

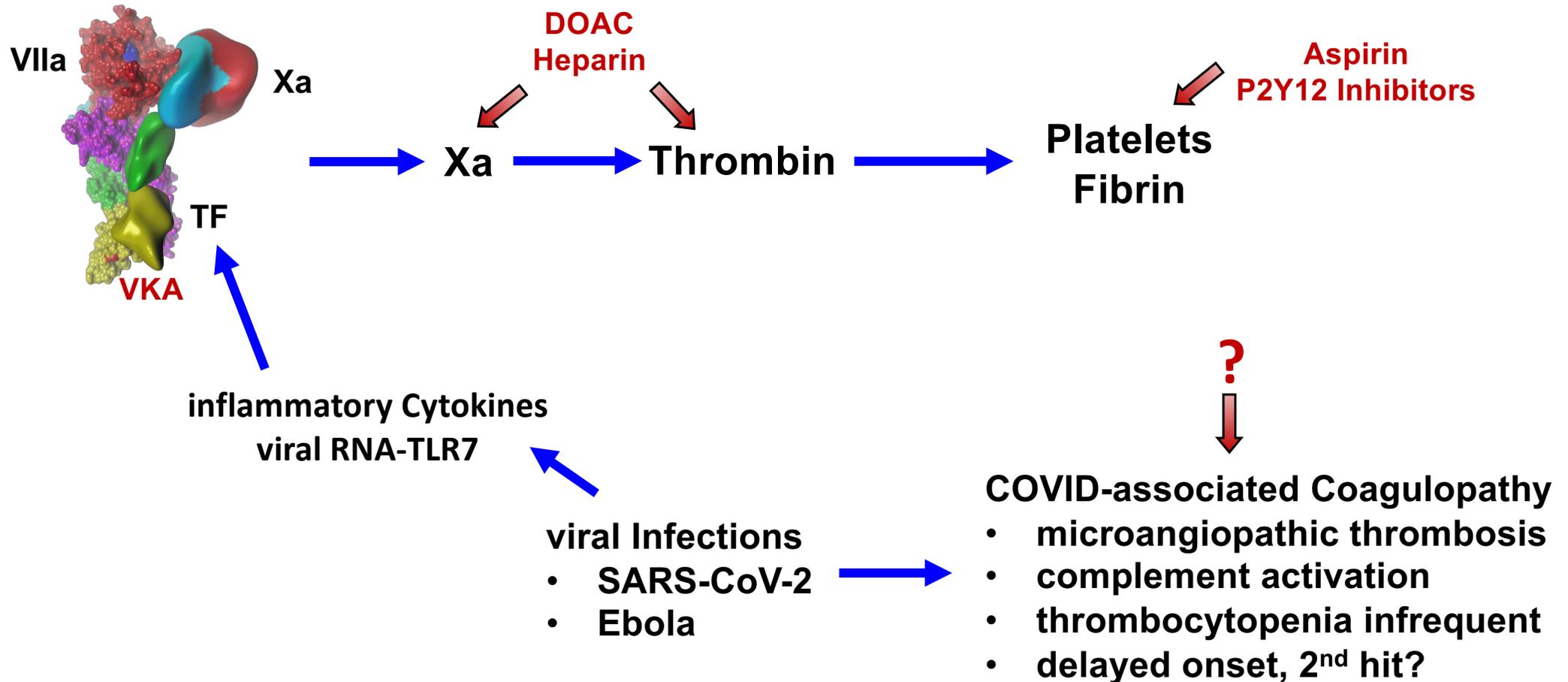
# *Zielstruktur für Antiphospholipid Antikörper: Therapeutische Optionen in Autoimmunität und COVID-19*

**Prof. Dr. Wolfram Ruf**

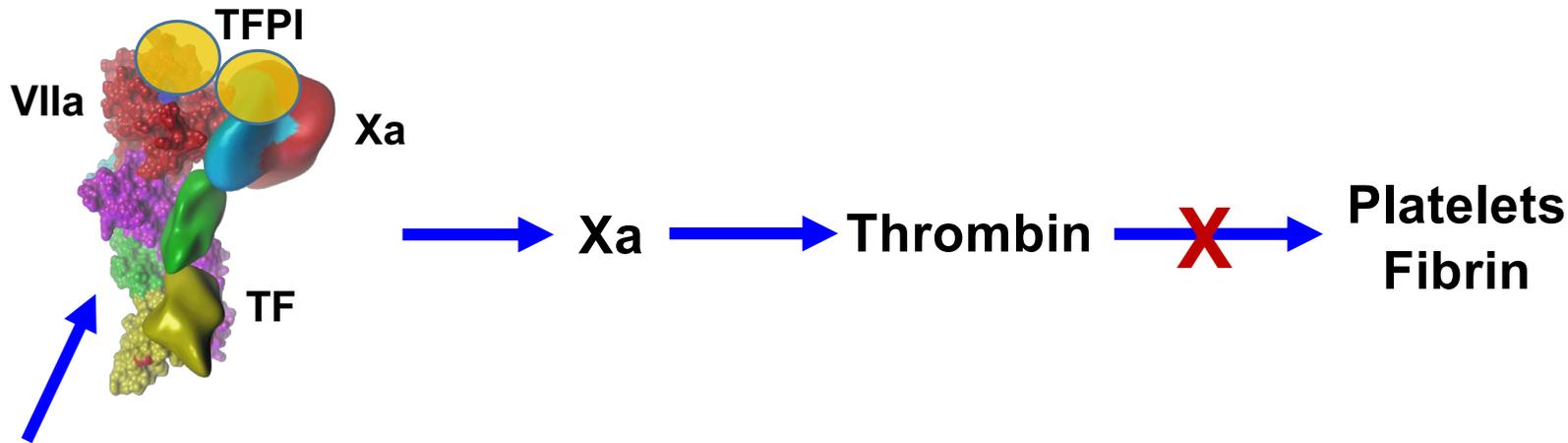
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# Coagulation Cascade Targets in Cardiovascular Diseases



# Antiphospholipid Antibodies (aPL) activate the TF Complex



**Antiphospholipid antibodies (aPL)**

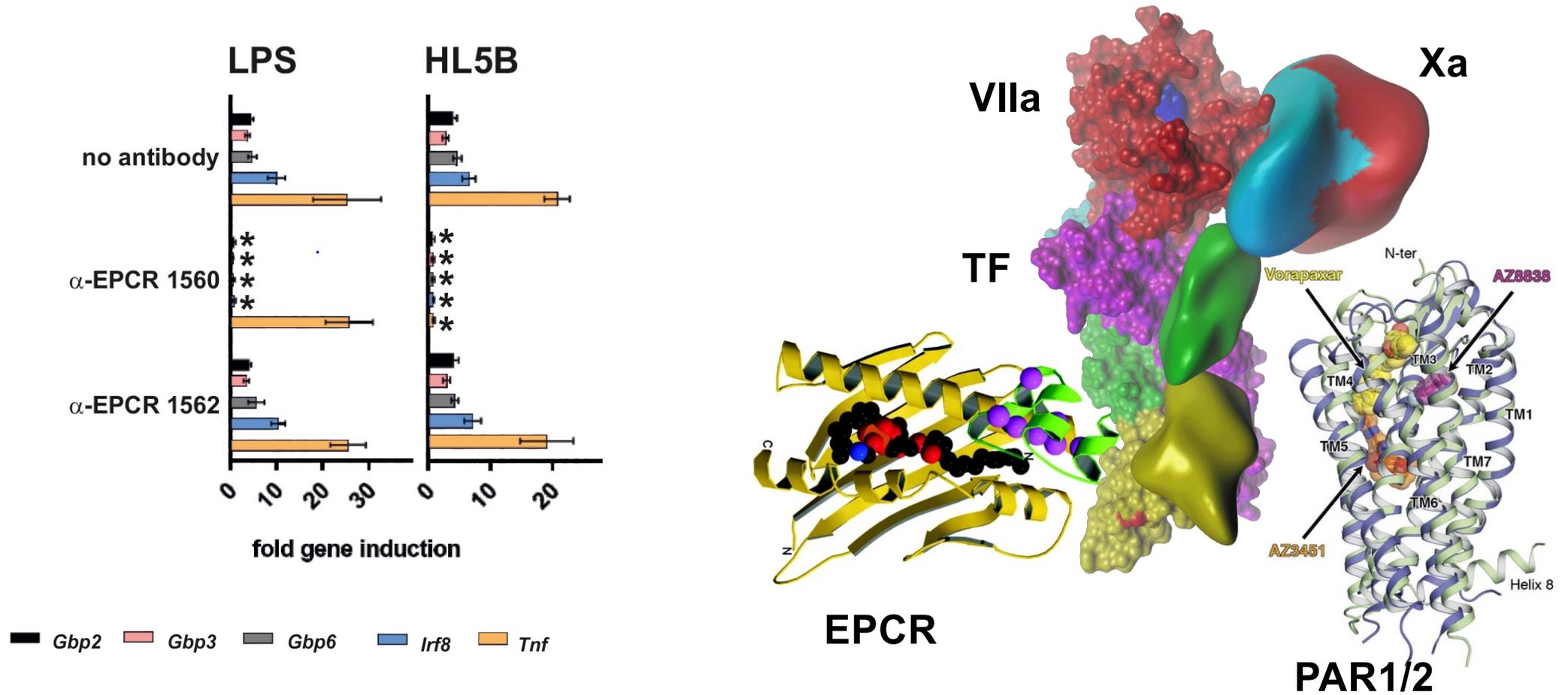
- develop in viral infections and autoimmune diseases
- diagnostic reactivity with cardiolipin
- cross-reactivity with plasma proteins ( $\beta$ 2GPI, prothrombin, PS)
- cause venous and arterial thrombosis and pregnancy complications



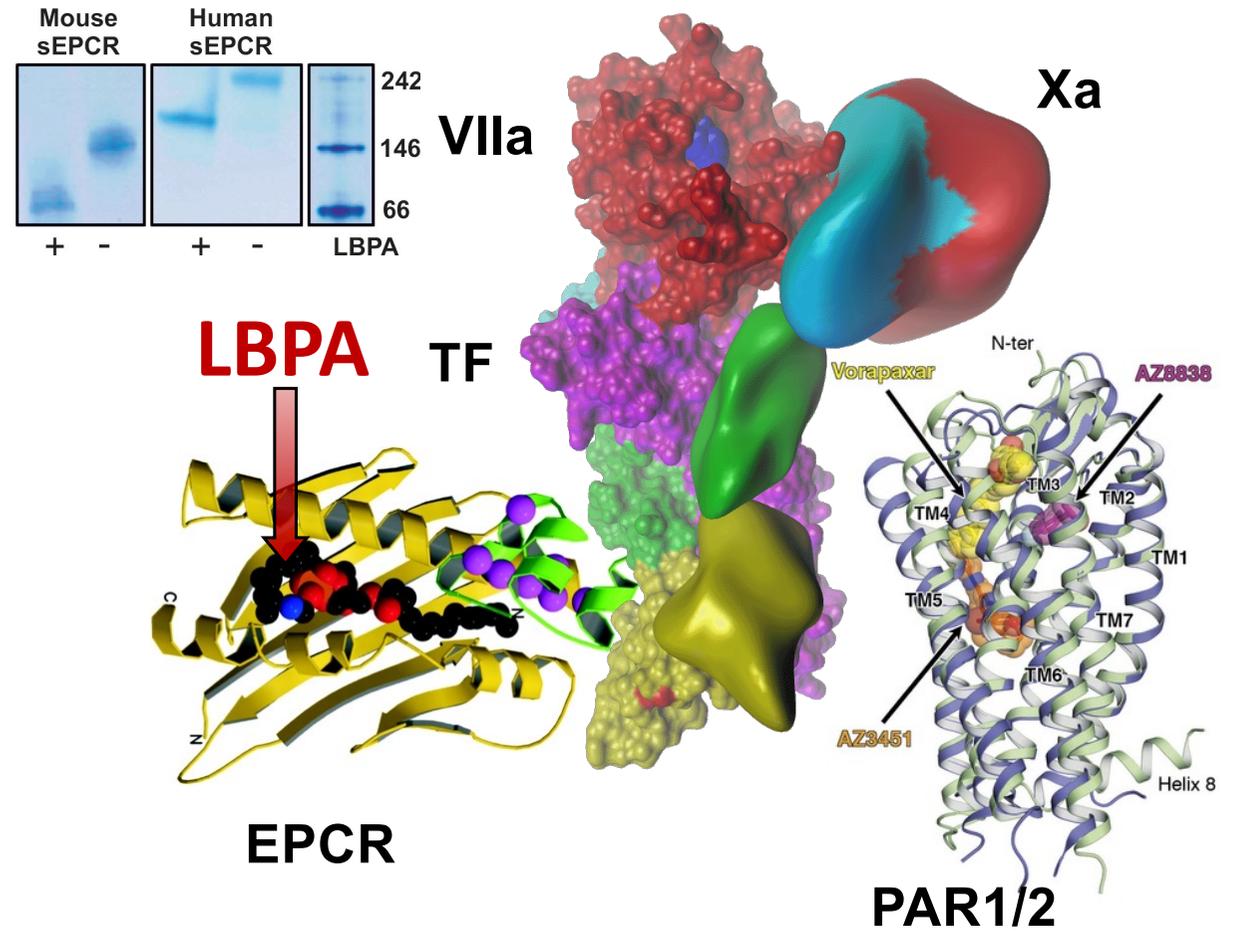
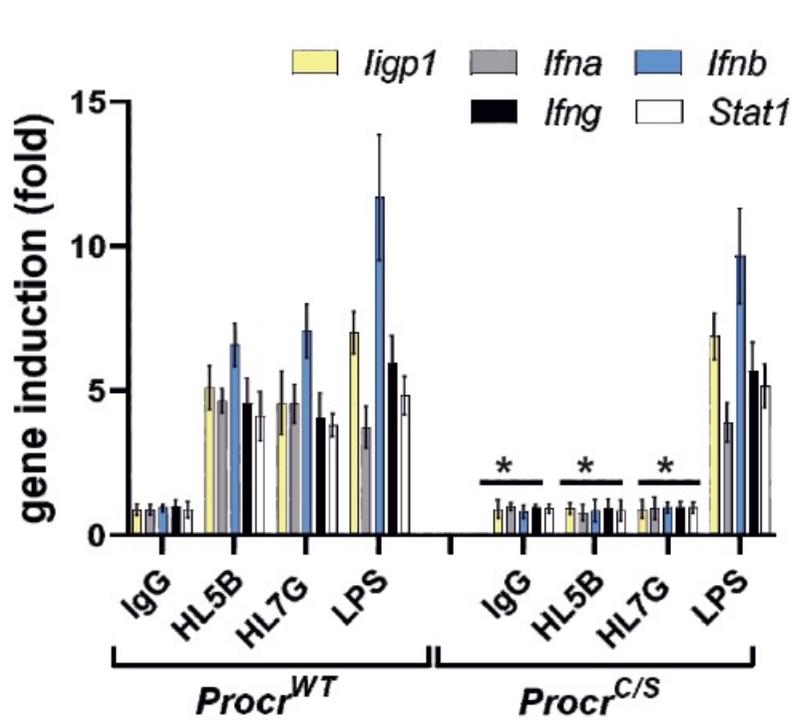
**aPL activate TF-thrombin-PAR signaling to cause**

- complement-dependent upregulation of inflammation (TNF) and coagulation (TF)
- endosomal ROS production
- type I interferon induction

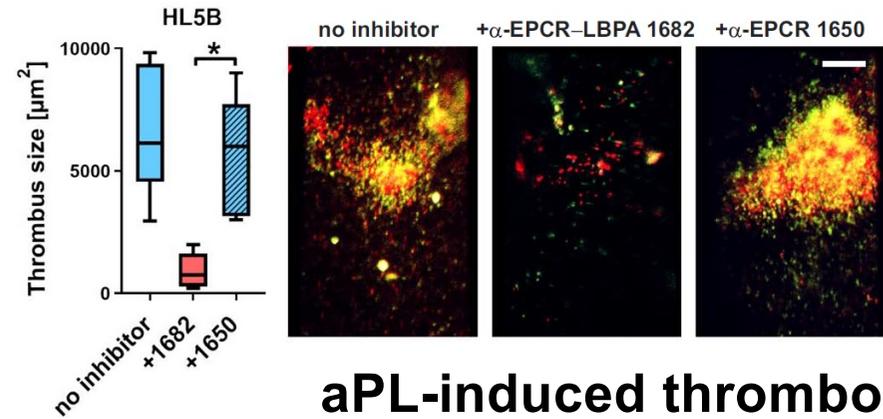
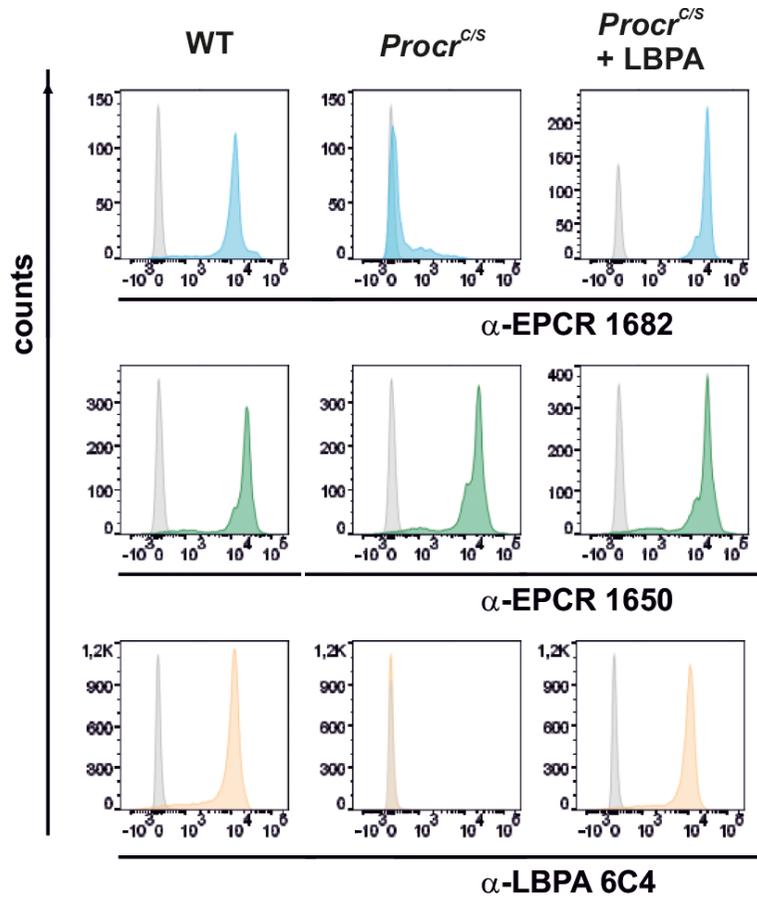
# aPL directly bind to EPCR for endosomal Trafficking



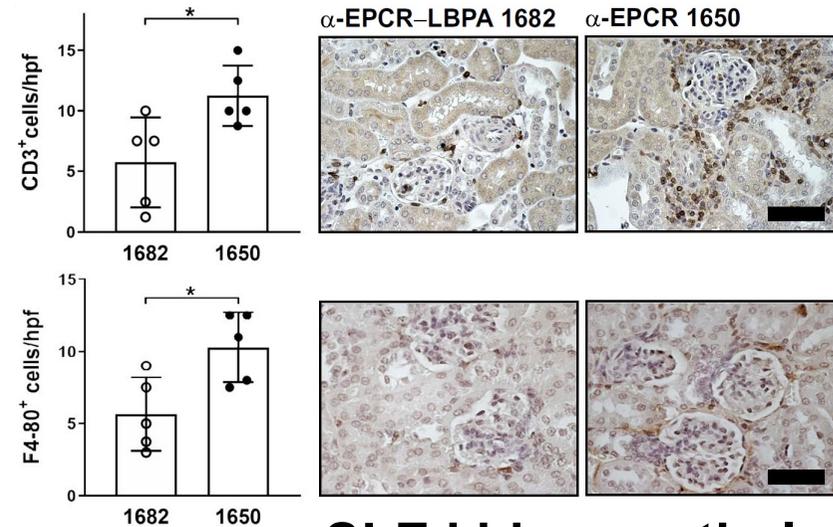
# aPL recognize EPCR after endosomal Lipid-Exchange



# Identification of specific Inhibitor of EPCR-LBPA

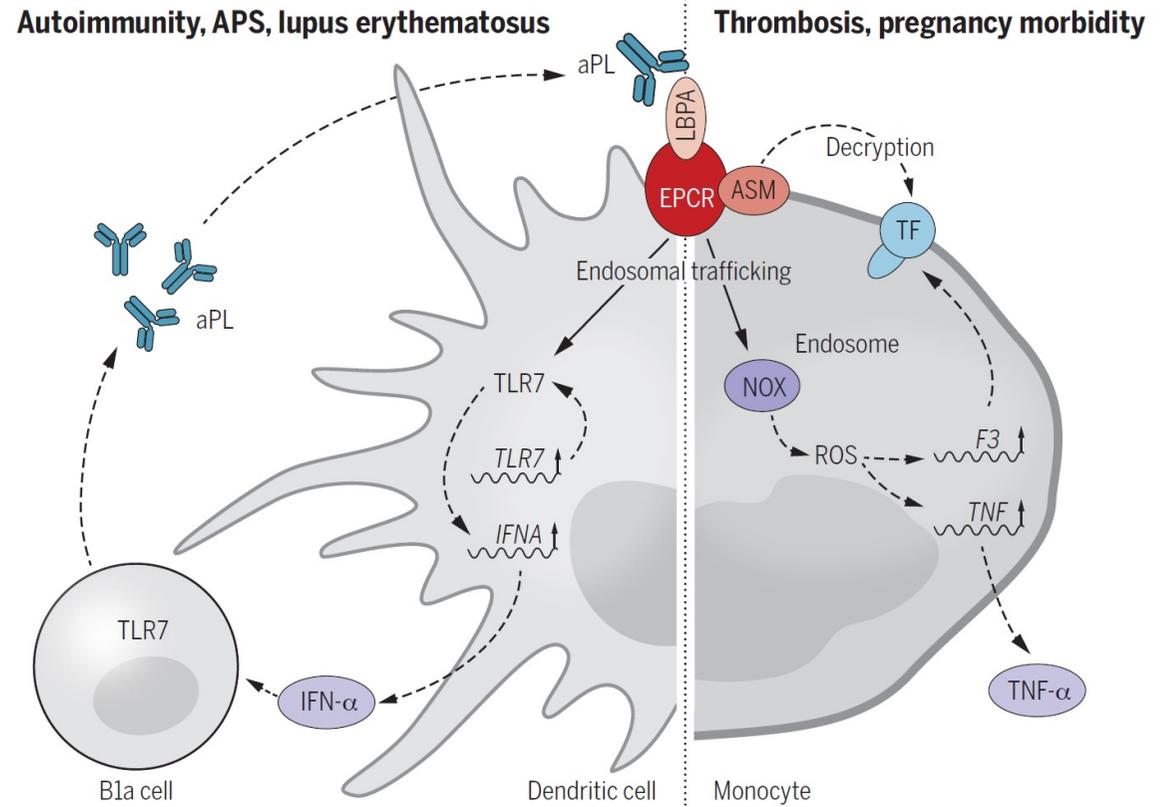
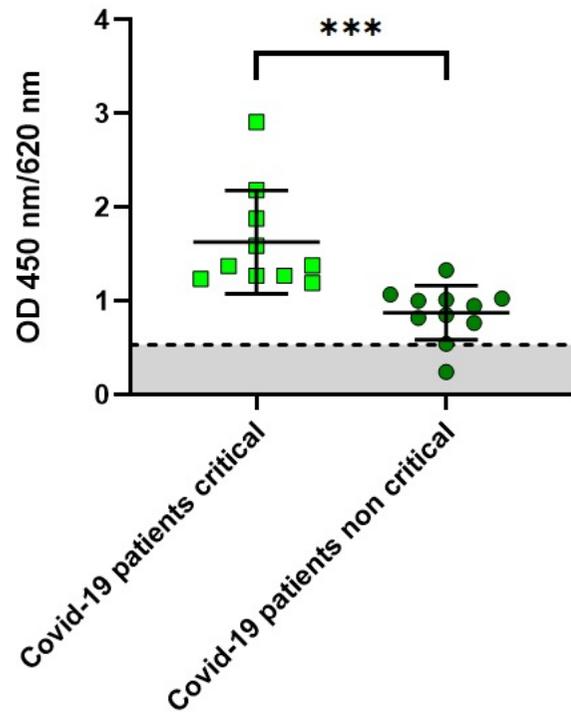


## aPL-induced thrombosis

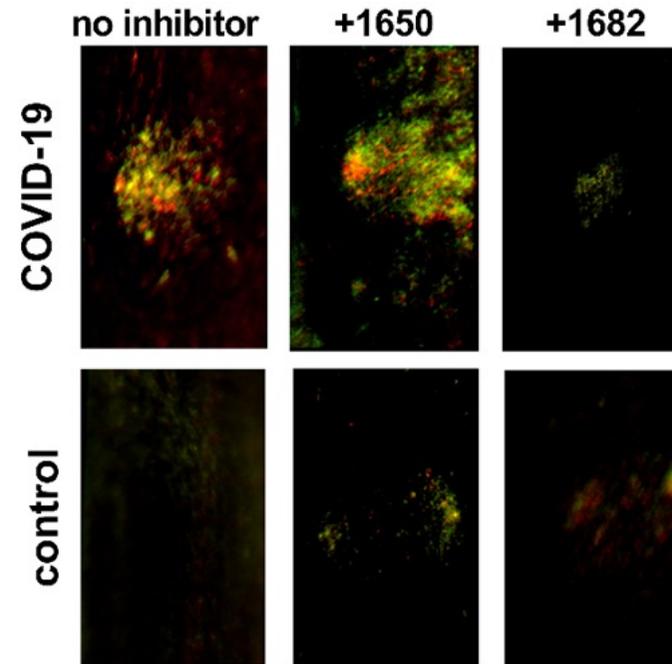
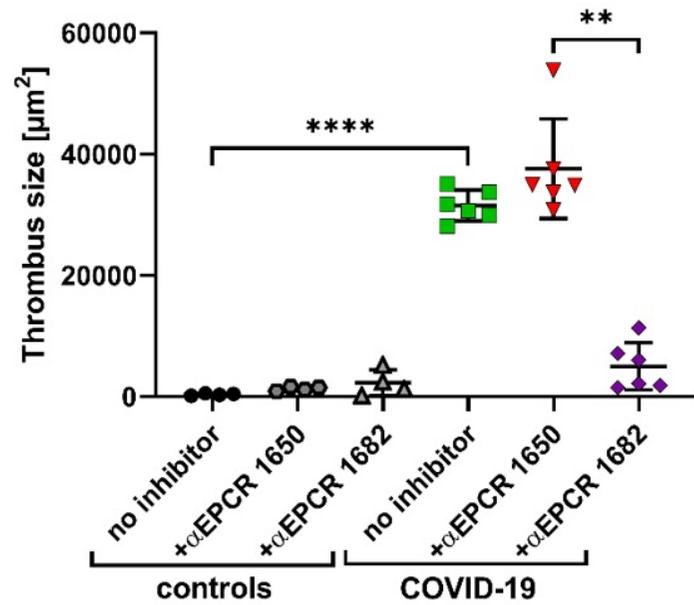


## SLE kidney pathology

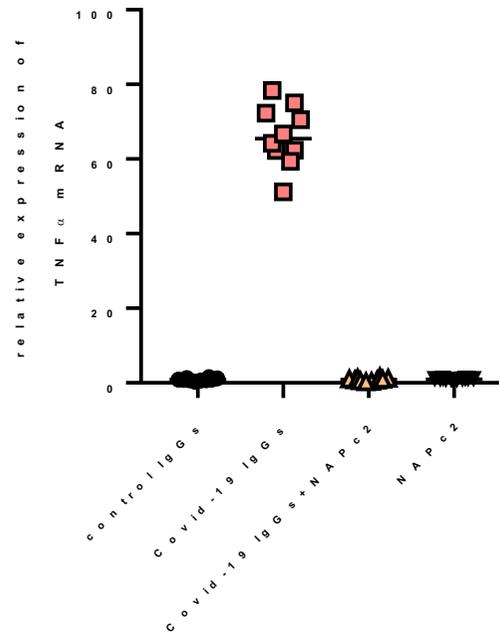
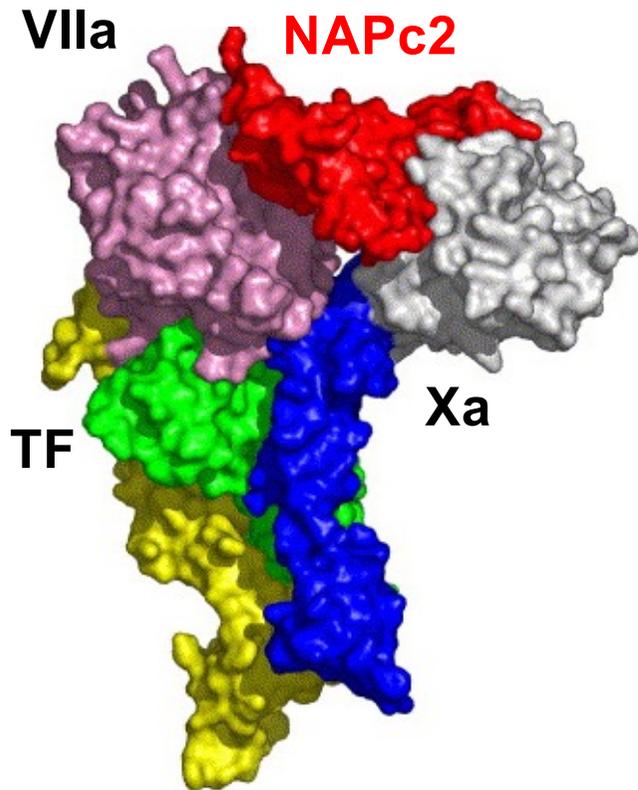
# aPL in severe COVID-19



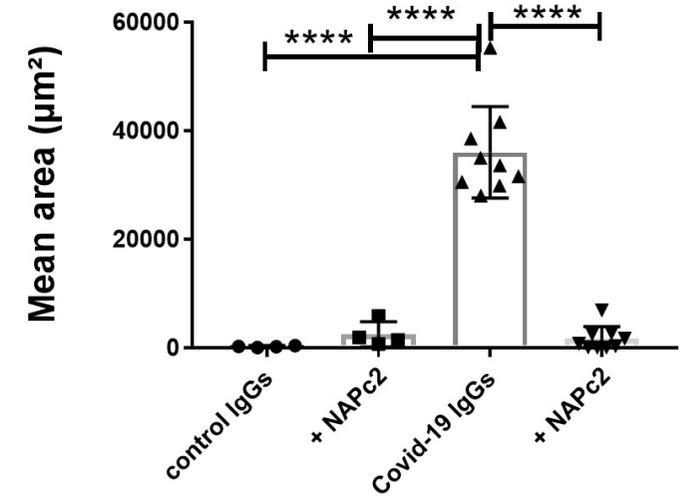
# aPL in severe COVID-19 cause EPCR-LBPA-dependent Thrombosis



# Stabilizing the TF Complex prevents aPL-induced Thrombosis



aPL-induced inflammation



aPL-induced thrombosis

# Targeting pathogenic TF Complex Signaling

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