Can platelet microparticles replace platelets in thrombocytopenia?

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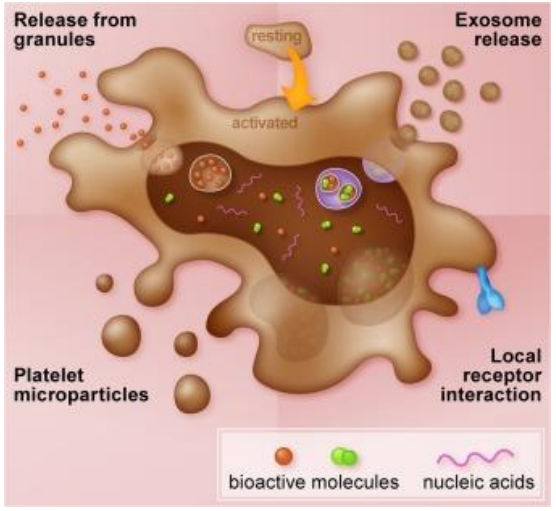
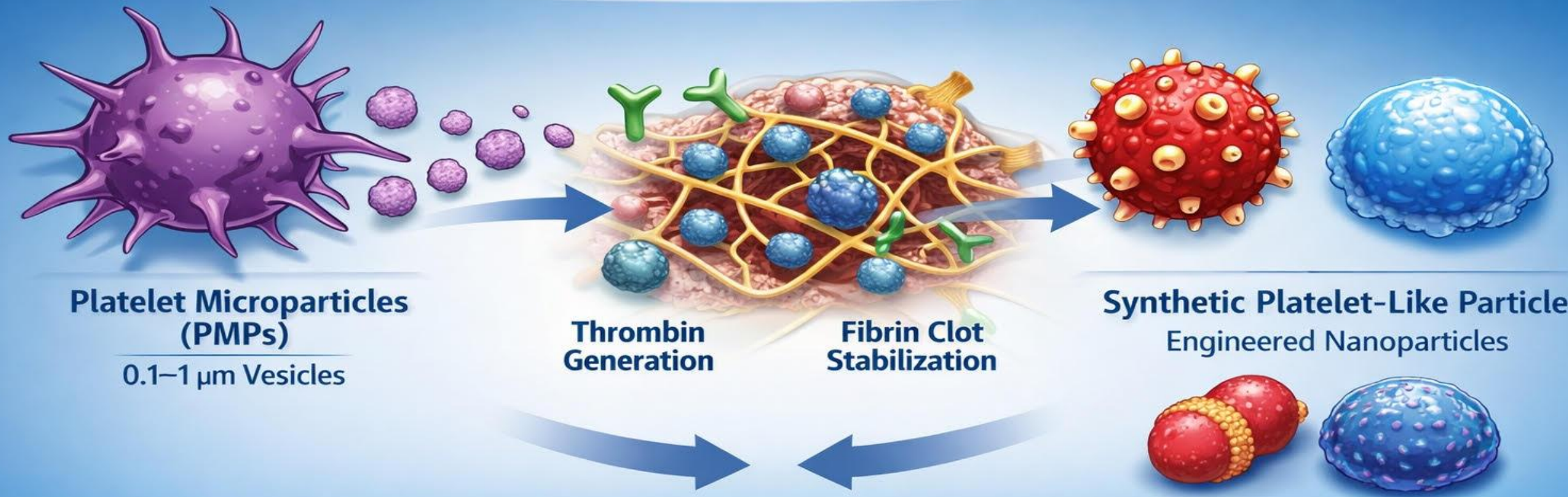


Platelet Micro- and Macro-Particles:

From Biology to Clinical Applications



Hemostasis & Bleeding Control

Therapeutic & Regenerative Medicine

Why

- Challenges platelet count dogma
- Transfusion shortages + trauma care pressure
- Biotech loves things that don’t need donors
- Safety is the biggest barrier to trials
- Procoagulant vs prothrombotic paradox
- Standardization problem
- Interaction with antiplatelet and anticoagulant therapy

Absolute Platelet Count

- **What it measures:**
  - Number of circulating platelets per µL.
- **What clinicians assume:**
  - Low count = high bleeding risk.
  - High count = safety.
- **Why this fails:**
  - Platelets are not functionally equal.
  - Doesn’t capture activation state, procoagulant surface, or thrombin generation.
  - Explains nothing in:
    - ITP patients with platelets 10–20 $\times 10^9$/L who don’t bleed
    - ICU or sepsis patients with “normal” counts who do bleed

Platelet Microparticles (PMPs)

- **What they are doing instead of sitting idle:**
  - Provide phosphatidylserine-rich surfaces
  - Amplify tenase and prothrombinase complexes
  - Boost thrombin generation per platelet equivalent
- ***One PMP can be more procoagulant than an intact platelet.***
  - Unfair, but biology doesn’t care about fairness.

PMP-to-Platelet Ratio (Functional Concept)

- **Definition:**
  - Number of circulating PMPs relative to platelet count
- **What it reflects:**
  - Platelet activation history
  - Net procoagulant potential
  - Functional hemostatic reserve
- **This ratio often rises when platelet count falls**.

Why the Ratio Beats the Count

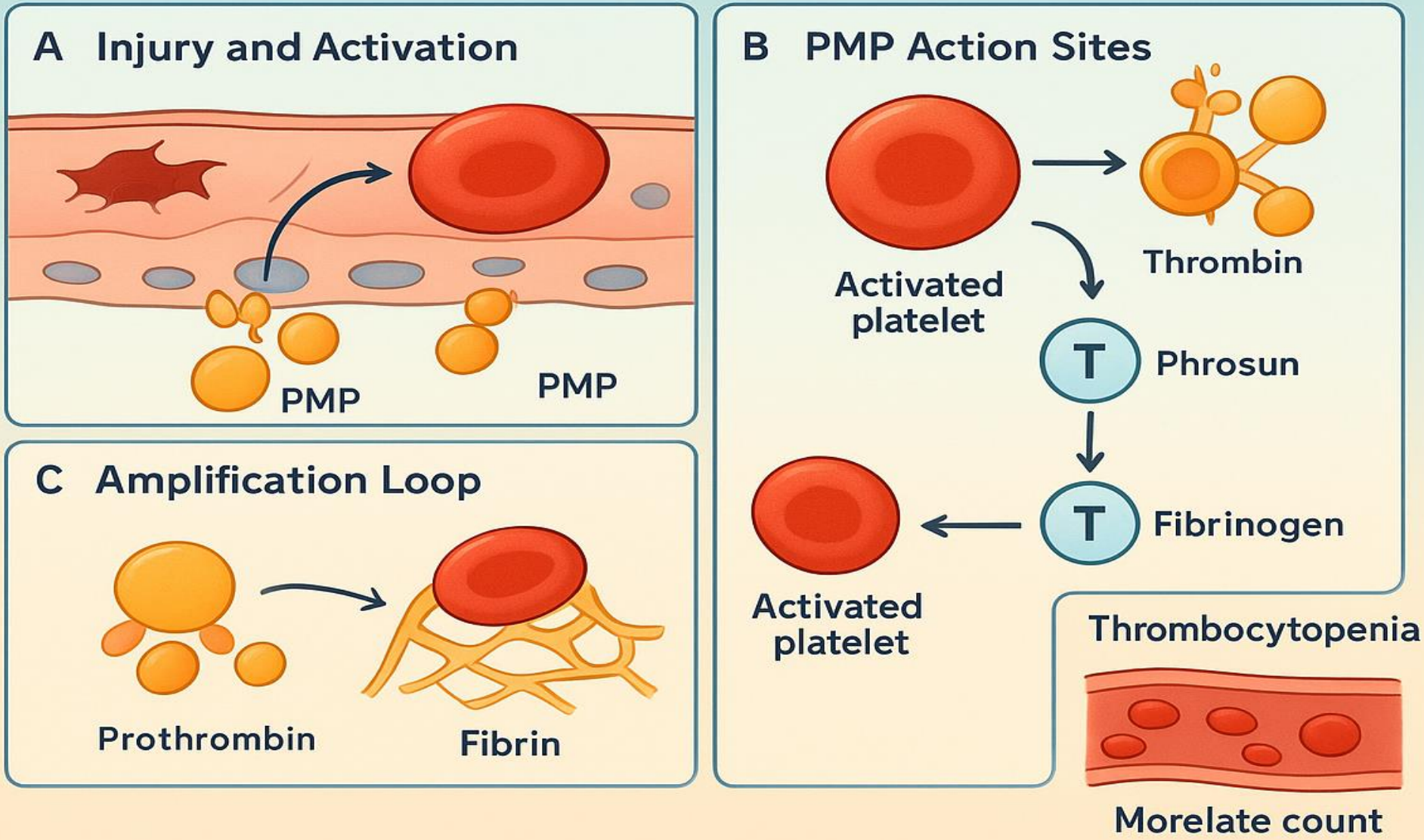
Scenario	Platelet Count	PMP Level	Bleeding Risk
ITP	Very low	High	Often mild
Chemotherapy	Low	Low	High
Sepsis	Normal/low	Very high	Thrombosis ± bleeding
HSCT	Low	Variable	Unpredictable

Two patients with the same platelet count can have opposite bleeding risks depending on PMP availability.

Mechanistic Explanation

- Platelet activation → PMP shedding
- Fewer platelets but more procoagulant surface area
- Thrombin generation preserved despite thrombocytopenia
- This explains the clinical paradox better than platelet count ever will.

Mechanisms by which Platelet Microparticles Prevent Bleeding



Clinical Implications

- Platelet count alone is a blunt instrument
- **PMP-to-platelet ratio could:**
  - Refine bleeding risk prediction
  - Prevent unnecessary platelet transfusions
  - Identify patients protected despite severe thrombocytopenia

Why It’s Not in Guidelines Yet

- No standardized PMP measurement
- Flow cytometry variability
- No prospective bleeding-endpoint trials

Clinical Trials Landscape on PMP on Human

Category	Trial Type	Status / Focus	References
Phase I EV Therapy	Allogeneic platelet EV administration	*Safety established in healthy volunteers (wound healing context)* PubMed	Johnson J First-in-human clinical trial of allogeneic, platelet-derived extracellular vesicles as a potential therapeutic for delayed wound healing. J Extracell Vesicles. 2023 Jul;12(7):e12332.
Observational Biomarker Studies	Circulating platelet EVs	Recruiting or completed observational work on platelet EVs as biomarkers in thrombosis/cardiovascular conditions ICHGCP	Clinical Trial NCT06298682
Future Potential	Interventional bleeding/hemostasis target	None yet	

Why Bleeding Endpoints Were Not Tested Yet

- Phase I studies are designed for safety, not efficacy
- Small sample sizes → underpowered for clinical outcomes
- EV product heterogeneity
- Lack of GMP-standardized PMP isolation and dosing
- Regulatory & ethical considerations
- Hard to recruit patients at high bleeding risk without proven safety
- Unclear target population
- Who would benefit most (ITP vs trauma vs thrombocytopenia)?
- No consensus yet

Take-home Message

- Platelet count tells you how many cells you have
- PMP-to-platelet ratio tells you how much coagulation power you actually have

Take-home Message

- Human clinical research on platelet microparticles has begun.
- Safety in administered platelet EVs is established via a Phase I trial, but efficacy in bleeding or hemostatic therapy remains to be demonstrated in future controlled trials.

ANY Questions?