Trauma, haemorrhagic shock and endothelial function

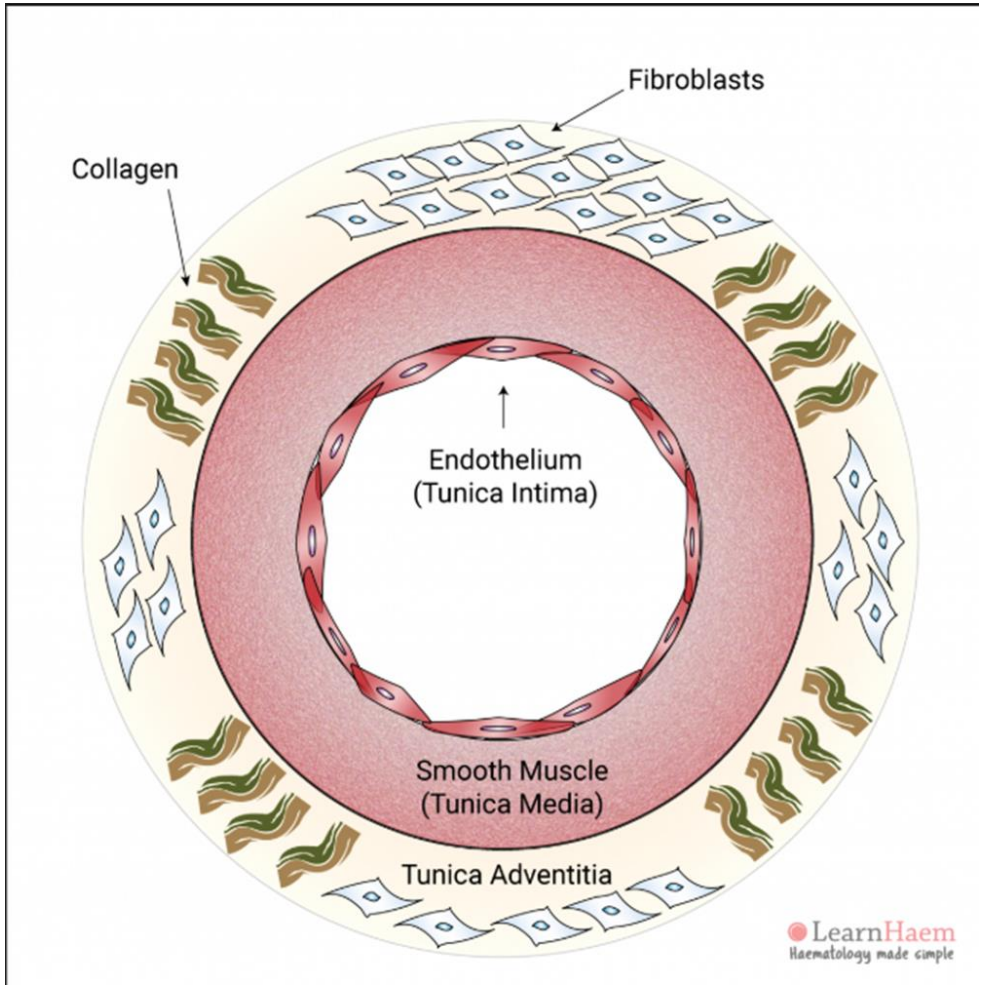
THOR, May 2025

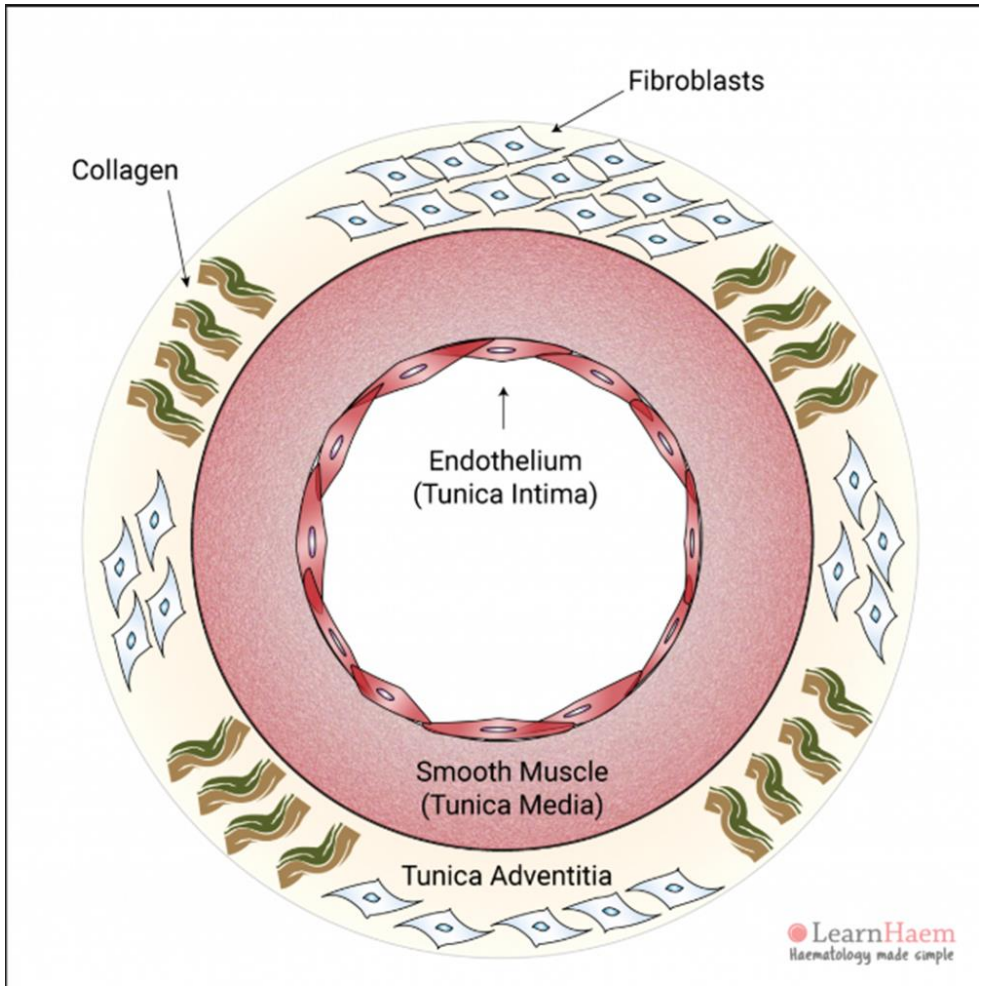
Norway

Nikki Curry

Oxford University Hospitals NHS Foundation Trust

Radcliffe Dept of Medicine, University of Oxford


Fibroblasts
Collagen
Endothelium
(Tunica Intima)
Smooth Muscle
(Tunica Media)
Tunica Adventitia
LearnHaem
Haematology made simple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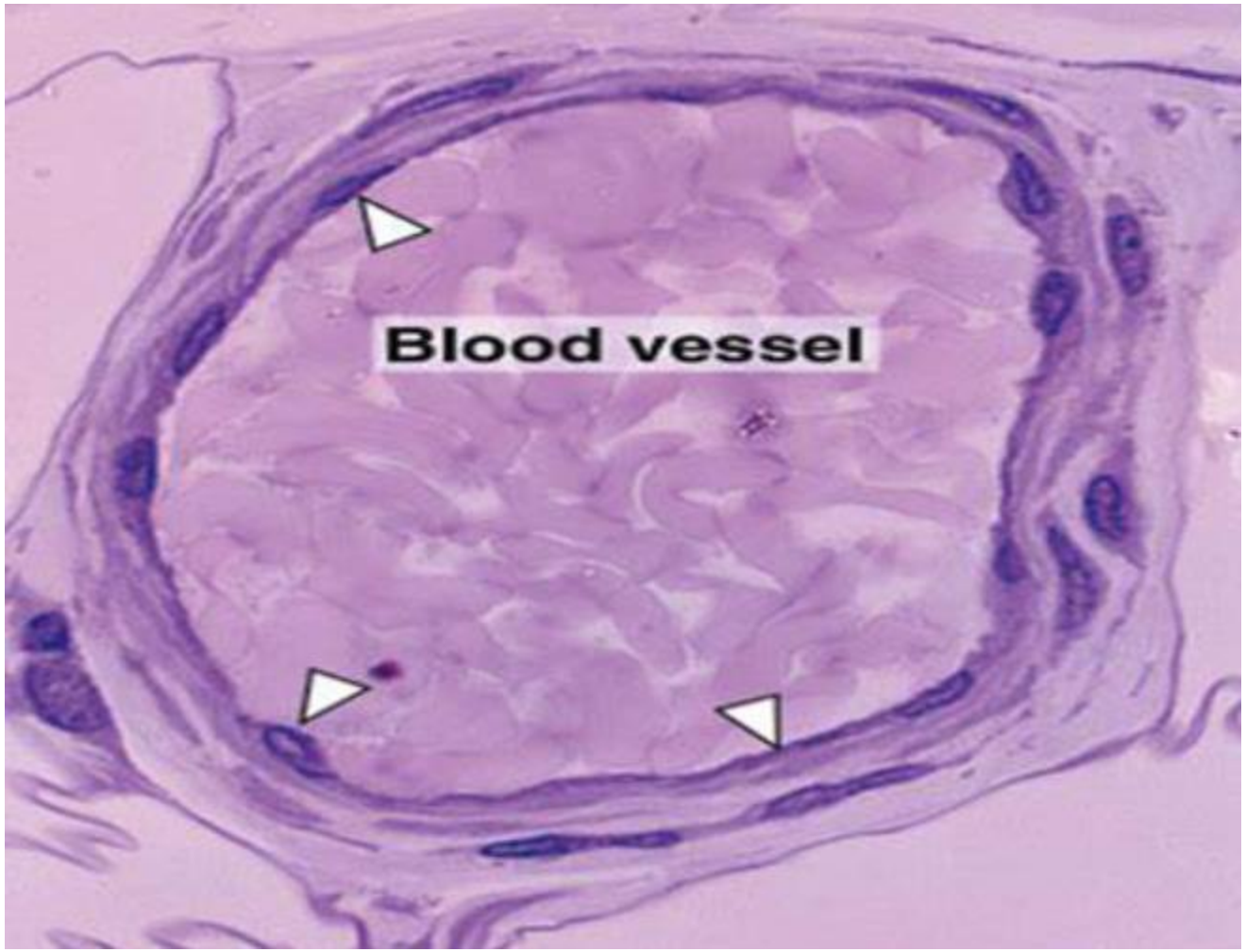
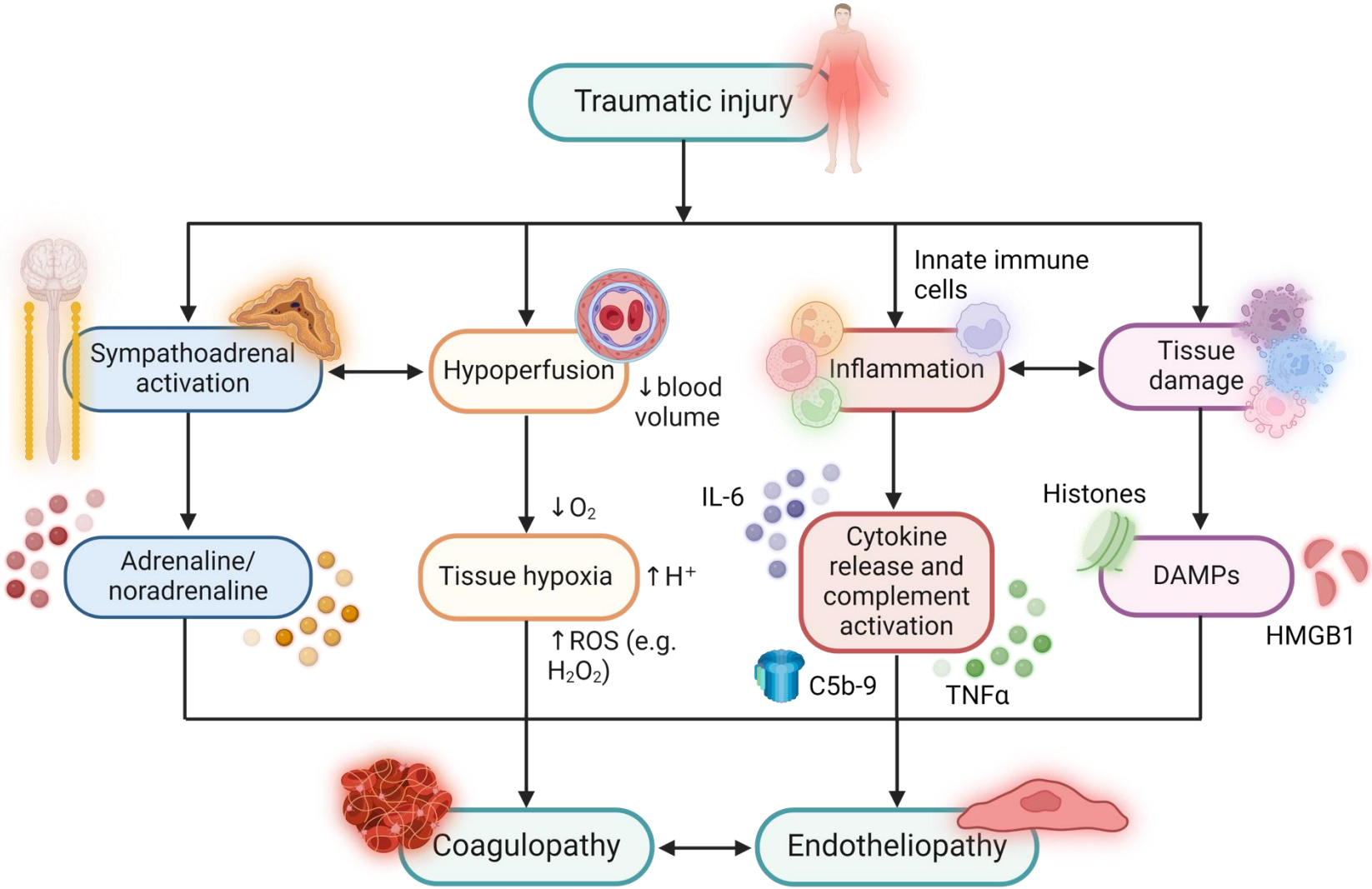
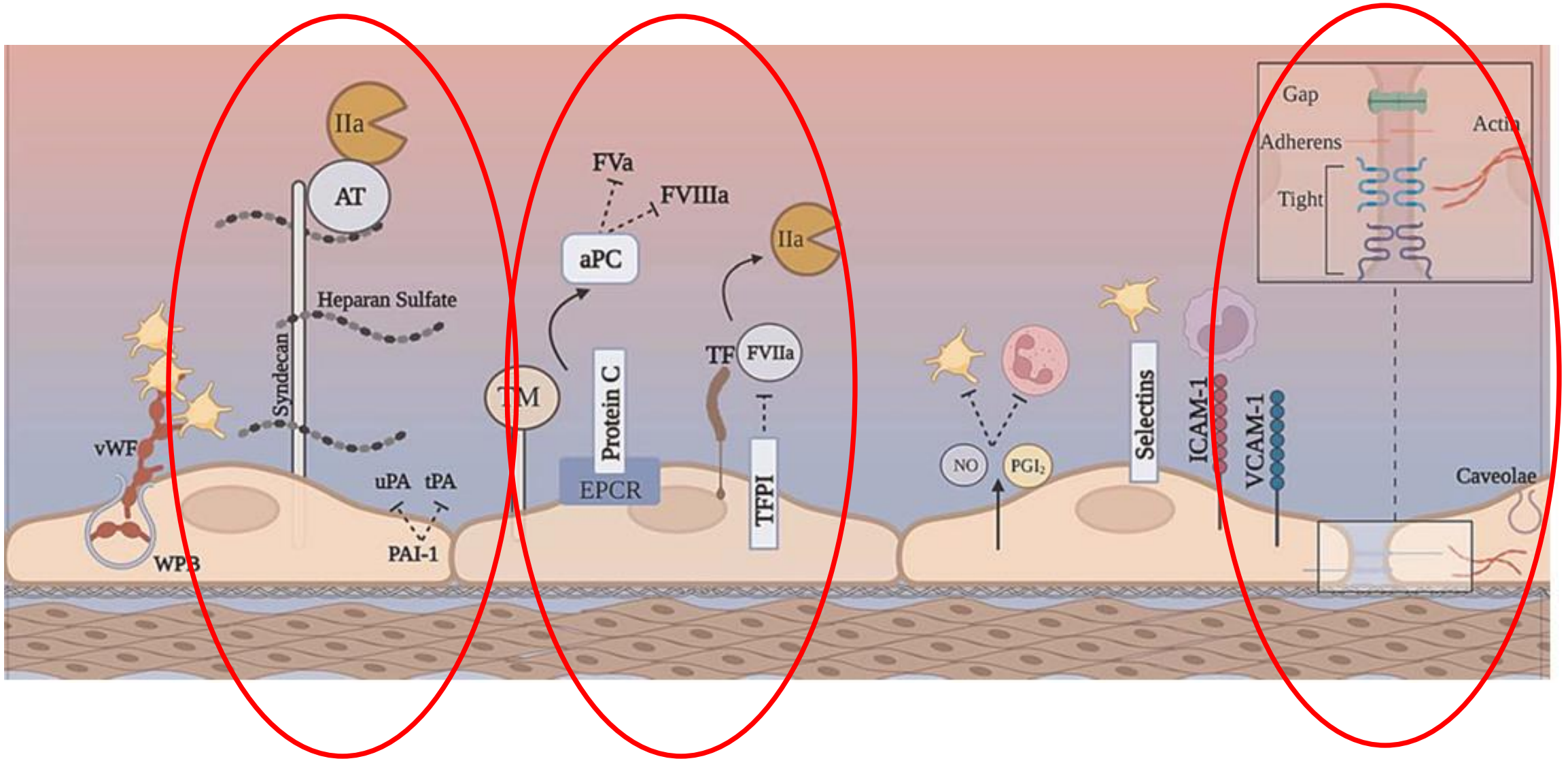

Blood vessel

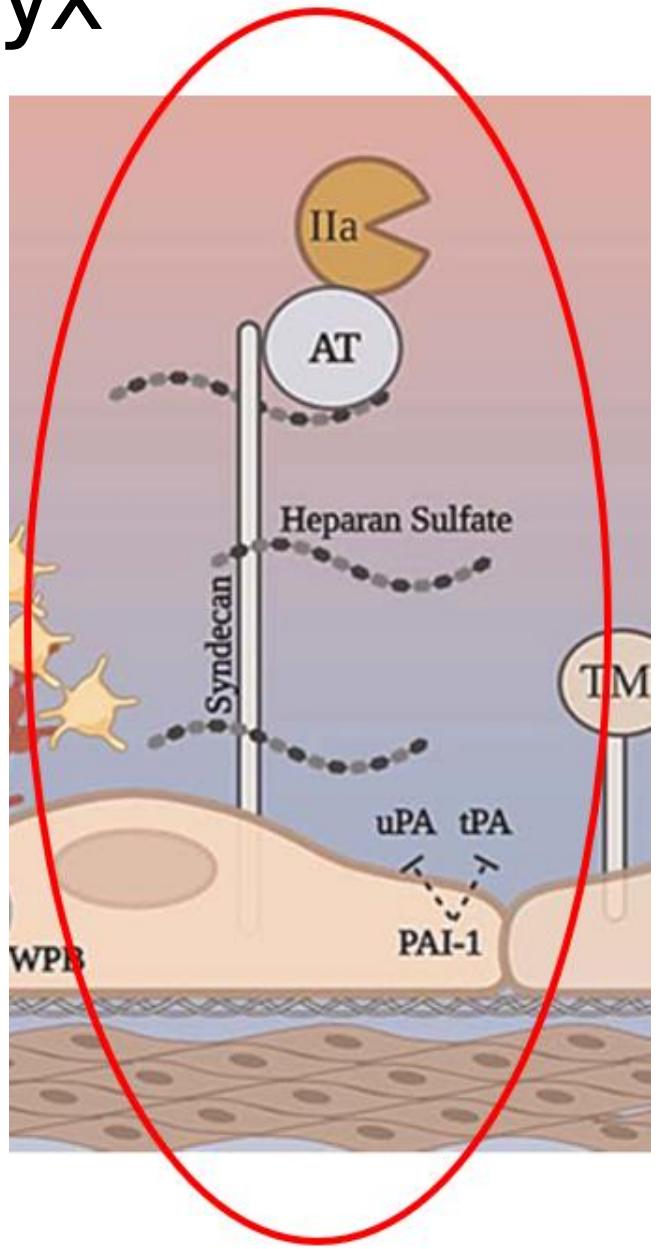
Trauma-induced endotheliopathy



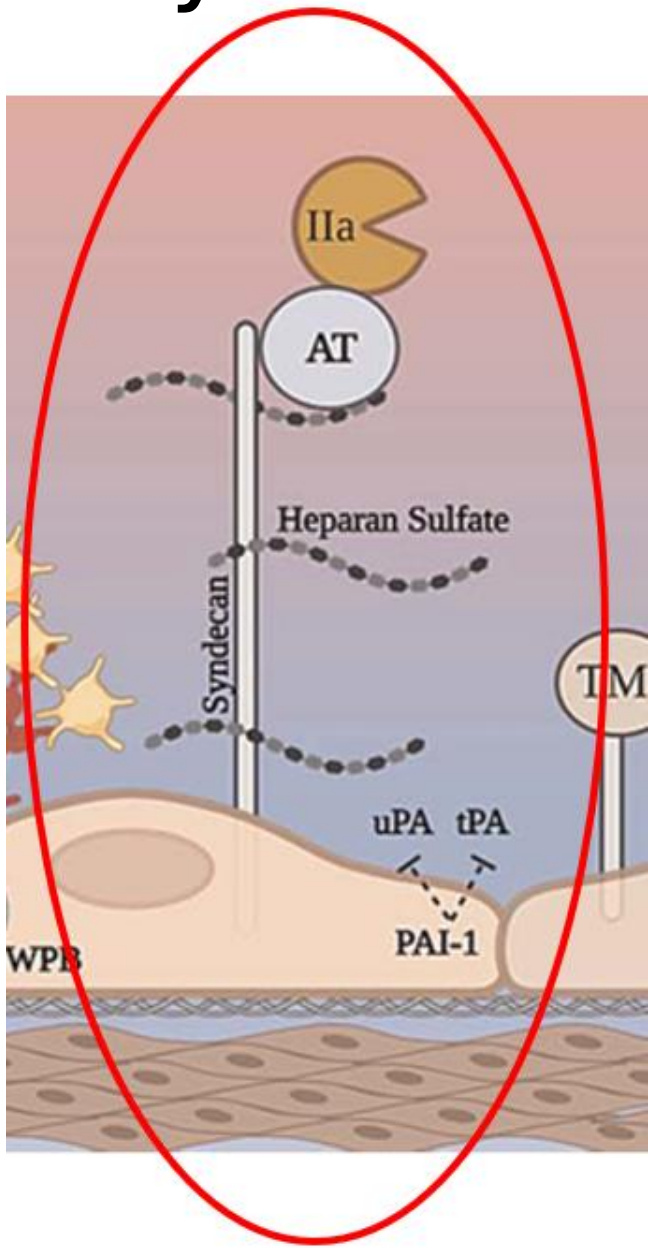


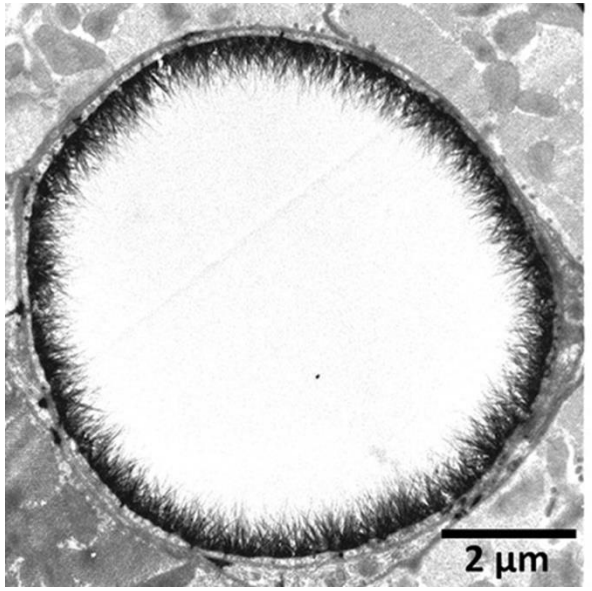
Cardenas et al, J Trauma 2023

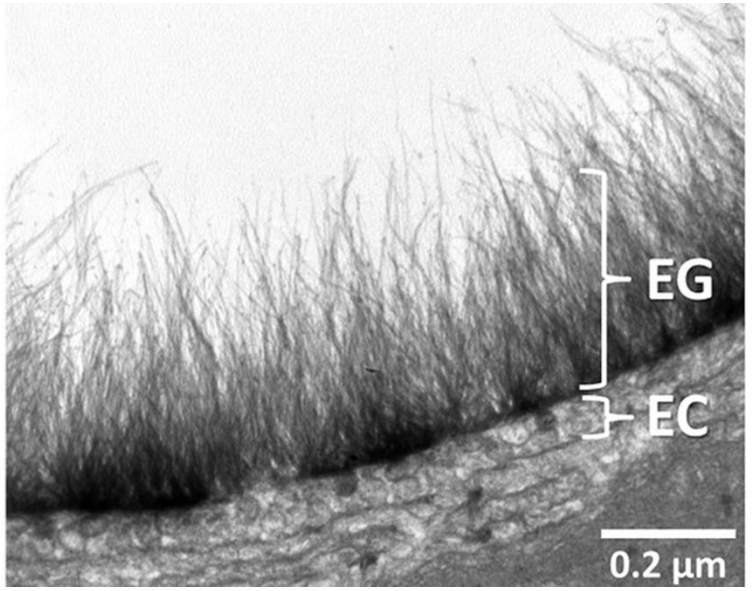
Glycocalyx



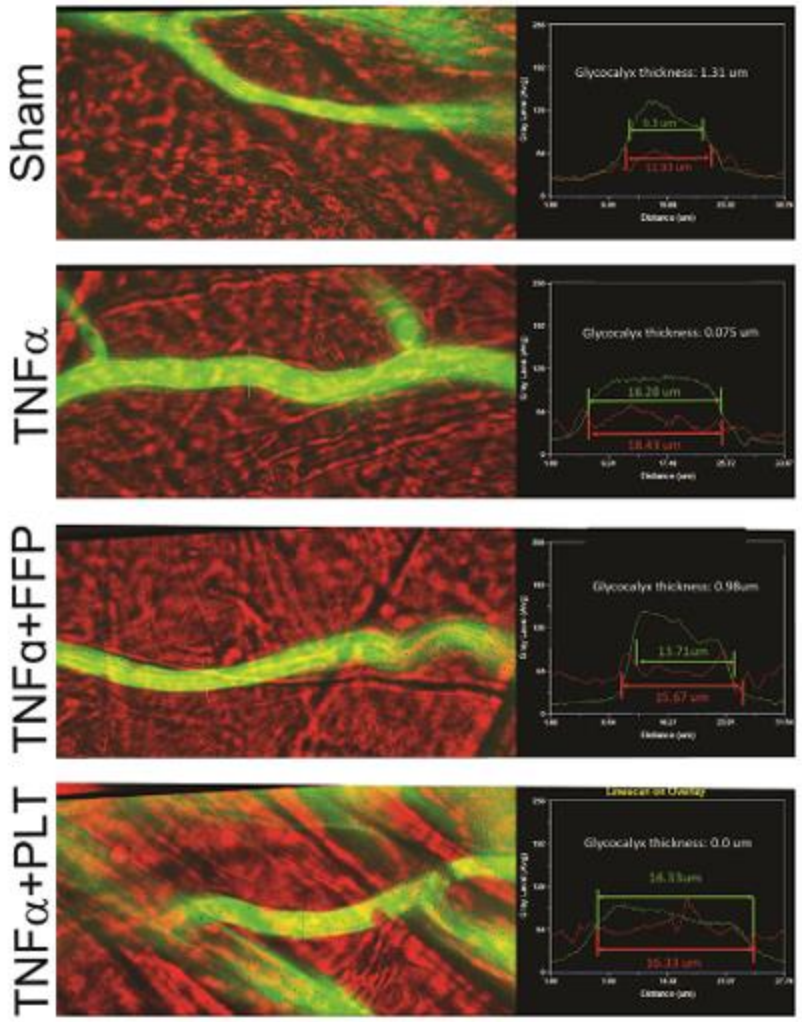
Glycocalyx

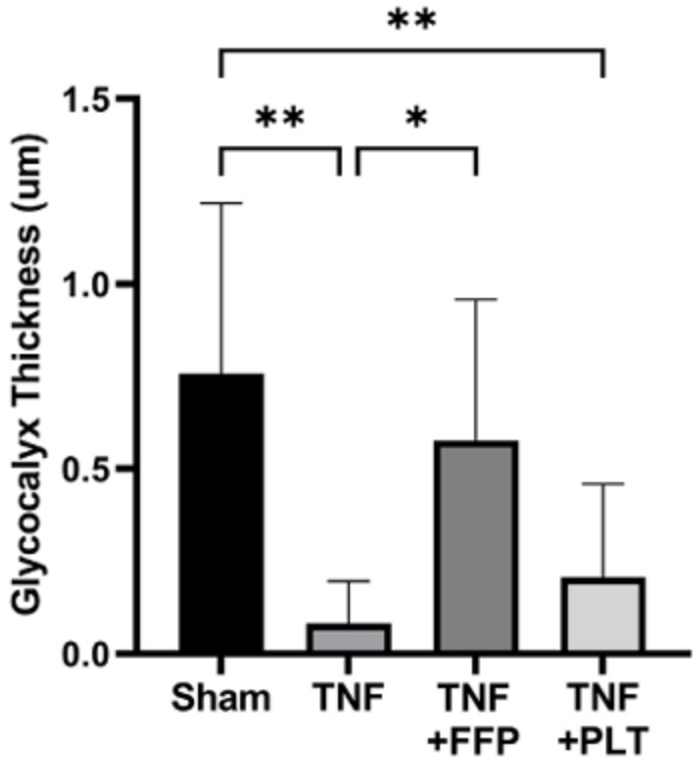

IIa
AT
Heparan Sulfate
Syndecan
TM
uPA
tPA
PAI-1
WPB


2 µm


EG
EC
0.2 µm

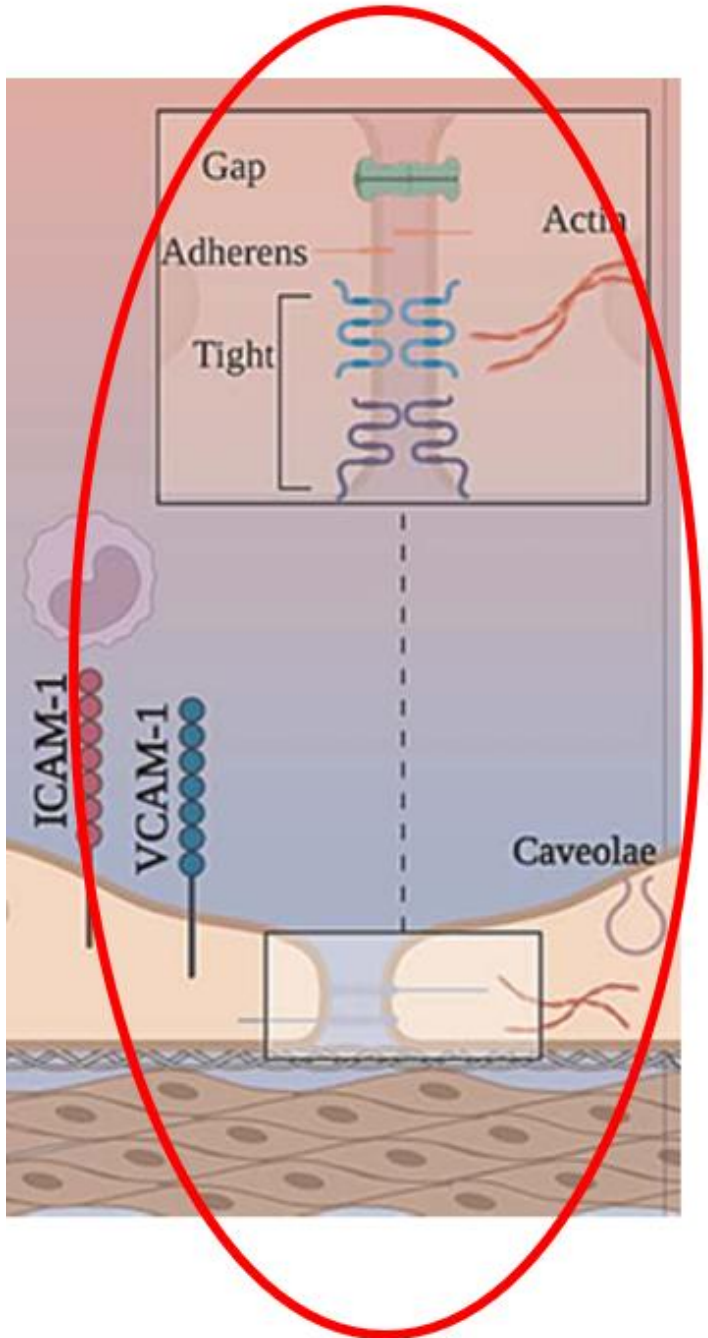
Effect of blood products on glycocalyx



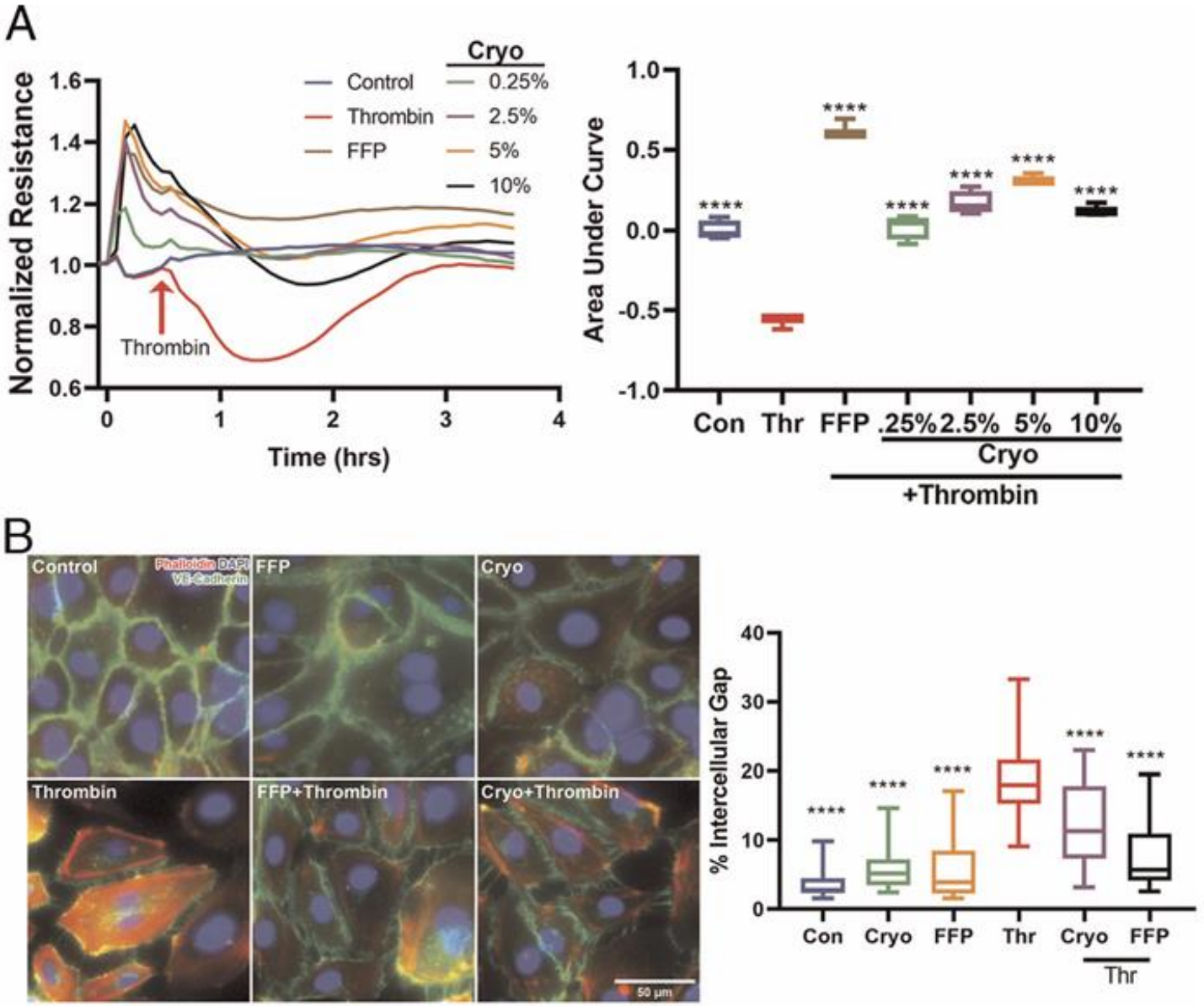


Barry & Pati. Materials Biology 14 (2022) 100107

Tight junctions



Fibrinogen replacement



Barry et al. (2021) J Trauma Acute Care Surg Volume 90(6):1022-31

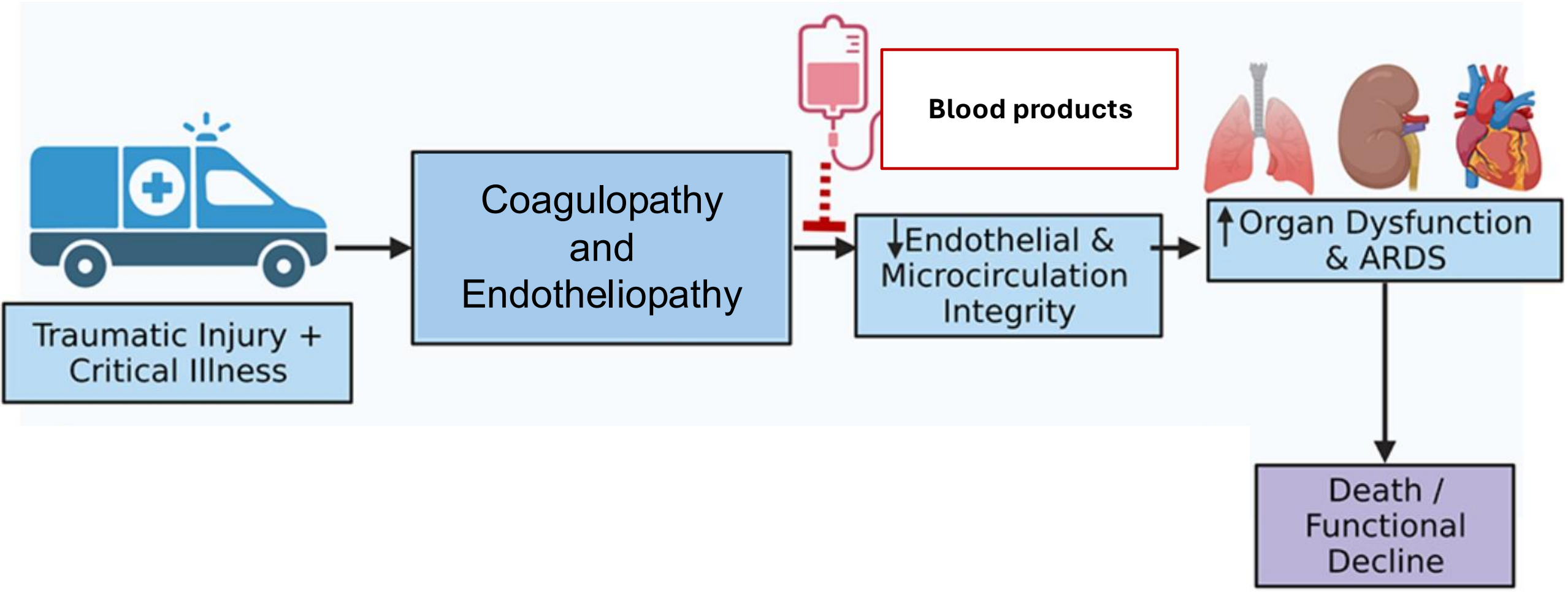
Traumatic Injury + Critical Illness

Coagulopathy and Endotheliopathy

↑Organ Dysfunction & ARDS

Death / Functional Decline

Adapted from: Douin et al, Anaesthesiology, 2022



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JAMA Surgery | Original Investigation

Association of Trauma Molecular Endotypes With Differential Response to Transfusion Resuscitation Strategies

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JAMA Surg. 2023;158(7):728-736. doi:10.1001/jamasurg.2023.0819
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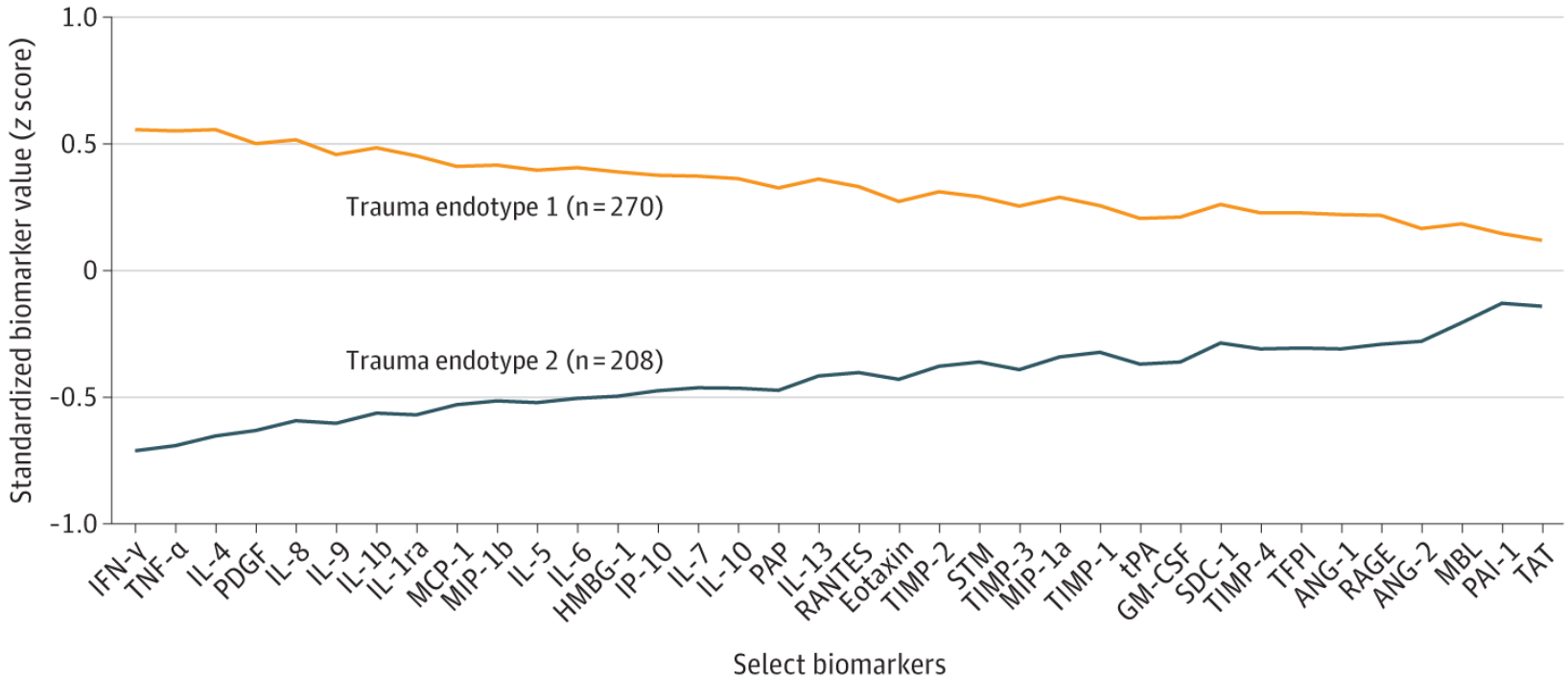

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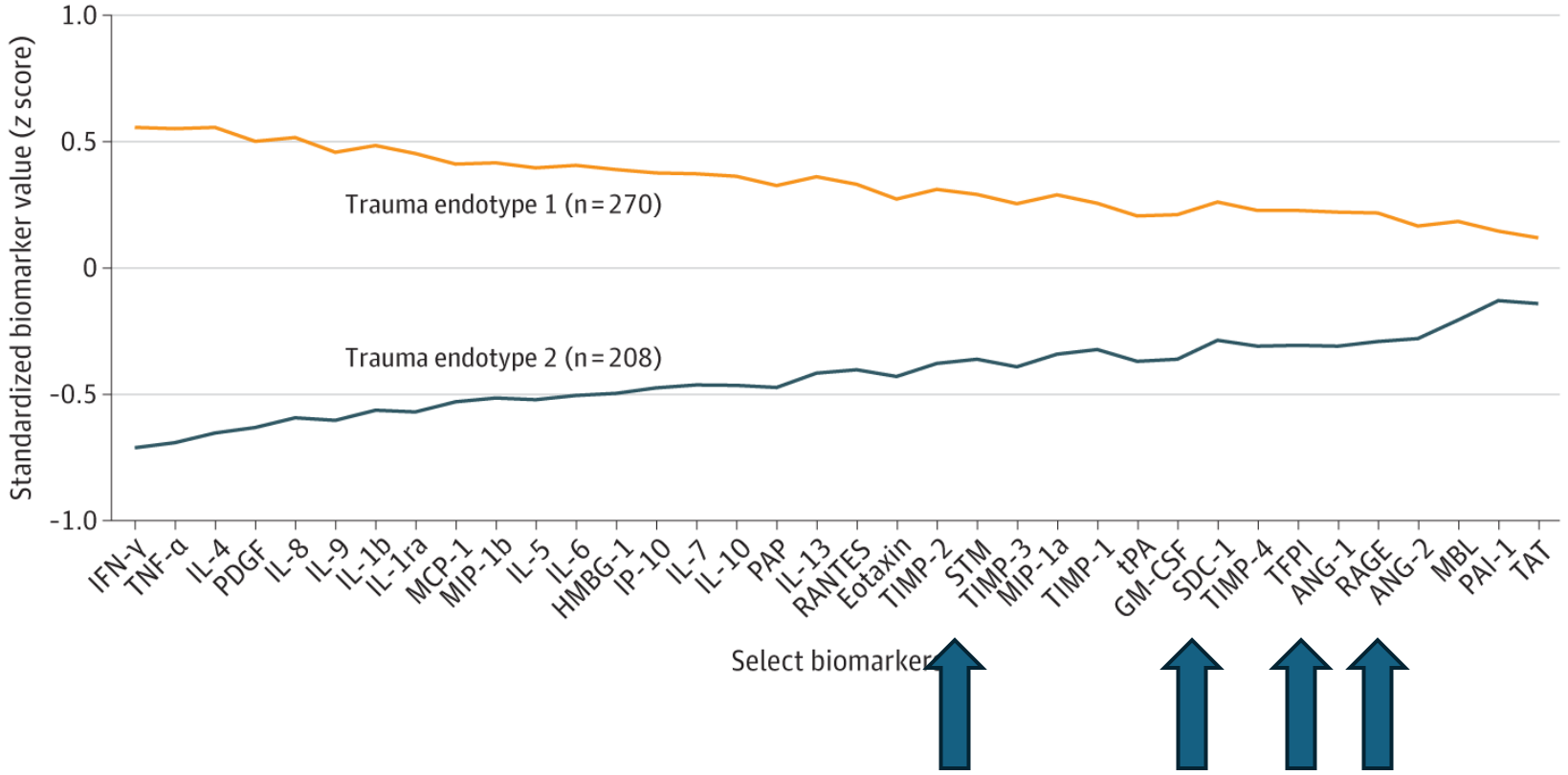

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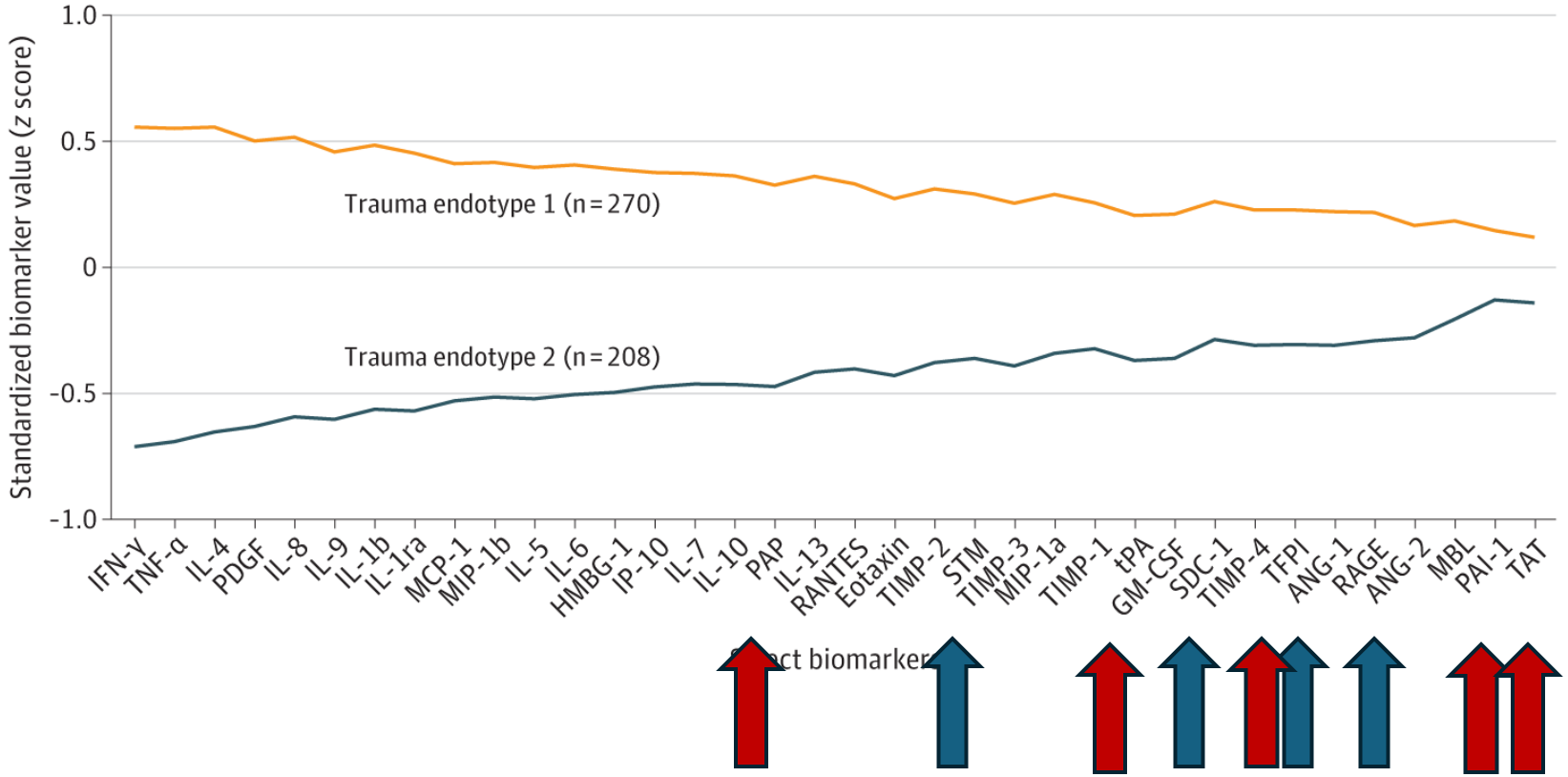

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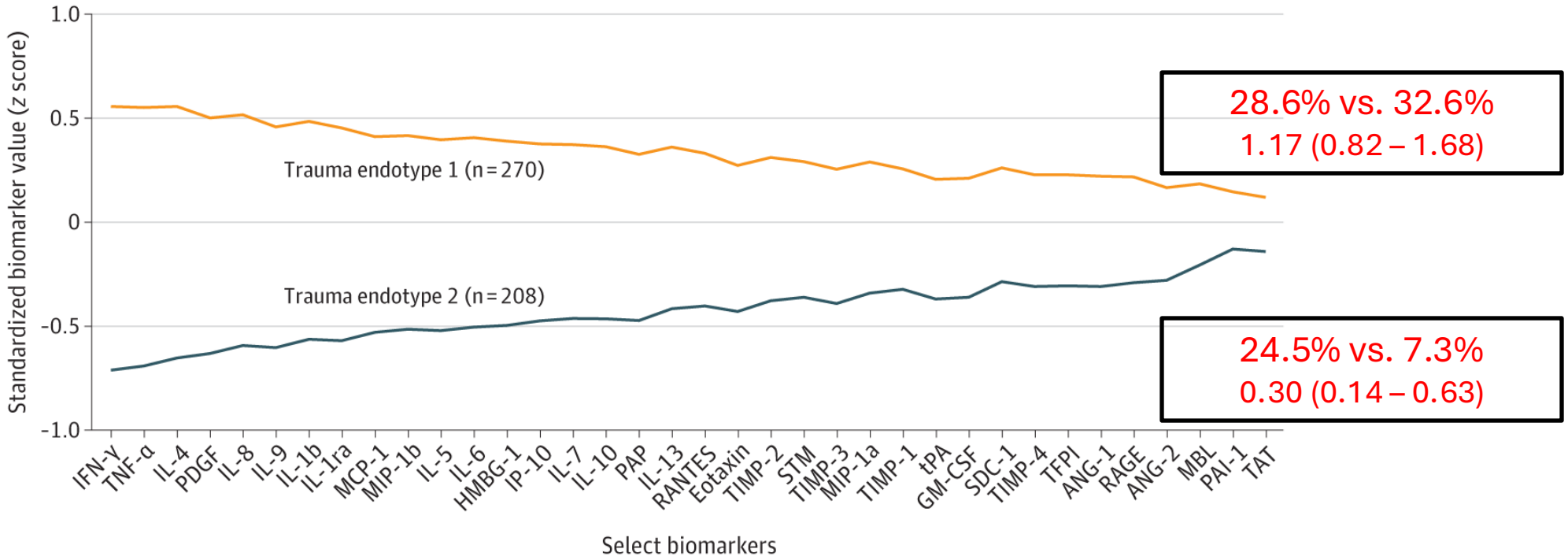
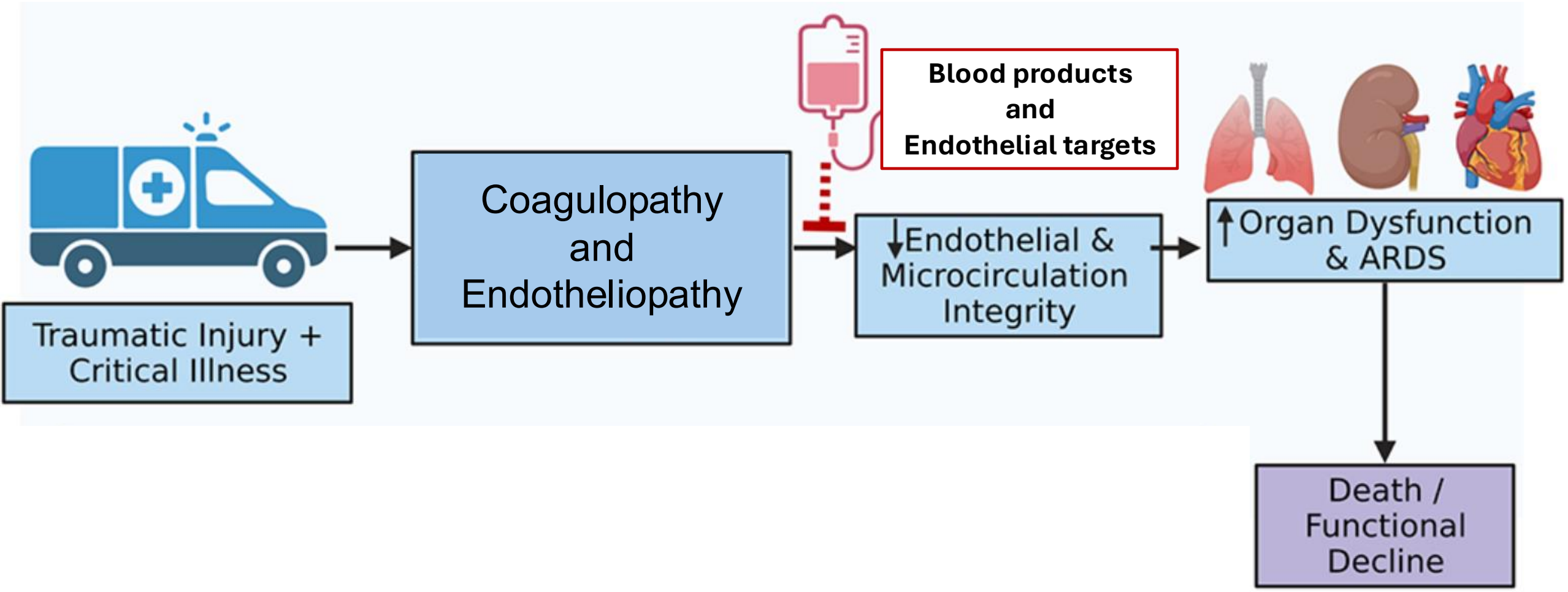


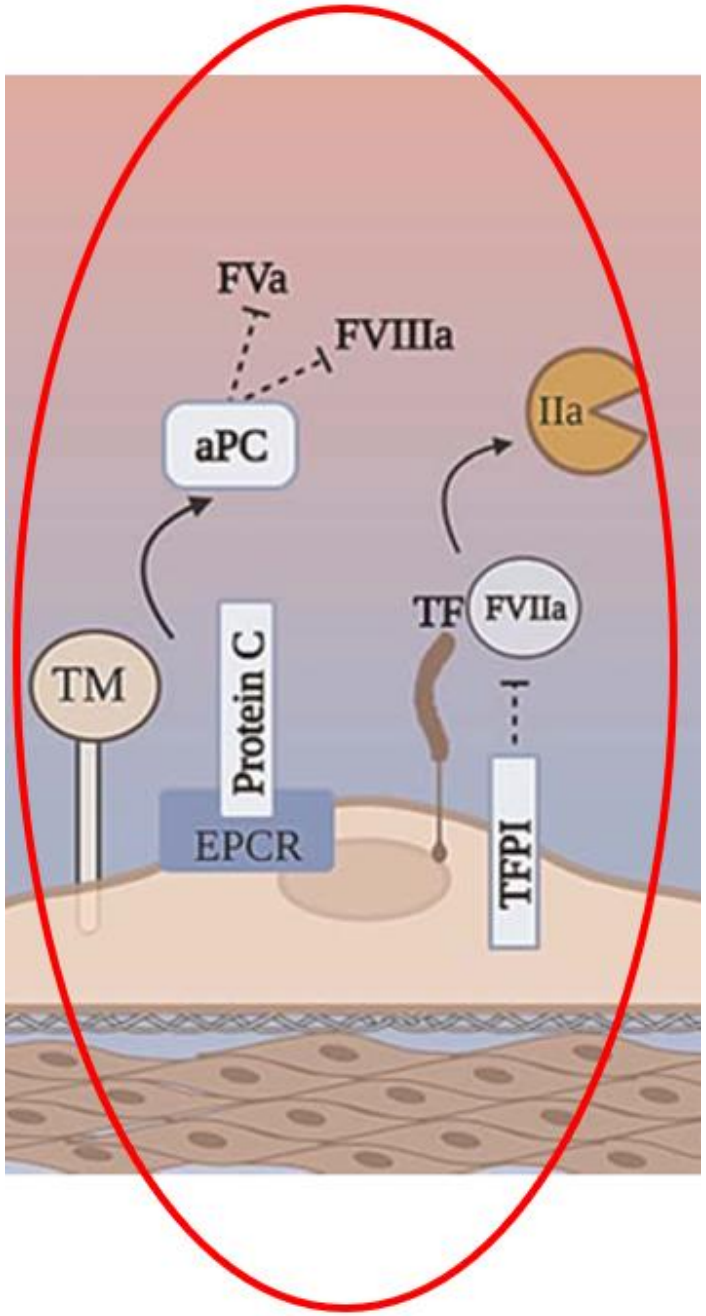
28.6% vs. 32.6%
1.17 (0.82 – 1.68)

24.5% vs. 7.3%
0.30 (0.14 – 0.63)



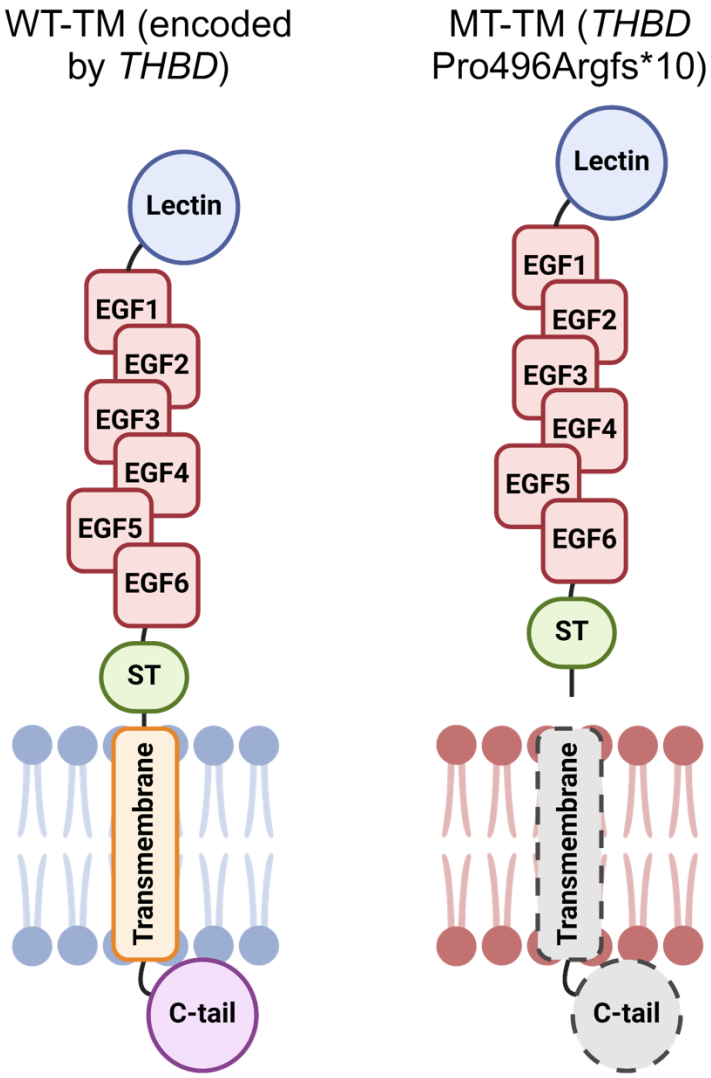
Adapted from: Douin et al, Anaesthesiology, 2022

Haemostatic surface



Endothelial thrombomodulin in health and trauma

Dr. J. Abu-Hanna



Patients with this truncating TM variant bleed abnormally

Endothelial thrombomodulin in health and trauma

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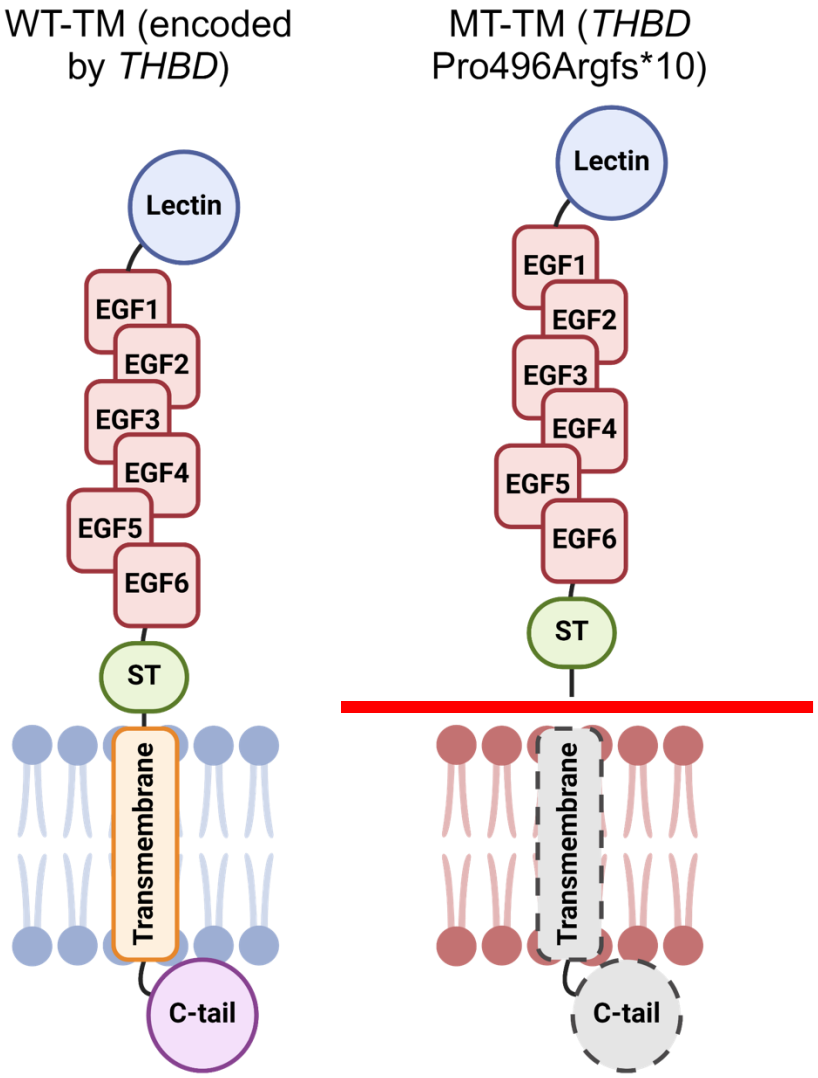

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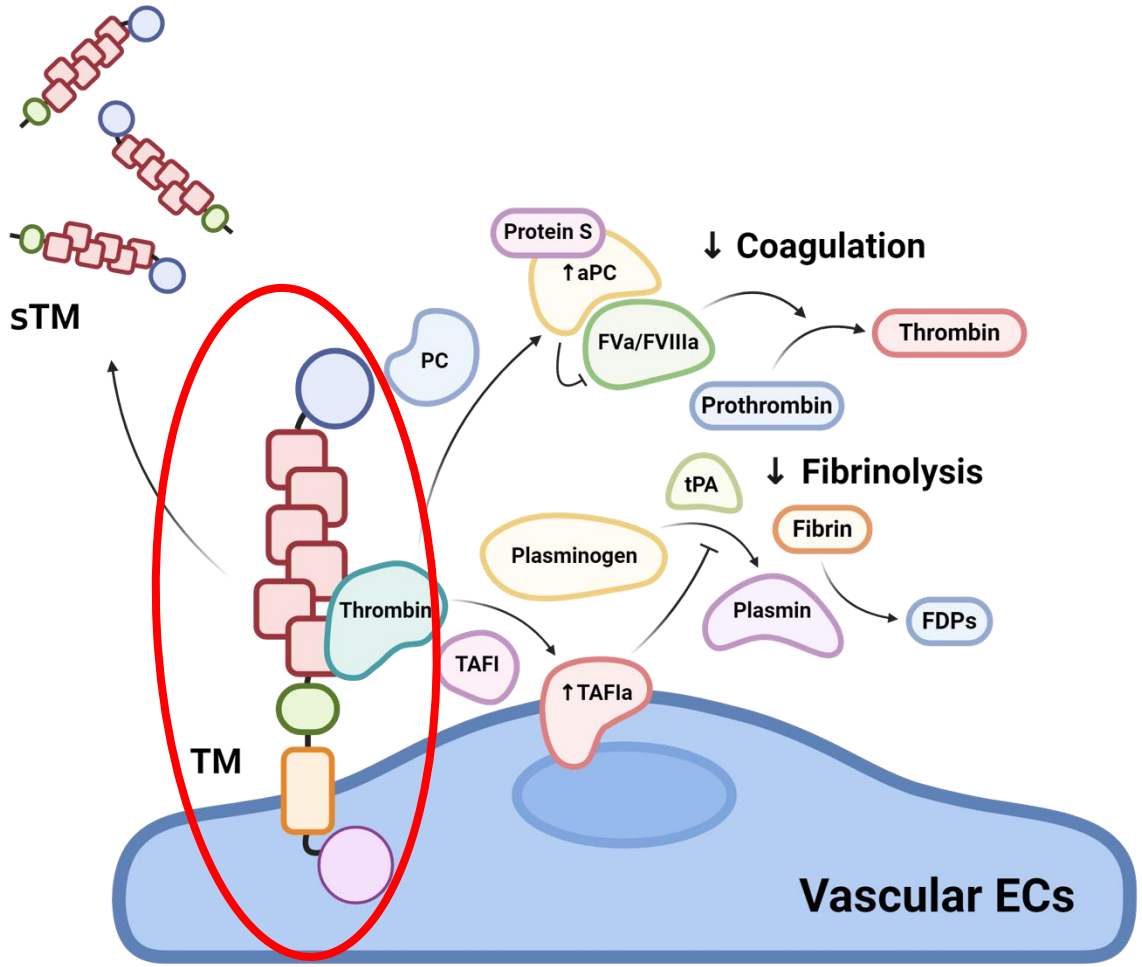
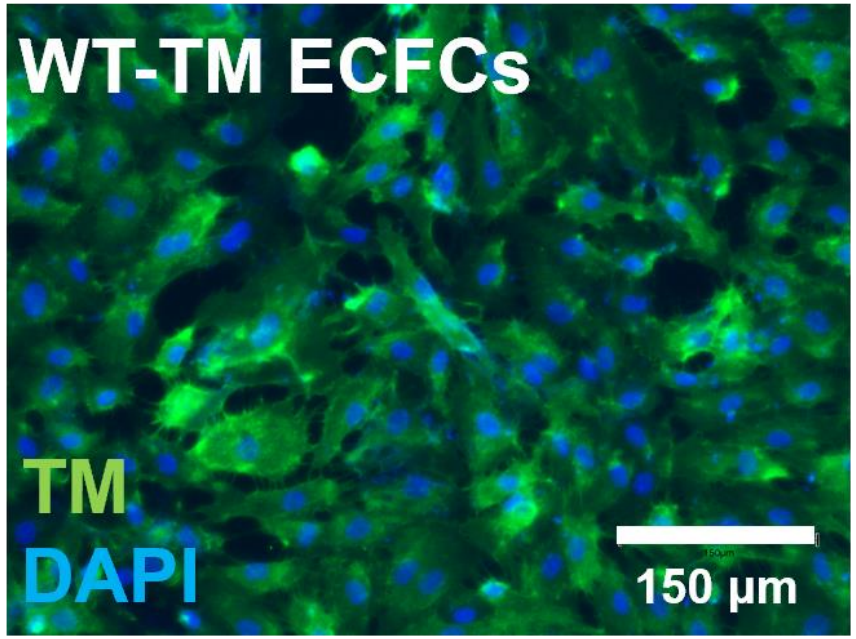
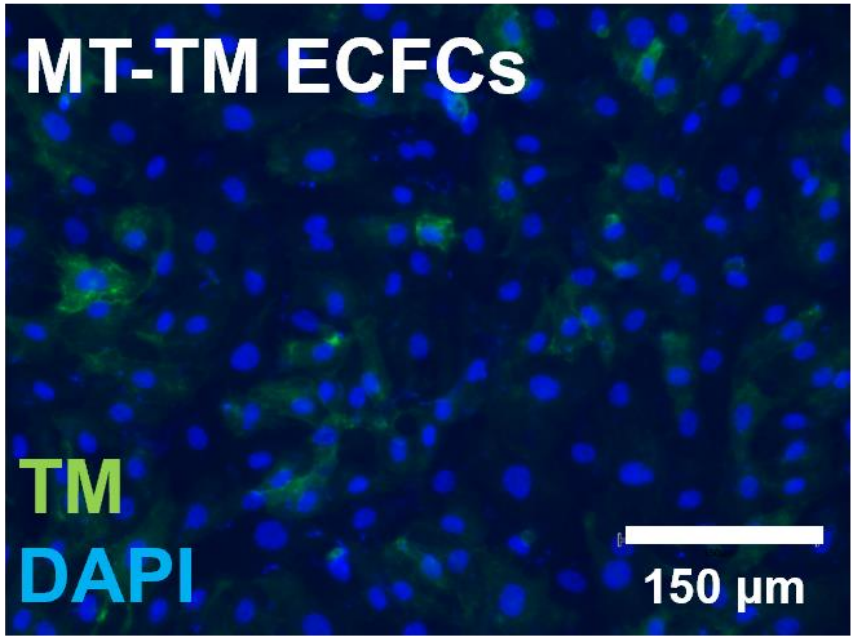


Clotting

Clot breakdown

TM variant releases TM and has low surface levels

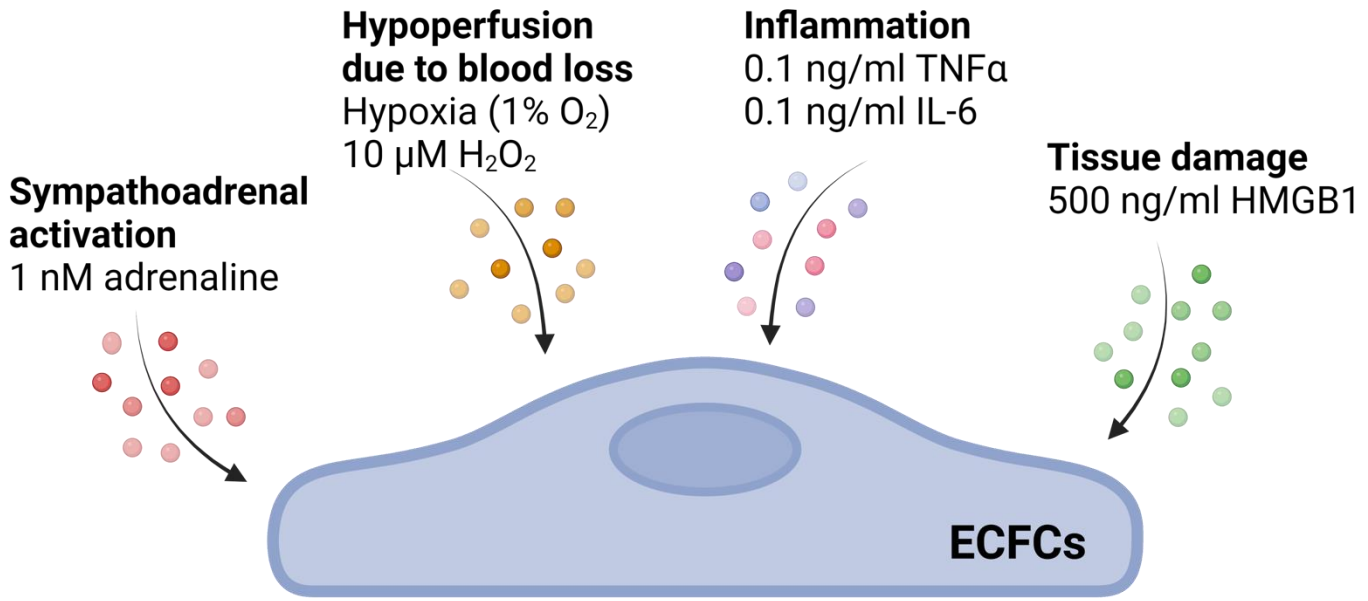




Simulating trauma conditions *in vitro* induces surface TM shedding in WT-TM ECFCs

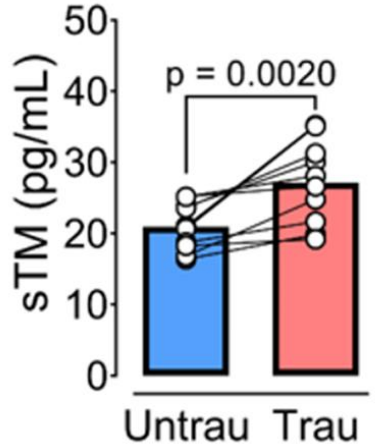
Hypothesis: Simulating trauma conditions heightens shedding of surface TM in WT-TM ECFCs

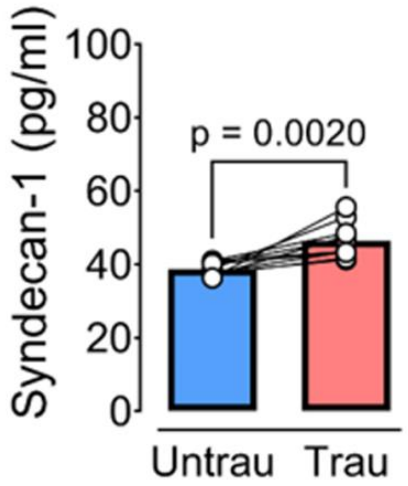
In vitro
"traumatisation"



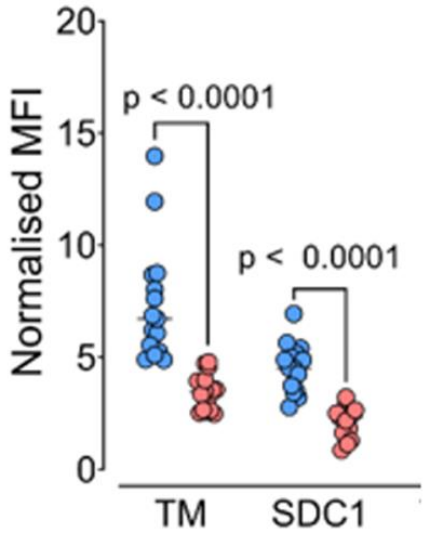
Simulating trauma conditions *in vitro* induces surface TM shedding in WT-TM ECFCs

Supernatant

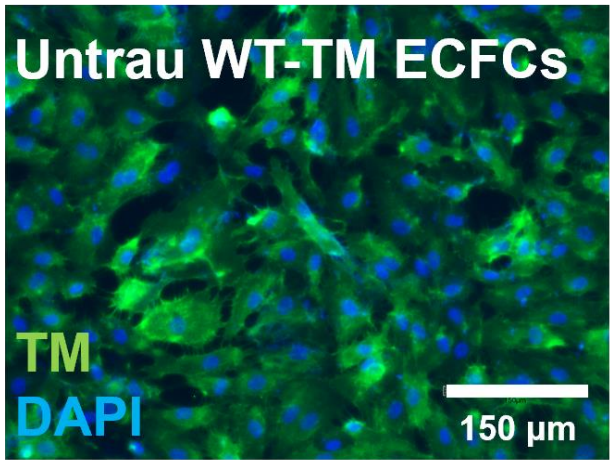


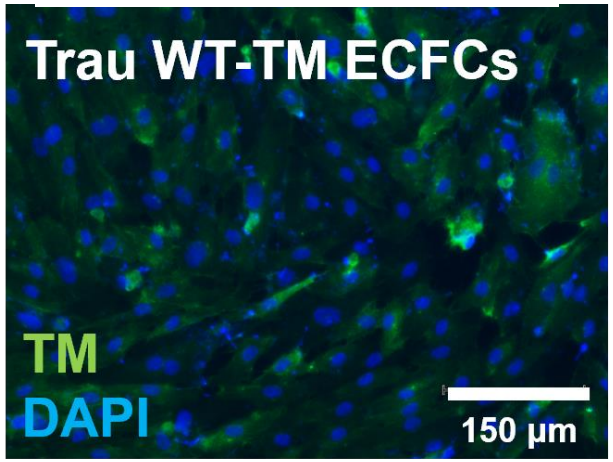


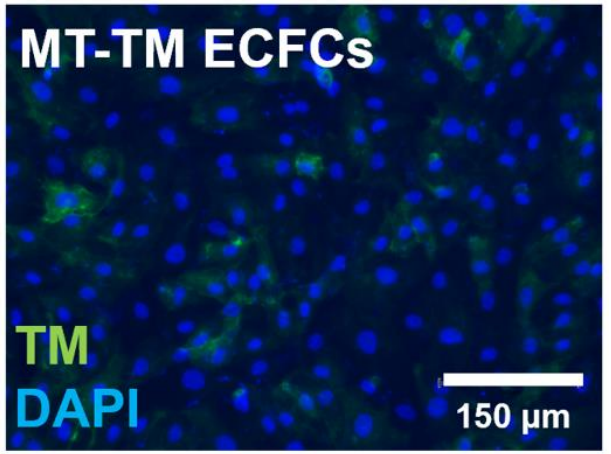
Endothelial cell surface



Untrau WT-TM ECFCs
Trau WT-TM ECFCs

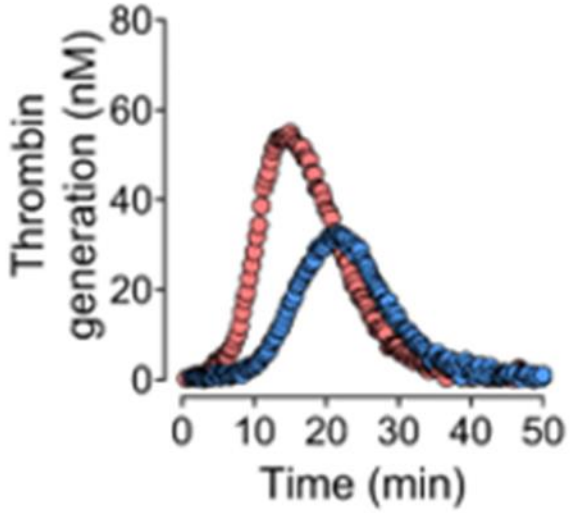


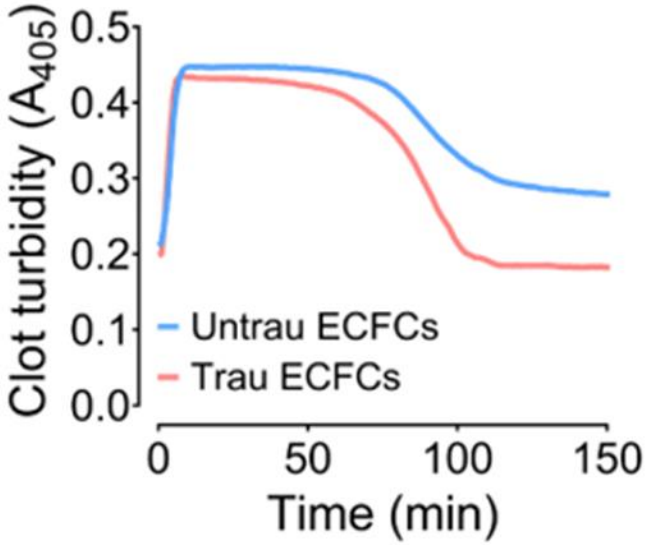




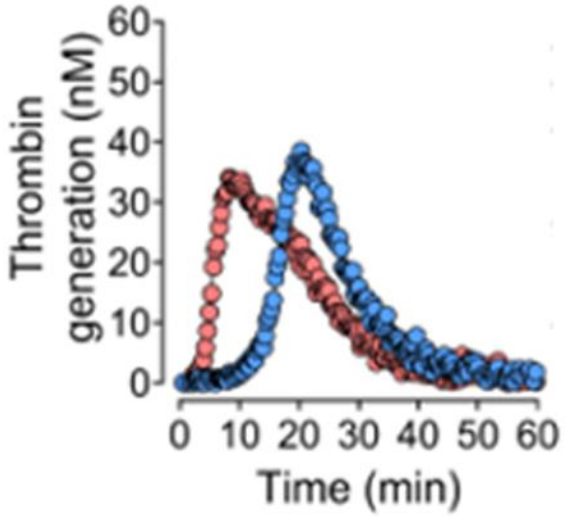
In vitro traumatisation alters haemostatic potential of WT-ECFC surface and its supernatant

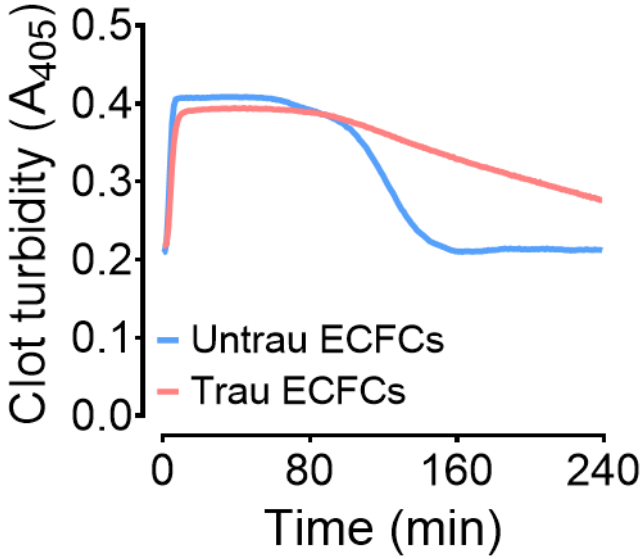
Endothelial cell surface





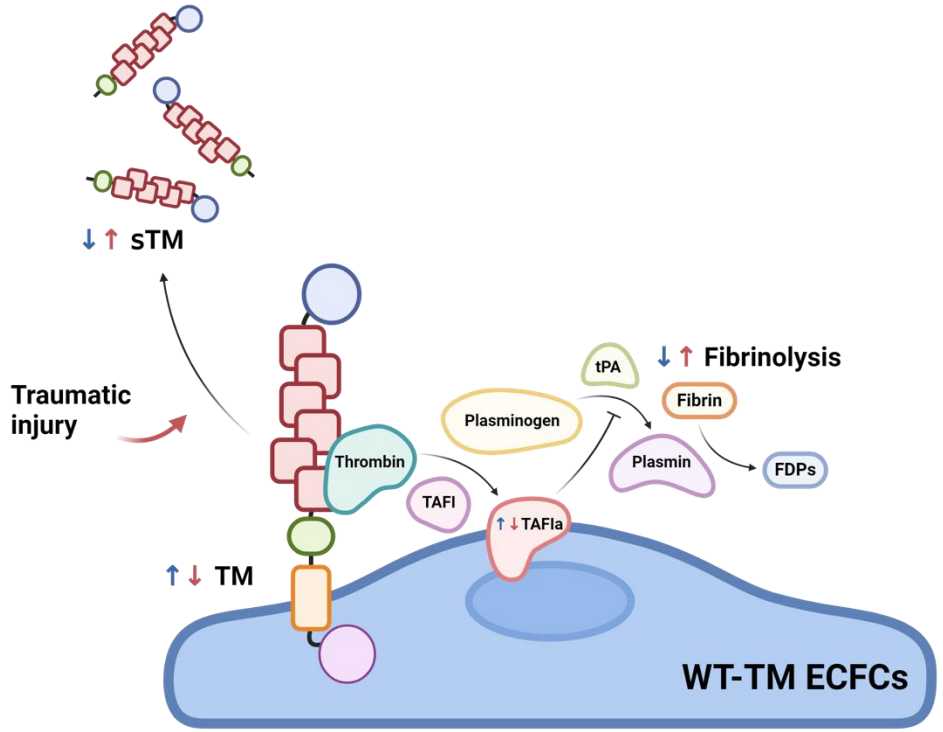
Supernatant





Untrau WT-TM ECFCs
Trau WT-TM ECFCs

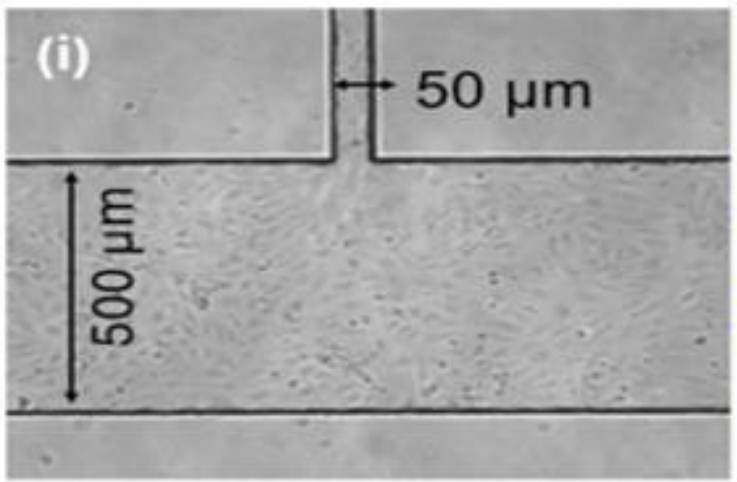
In vitro traumatisation alters haemostatic potential of WT-ECFC surface and its supernatant

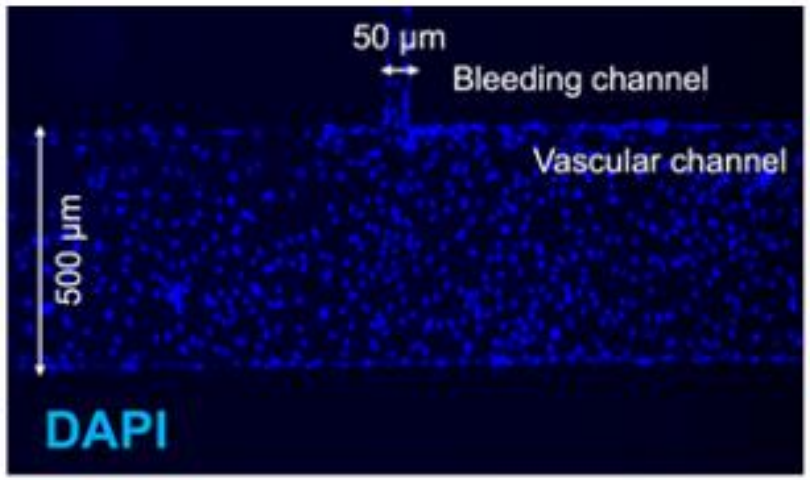


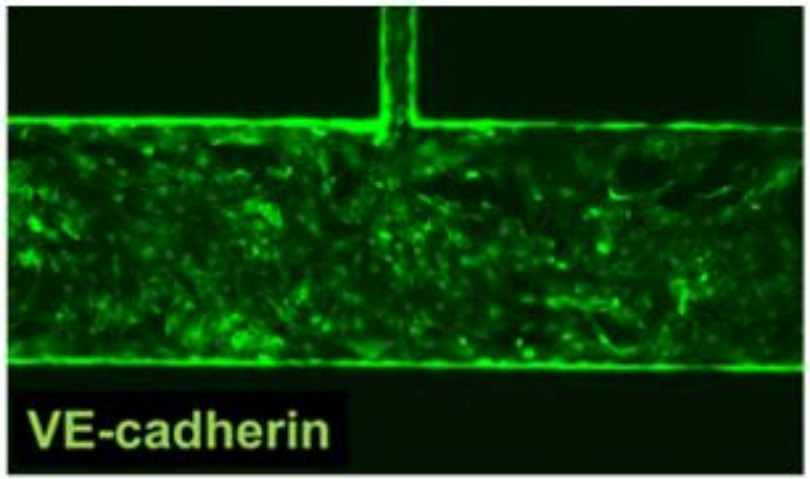
Traumatisation:

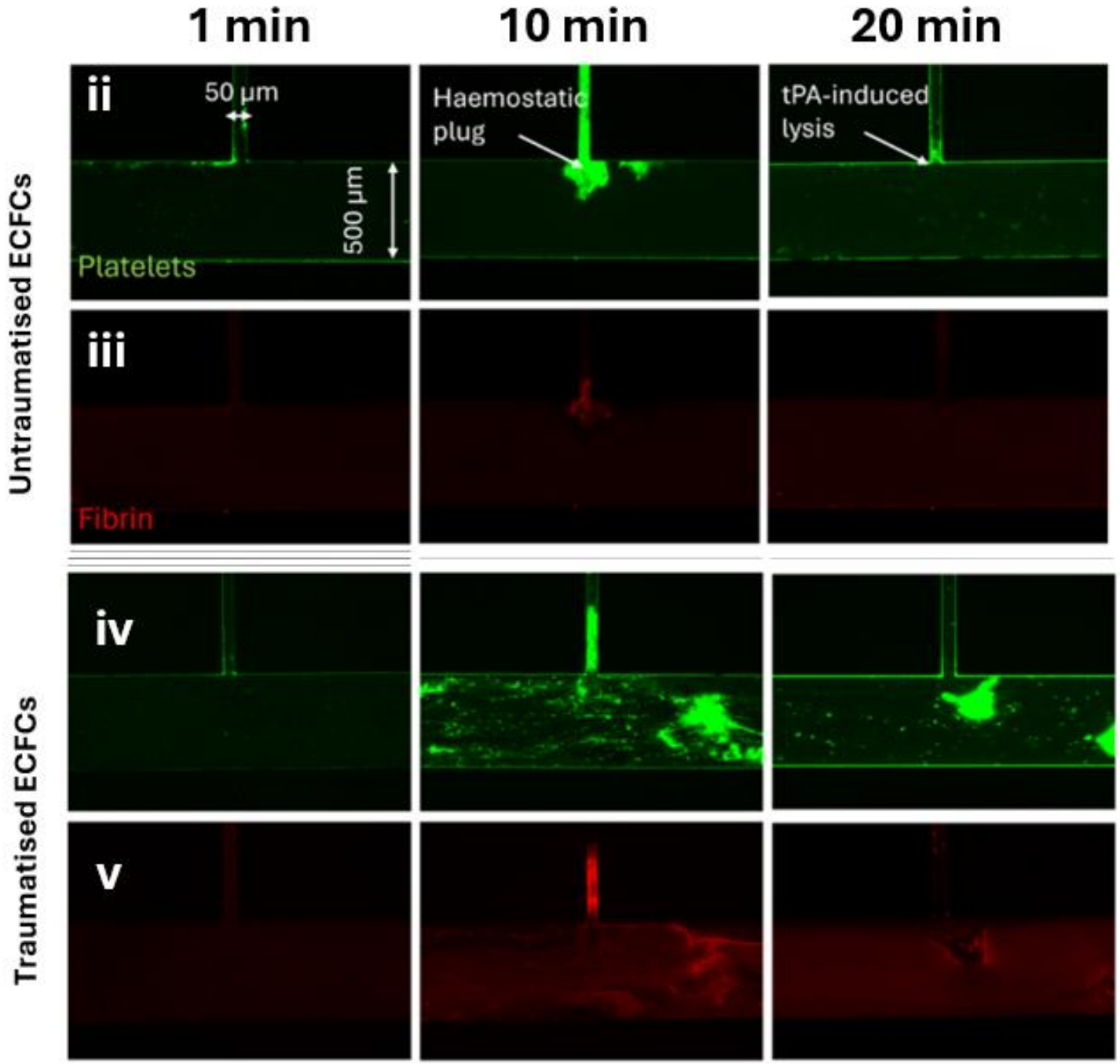
- Increases TM shedding
- Low surface TM:
  - Greater fibrinolysis
  - Greater clot formation
- Higher soluble TM:
  - Slower clot lysis

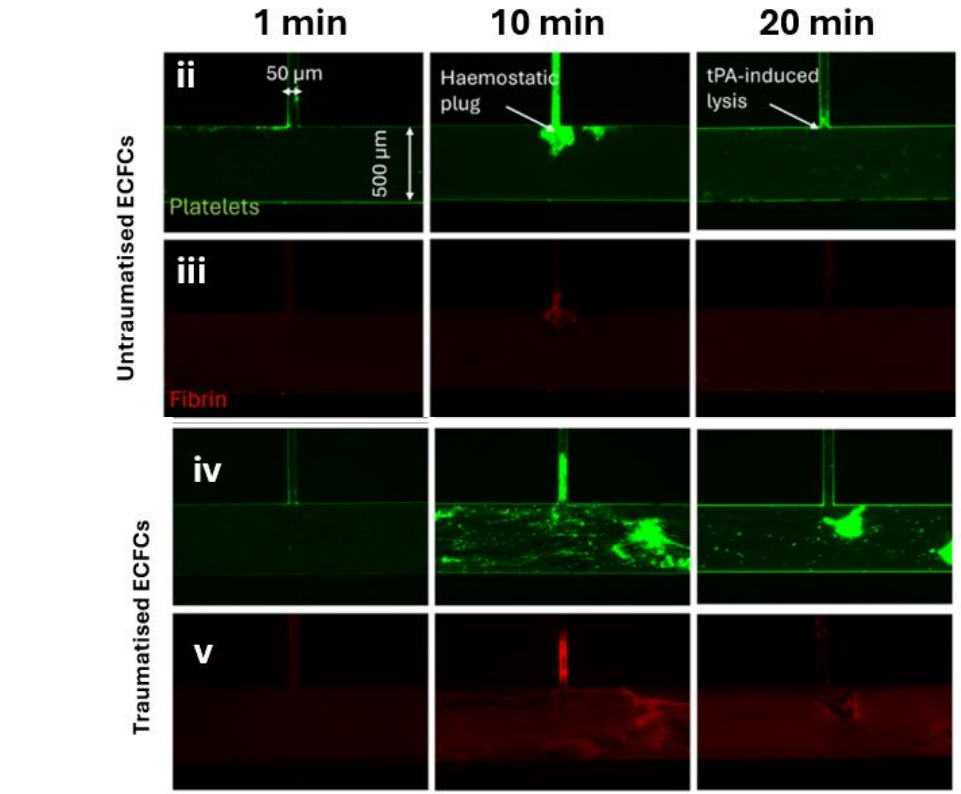
Trauma endothelial model under flow








1 min
10 min
20 min
Untraumatised ECFCs
Traumatised ECFCs
ii
50 µm
500 µm
Platelets
Haemostatic plug
tPA-induced lysis
iii
Fibrin
iv
v


1 min
10 min
20 min
ii
50 µm
500 µm
Platelets
Haemostatic plug
tPA-induced lysis
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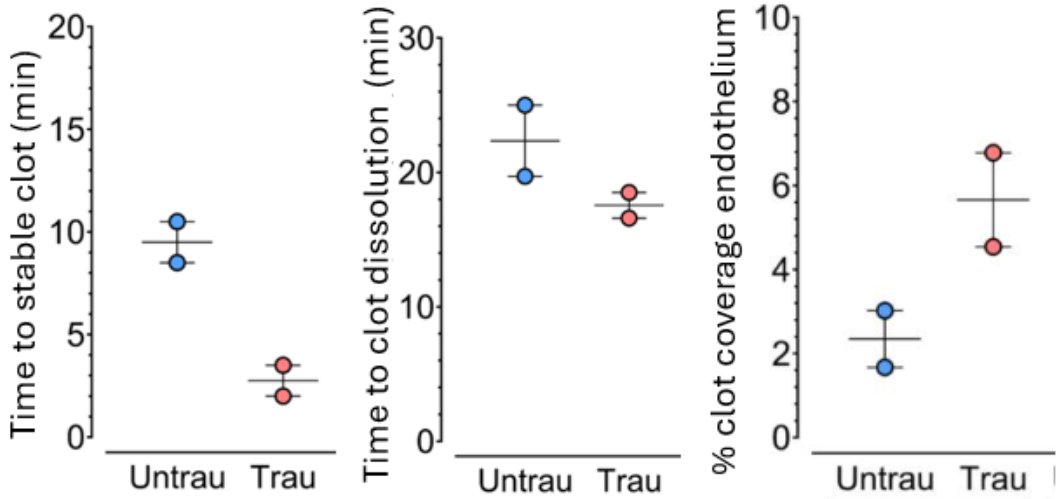
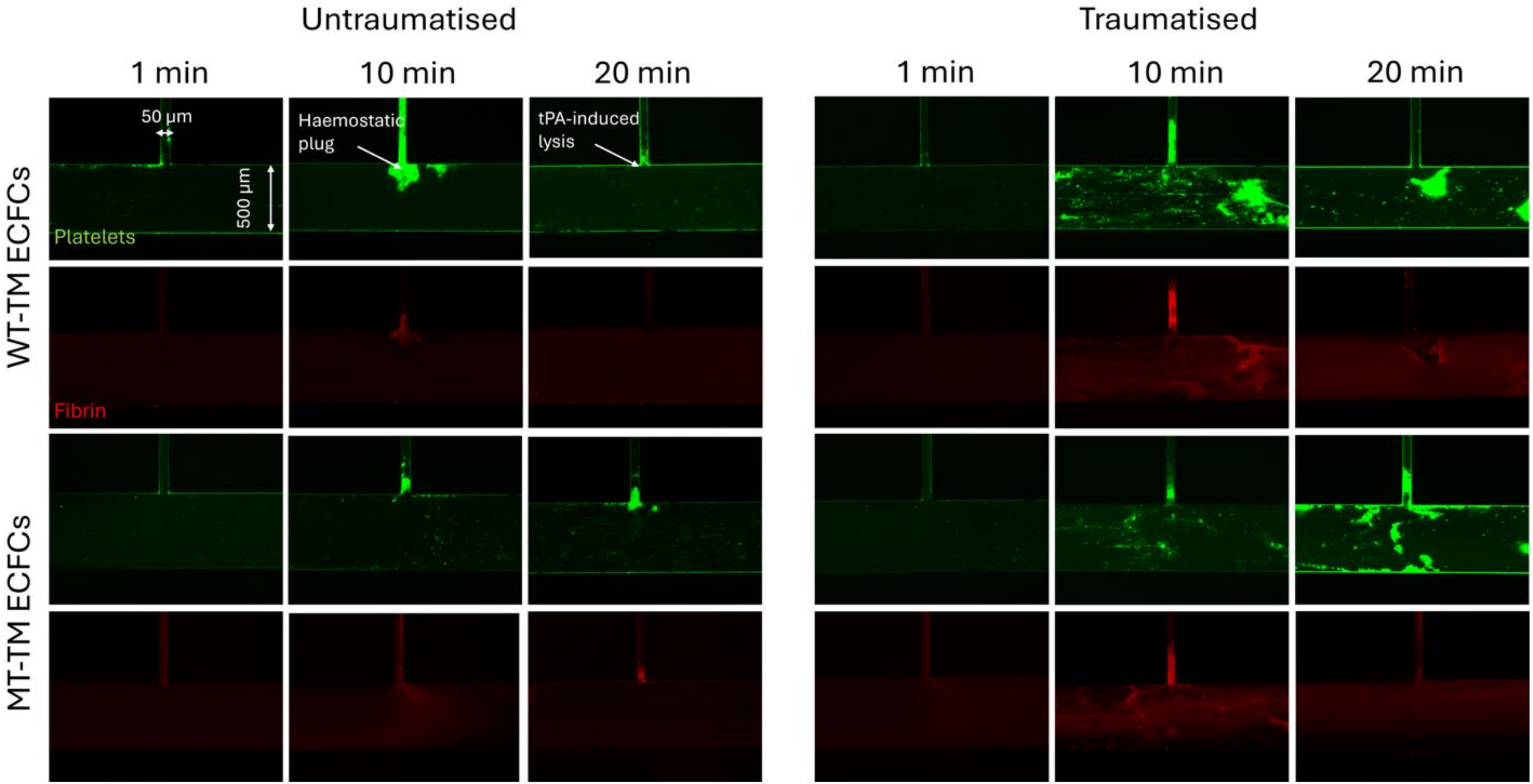
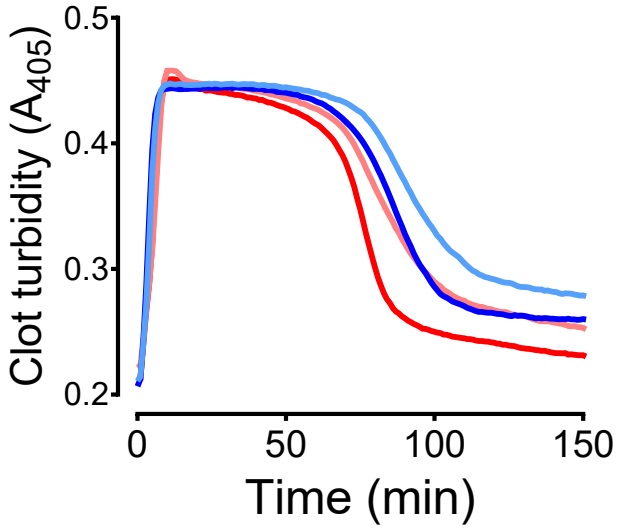
Fibrin
Untraumatised ECFCs
iv
v
Traumatised ECFCs


Time to stable clot (min)
0
5
10
15
20
Untrau
Trau
Time to clot dissolution (min)
0
10
20
30
Untrau
Trau
% clot coverage endothelium
0
2
4
6
8
10
Untrau
Trau

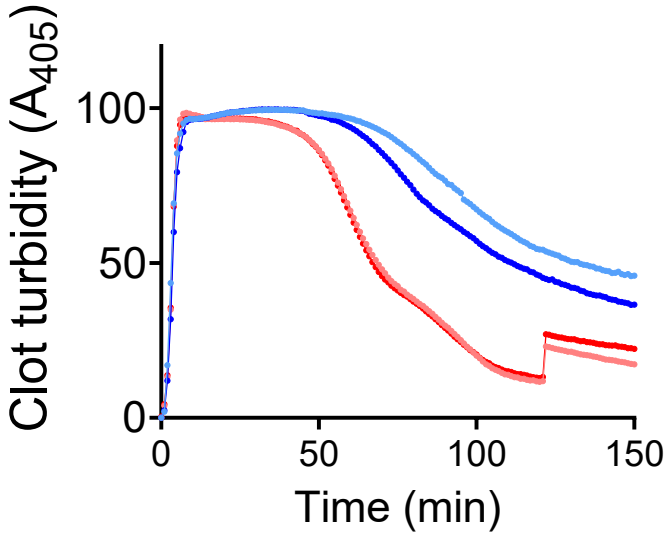

Untraumatised
Traumatised
1 min
10 min
20 min
1 min
10 min
20 min
WT-TM ECFCs
MT-TM ECFCs
50 µm
500 µm
Platelets
Fibrin
Haemostatic plug
tPA-induced lysis

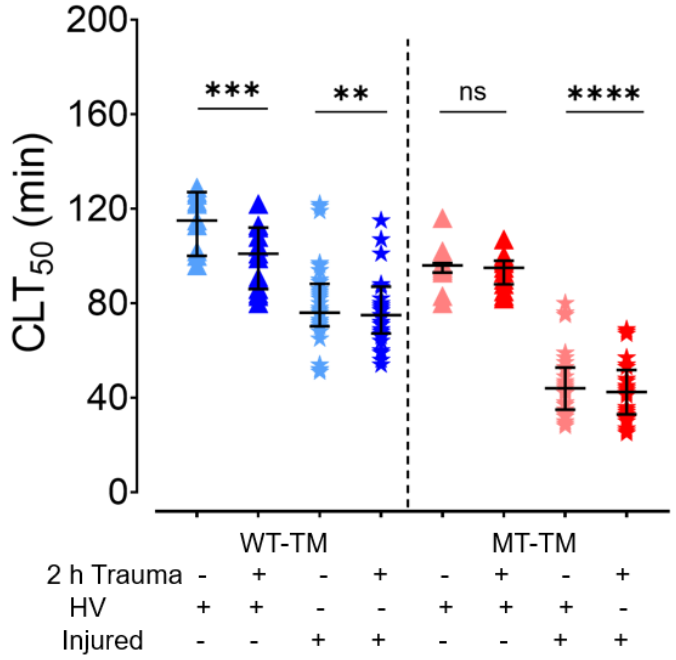
Endothelial coagulation interface

Healthy volunteer plasma



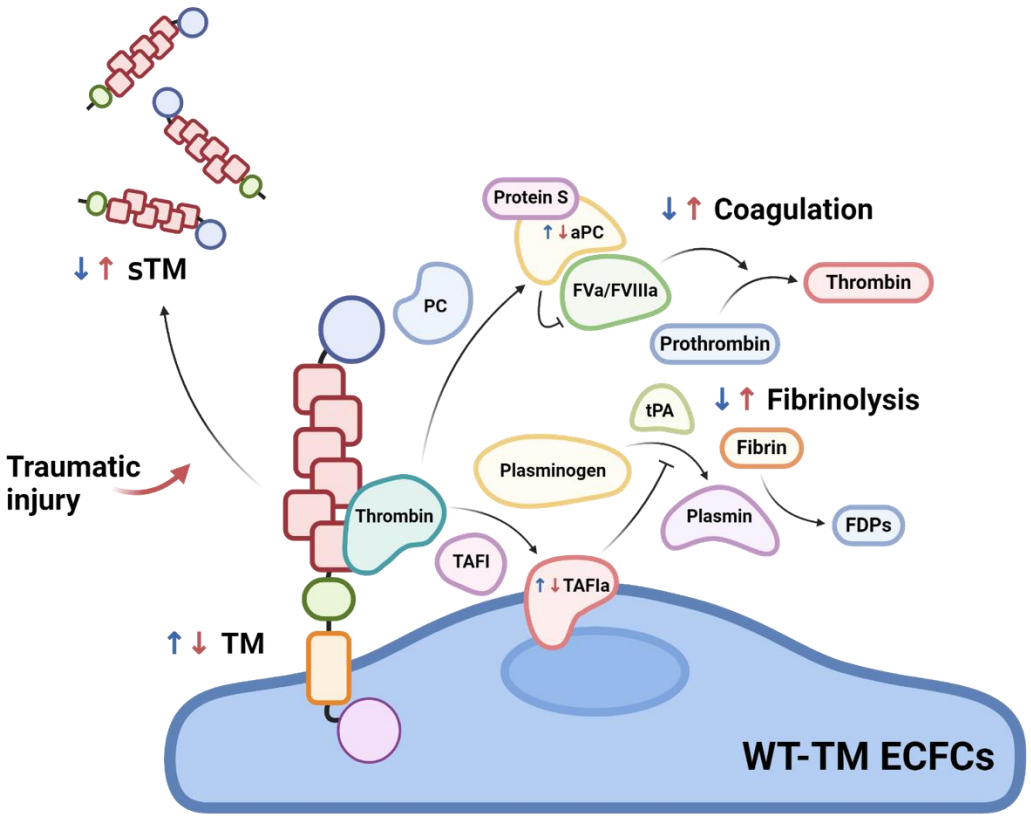
Trauma patient plasma





Untraumatised WT-TM
Traumatised WT-TM
Untraumatised MT-TM
Traumatised MT-TM

Conclusions



- Endothelial-coagulation interface should be viewed as a continuum

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