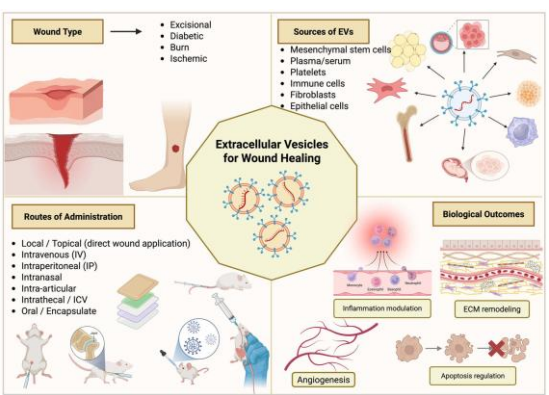
Dishon W. Hibner et al., *Blood Advances*, DOI: 10.1182/bloodadvances.2025017995

Platelets form a layered thrombus whose dense core depends on sustained contractility. The study shows that 1 U ml^{-1} thrombin increases platelet traction forces by 50 % after one hour, exceeding the modest effects of 5 μM ADP or 5 μg ml^{-1} CRP. Maximal contractility requires simultaneous PAR1 and PAR4 activation, mimicking thrombin without changing adhesion signalling. Thrombin uniquely maintains ROCK2 and MYL9 phosphorylation, raises MYL9 protein, and induces ROCK1 pre-mRNA splicing, defining a PAR→$G\alpha_{13}$→RhoA→ROCK→pMLC pathway. Anti-platelet drugs (aspirin, AR-C69931, Glenzocimab) dose-dependently reduce clot contraction, especially at low thrombin stimulation, warning that combined antiplatelet-anticoagulant therapy may increase bleeding risk.

The use of therapeutic exosomes for in vivo wound healing

Bigliardi E, et al., International Journal of Molecular Sciences, DOI:10.1177/09636897261418580

This review evaluates the therapeutic application of exosomes as cell-free regenerative agents for in vivo wound healing. Exosomes derived from mesenchymal stem cells and other progenitor sources promote angiogenesis, modulate inflammation and stimulate fibroblast and keratinocyte proliferation and migration through delivery of bioactive cargo including microRNAs and proteins. The authors discuss delivery strategies, dosing considerations and manufacturing challenges, highlighting key translational barriers to clinical implementation.

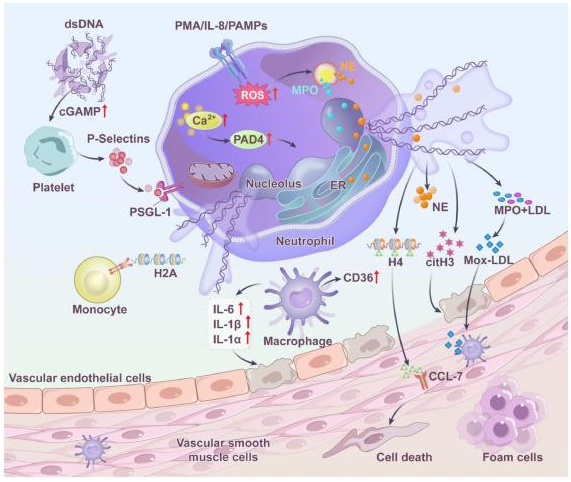


Papers

The effect of neutrophil extracellular traps in atherosclerosis

Zhang H et al., Current Research in Translational Medicine, DOI:10.1177/09636897261418580

This review examines the role of neutrophil extracellular traps (NETs) in the development and progression of atherosclerosis. NETs, composed of decondensed chromatin decorated with histones and granular proteins, contribute to endothelial dysfunction, lipid deposition and amplification of vascular inflammation. The authors summarise evidence that NETs promote monocyte recruitment, macrophage activation and foam cell formation, and enhance thrombus formation following plaque rupture. Mechanistically, NET-associated components such as histones and neutrophil elastase drive pro-inflammatory and pro-thrombotic signalling within the atherosclerotic milieu. The review also discusses therapeutic strategies targeting NET formation or promoting NET degradation as potential approaches to limit plaque progression and atherothrombosis.



Implications of hemoglobin, albumin, lymphocyte, platelet (HALP) score as a predictor of neoadjuvant chemotherapy response in bladder cancer patients

Stempel M et al., Urologic Oncology: Seminars and Original Investigations, DOI: 10.1016/j.urolonc.2026.111005

This study evaluates the HALP score - a composite index incorporating haemoglobin, albumin, lymphocyte count and platelet count - as a predictor of response to neoadjuvant chemotherapy (NAC) in bladder cancer. Using retrospective clinical data, the authors assess whether pre-treatment HALP scores correlate with pathological response at cystectomy and oncological outcomes. Lower HALP scores, reflecting poorer nutritional and immunological status and higher systemic inflammation, were associated with reduced likelihood of favourable response to NAC. The findings support the HALP score as a readily accessible biomarker integrating systemic inflammation and host condition, with potential utility for risk stratification and treatment decision-making in bladder cancer.

Emerging Perspectives on Platelet-Activating Factor in Relation yo Magnesium Levels at the Cellular, Tissue, and Systemic Levels in Disease States

Amanda Kaine at al., Cells, DOI: Emerging Perspectives on Platelet-Activating Factor in Relation to Magnesium Levels at the Cellular, Tissue, and Systemic Levels in Disease States | MDPI

Magnesium and platelet-activating factor (PAF) have an antagonistic relationship in cells and tissues with implications for various diseases. Hypomagnesemia increases PAF activity, platelet aggregation, and intracellular Ca^{2+} which drives vascular inflammation and atherogenesis. In chronic kidney disease (CKD) stages 3–4, PAF-acetylhydrolase (PAF-AH) activity rises and correlates with cardiac valve calcification and glomerular injury. Primary glomerulonephritis patients also show significantly higher urinary and plasma PAF levels. Severe magnesium depletion is observed in over 50% of subarachnoid haemorrhage cases, potentially representing a compensatory anticoagulant response. Magnesium's role as a Ca^{2+} antagonist helps to reduce PAF-mediated signalling, thereby decreasing platelet activation and inflammatory cascades in cardiovascular, renal, neurological, and metabolic disorders. The review suggests that targeted magnesium supplementation could counteract PAF-driven pathology, though further mechanistic studies are needed.