Hemorrhage Control and Resuscitation

SynthoPlate, a Synthetic Platelet Substitute, Reduces Blood Loss, Stabilizes Blood Pressure, and Significantly Improves Survival Following Multiple Types of Traumatic Bleeding Injuries

Combat trauma-associated uncontrolled hemorrhage and coagulopathy remain the leading causes of morbidity and mortality in the military. Overwhelming evidence from military-based resuscitation studies has indicated that platelet transfusion can significantly reduce these events in prolonged field care scenarios. However, platelet transfusion suffers from unique logistical and functional challenges in a military setting due to the limited availability and portability of platelet concentrates, special storage requirements, high risk of bacterial contamination, and very short shelf-life of plasma products. Furthermore, blood type compatibility issues can limit early in-field and en route intervention.

These challenges have led to robust research efforts for creating a shelf-stable, highly portable, readily deliverable 'platelet surrogate' that can mimic platelet-mediated mechanisms of hemostasis, while avoiding a systemic immune response and unexpected harmful effects. To this end, researchers at Case Western Reserve University (Cleveland, OH), the University of Pittsburgh (Pittsburgh, PA) with the United States Army Institute for Surgical Research (USAISR; San Antonio, TX) developed a lipid-peptide conjugate-based intravenously administrable synthetic platelet nanotechnology, called SynthoPlate, that mimics the platelet's hemostatic mechanisms specifically at the hemorrhaging sites for targeted activity (Figure 1).

In two recent studies, the team examined the effect of SynthoPlate in two animal models of hemorrhagic injury (*Dyer et al., 2018; Hickman et al., 2018*). In the first study, mice sustained a liver injury and were administered SynthoPlate intravenously as pretreatment or after injury via transfusion. Regardless of treatment order, SynthoPlate reduced blood loss and delayed development of hypertension.

The second study investigated the impact of intravenous SynthoPlate administration in a femoral artery hemorrhage model in pigs, during the first couple of hours after injury, a time when interventions can have a significant impact on patient outcome. Again, SynthoPlate treatment reduced blood loss, stabilized blood pressure, and significantly improved survival.

Taken together, these findings support the potential use of SynthoPlate as a viable platelet surrogate for emergency management of traumatic bleeding in military and civilian settings. Development of a platelet surrogate could greatly resolve military-relevant challenges regarding hemostatic management of traumatic hemorrhage by platelet-transfusion and significantly advance prolonged field care treatment modalities in combat wound care.

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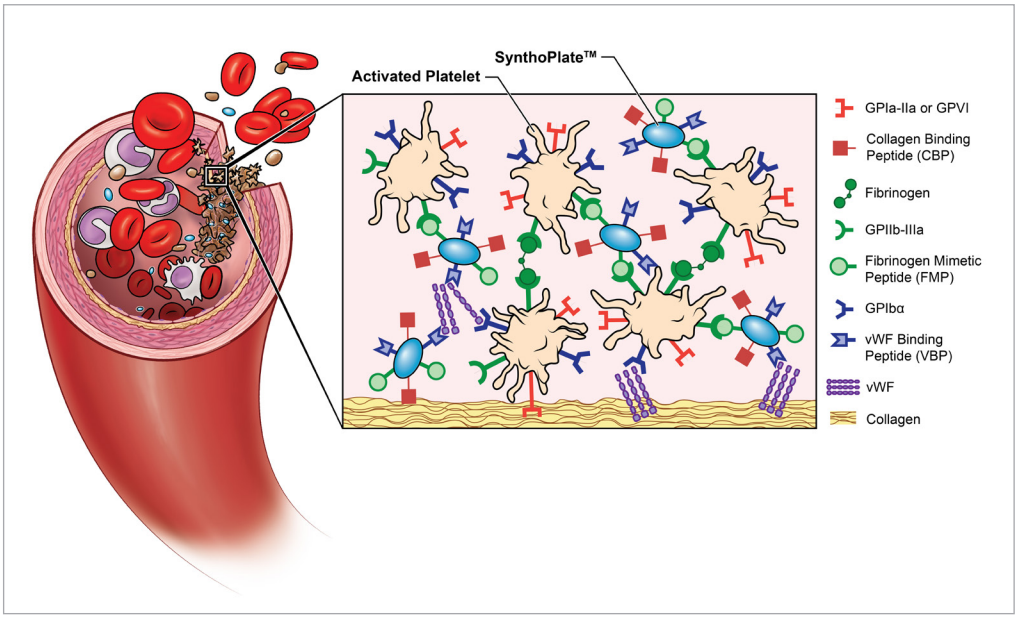

FIGURE 1: Illustration of the mechanism by which the synthetic platelet surrogate technology, SynthoPlate, augments hemostasis; SynthoPlate (blue particles) are nanoparticles decorated with a combination of protein components (peptides) that bind various blood proteins–vWF-binding peptides (VBP), collagen-binding peptides (CBP) and active platelet integrin GPIIb-IIIa binding fibrinogen-mimetic peptides (FMP); In the event of a hemorrhagic injury, SynthoPlate can target to the hemorrhaging site by binding to exposed vWF (a blood protein) and collagen (thus mimicking platelet's adhesion mechanism) and can aggregate with active platelets via binding to protein GPIIb-IIIa (thus mimicking platelet's aggregation mechanism); these mechanisms occurring in tandem accelerate hemostatic plug formation and improve hemorrhage control. (Figure used with permission from the authors).

REFERENCES:

Dyer, M. R., Hickman, D., Luc, N., Haldeman, S., Loughran, P., Pawlowski, C., . . . Neal, M. D. (2018). Intravenous administration of synthetic platelets (SynthoPlate) in a mouse liver injury model of uncontrolled hemorrhage improves hemostasis. J Trauma Acute Care Surg, 84(6), 917-923. doi:10.1097/TA.0000000000001893