



Endothelial cell-derived extracellular vesicles released upon stimulation with antiphospholipid antibodies: A genuine direct procoagulant mechanism or a new factor in the lupus anticoagulant paradox?

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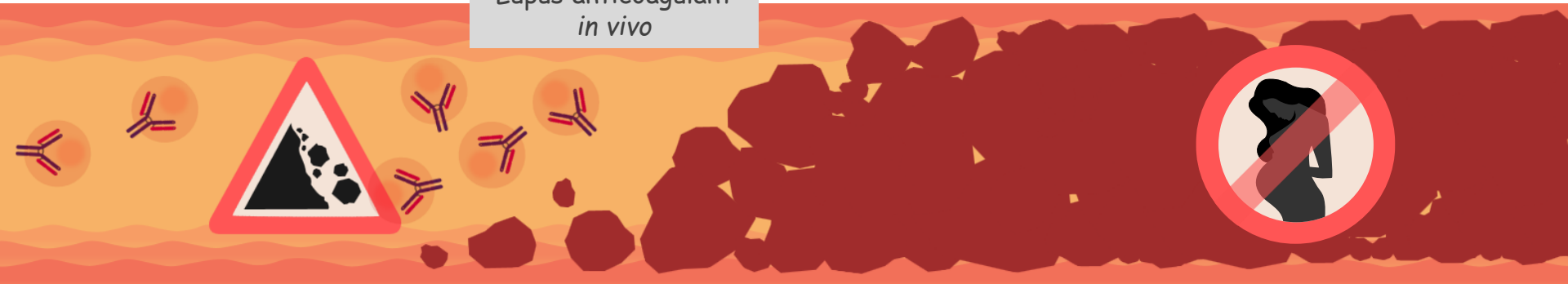
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Antiphospholipid syndrome and lupus anticoagulant

Vascular
thrombosis

Lupus anticoagulant
in vivo

Pregnancy-related
morbidity

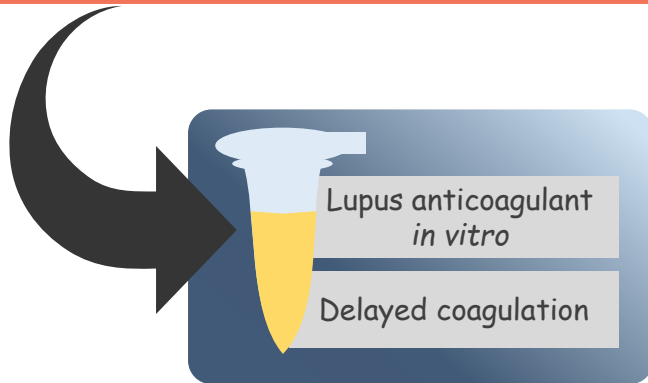
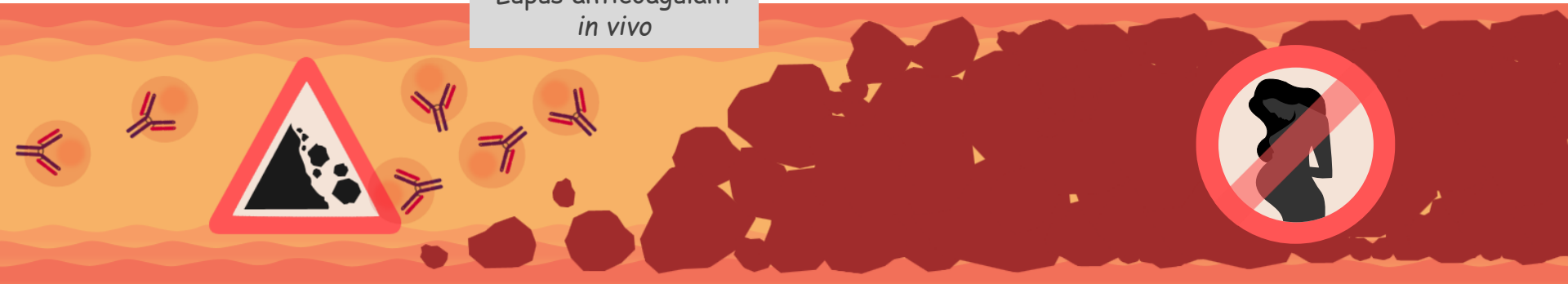


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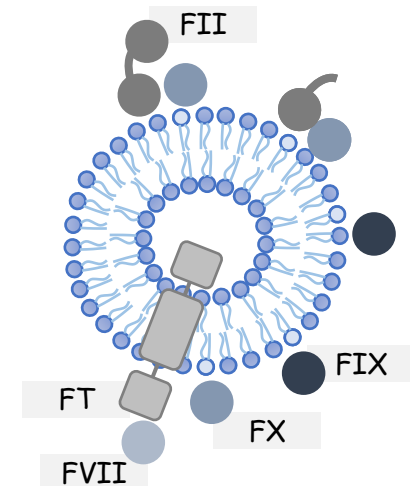
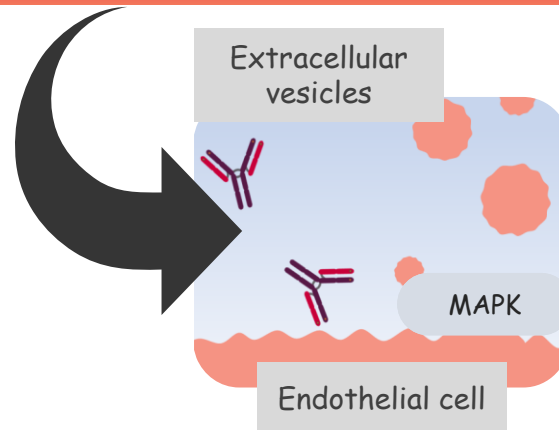
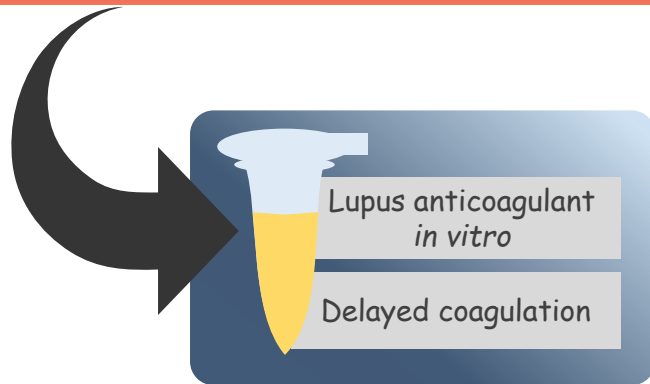
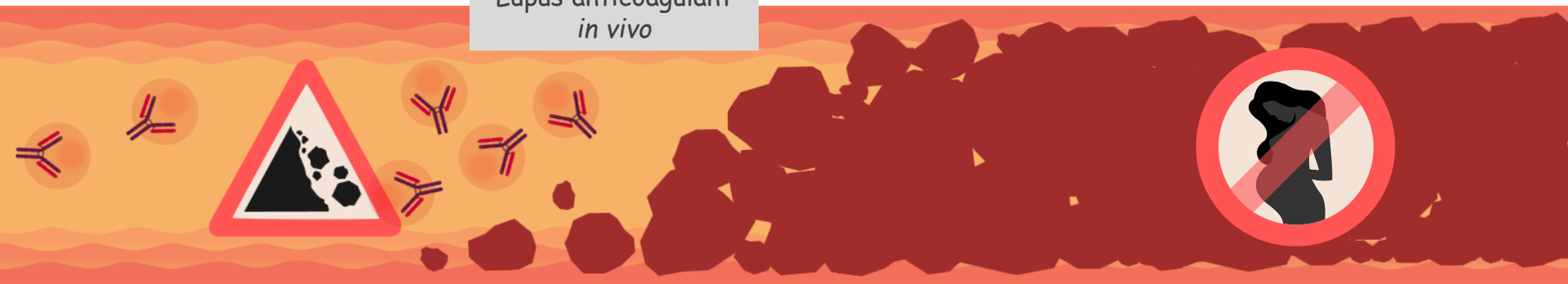


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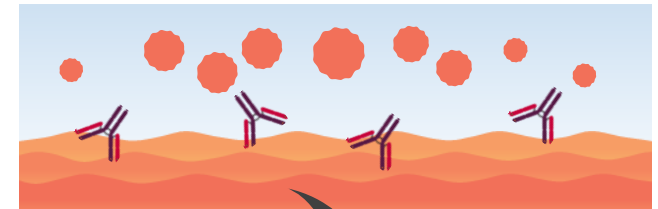
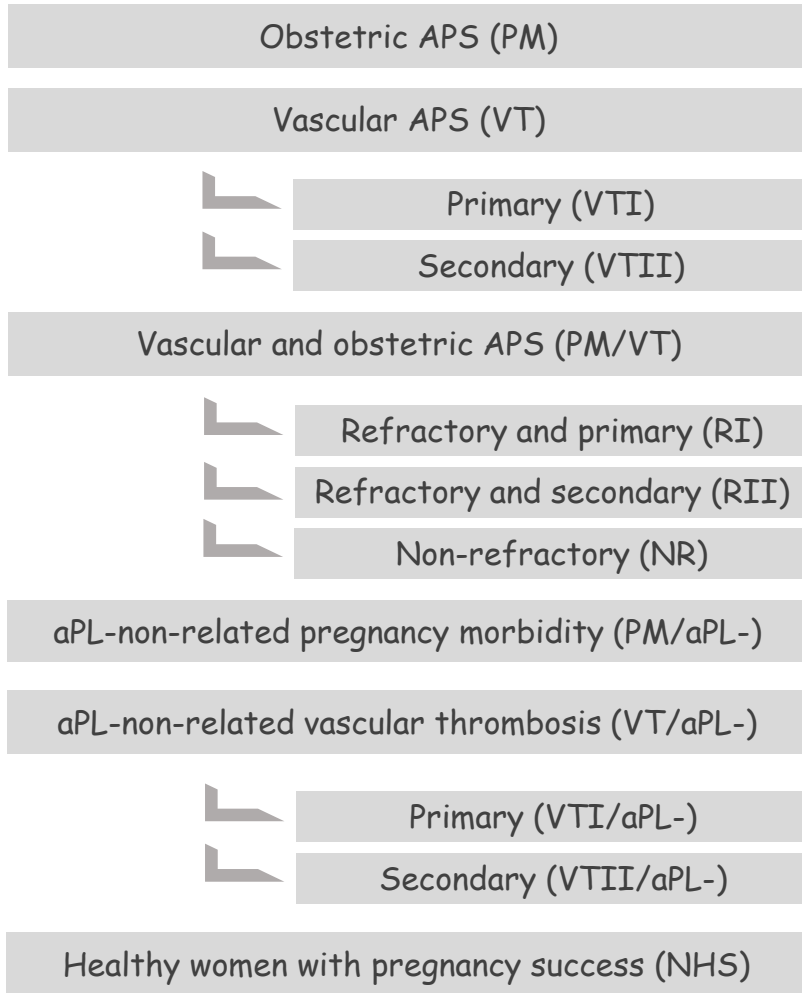
Lupus anticoagulant *in vivo*



Objective

To assess whether endothelial cell-derived extracellular vesicles released upon stimulation with aPL (aPL-EDEVs) are related or not to a higher direct coagulation activity.

Methods



HUVECs



Extracellular vesicle-rich supernatants

- EDEVs count by Flow cytometry
- Coagulation activity by recalcified plasma-based assay

Results

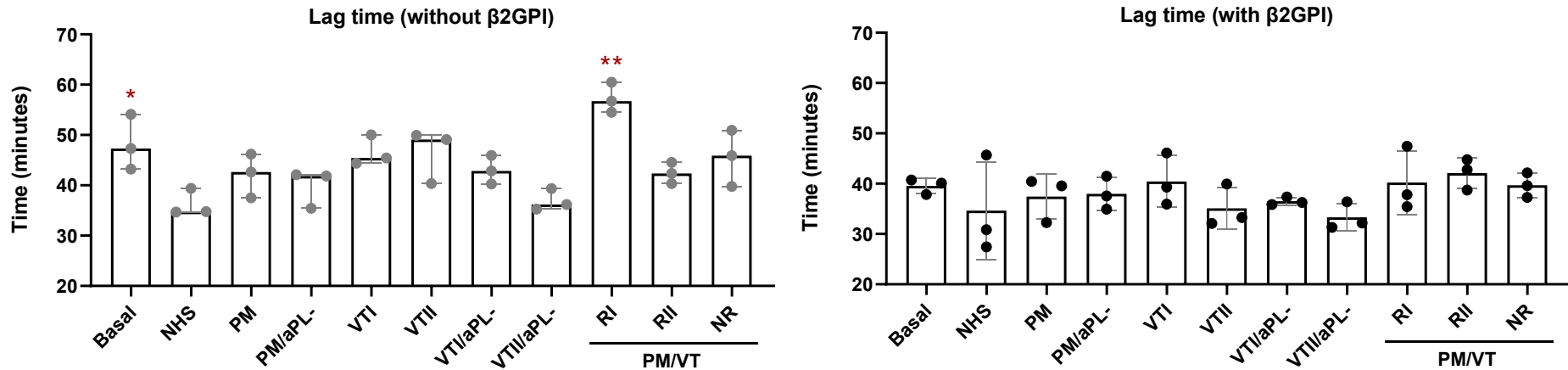


Figure 1. EDEV-rich supernatant from endothelial cells stimulated with IgG from RI patients exhibits a dampened coagulation activity. This anticoagulant effect is abrogated by using β 2GPI, main cofactor of aPL, during the stimulation of endothelial cells.

Results

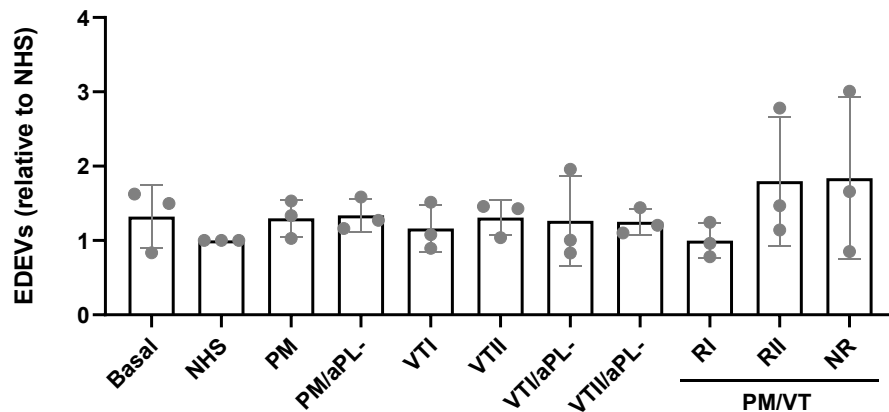


Figure 2. There are no statistically significant differences between the EDEV counts

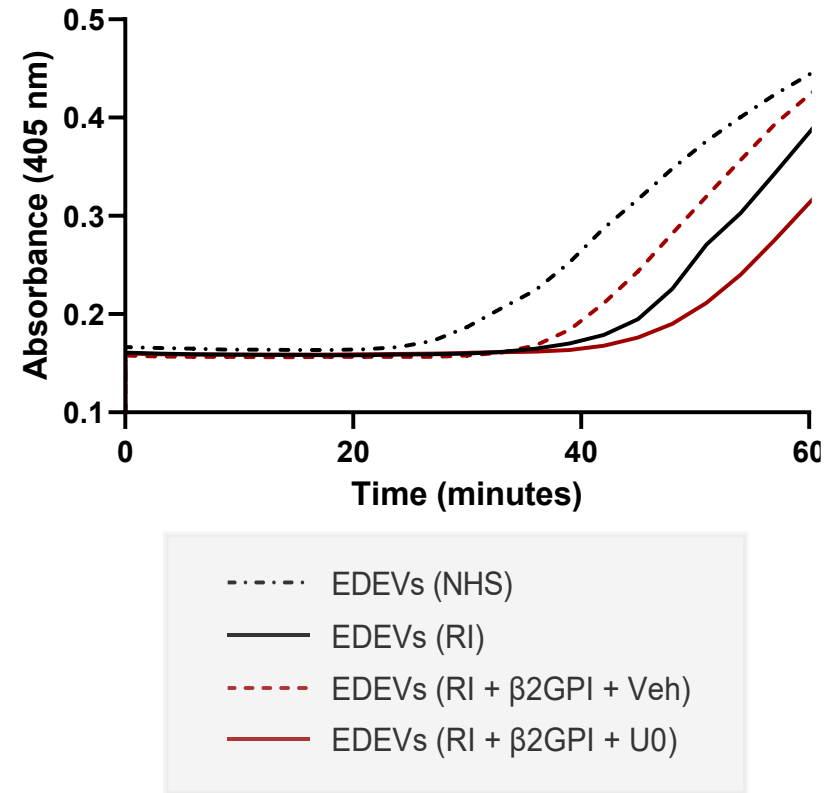
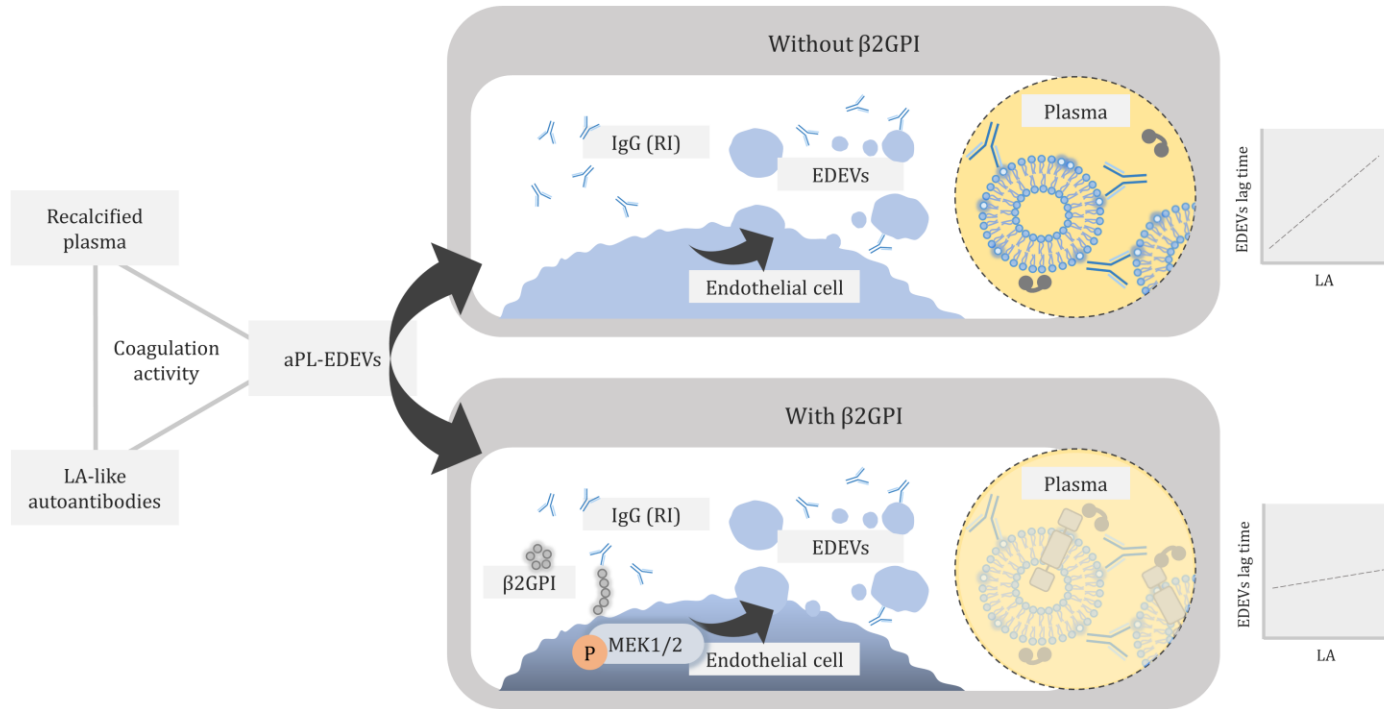


Figure 3. Inhibiting the MEK1/2 pathway hinders the procoagulant action of β 2GPI

Concluding model



Lupus anticoagulant-like autoantibodies exhaust the coagulation activity of the extracellular vesicle-rich supernatants. This anticoagulant effect can be countered by using $\beta 2\text{GPI}$ as a cofactor of IgG during endothelial cell stimulation. Inhibiting the MEK1/2 pathway prevents the restorative and procoagulant activity of $\beta 2\text{GPI}$.

Acknowledgements



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