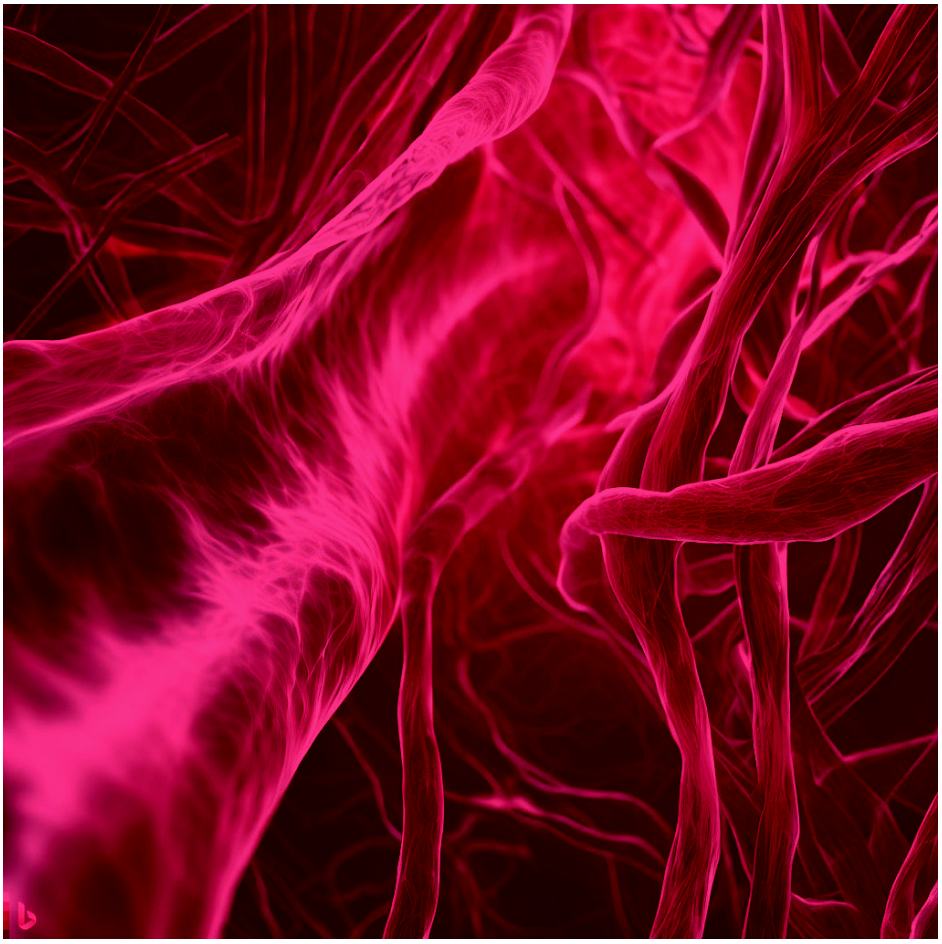
Newsletter of the Vascular Biology Institute – 2023/2



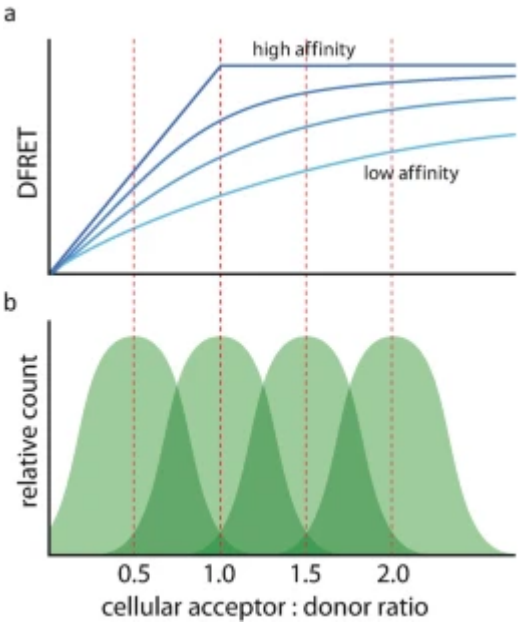
New publications with team members as first- or corresponding author

Teams (alphabetically) :

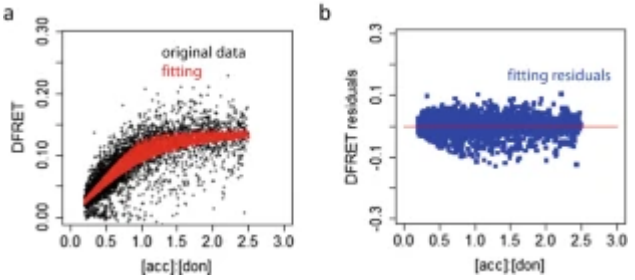
Assinger/Schrottmaier group

Editorial: Platelet and megakaryocyte dysfunctions in infectious diseases.
Assinger A, Capron C, Real F, Bomsel M.
Front Immunol. 2023 Mar 28;14:1175200. doi: 10.3389/fimmu.2023.1175200. eCollection 2023.

Schmid group



Estimating the Interaction Strength Between PTS1-Peptides and Their Receptor PEX5 in Living Cells Using Flow-Cytometer-Based FRET (flowFRET) Measurements.
Hochreiter B, Schmid JA, Berger J, Kunze M.
Methods Mol Biol. 2023;2643:413-434. doi: 10.1007/978-1-0716-3048-8_30.

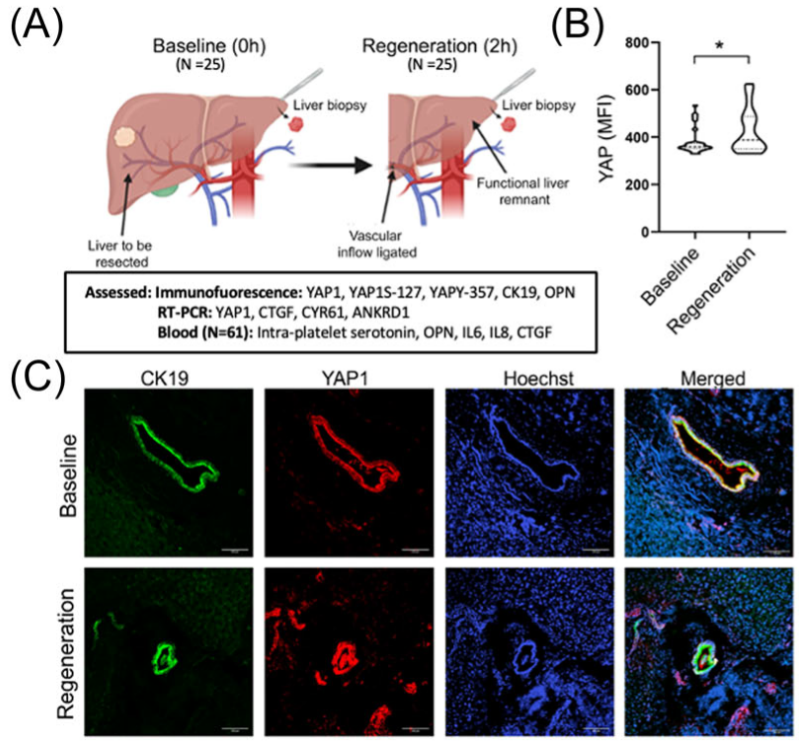


Zellner group

How can platelet proteomics best be used to interrogate disease?
Zellner M.
Platelets. 2023 Dec;34(1):2220046. doi: 10.1080/09537104.2023.2220046.

New publications as co-author

Assinger/Schrottmaier group



Tyrosine phosphorylation of YAP-1 in biliary epithelial cells mediates posthepatectomy liver regeneration and is affected by serotonin Patrick Starlinger, Laura Brunnthaler, Ryan Watkins, David Pereyra, Judith Stift, Michaela Finsterbusch, Jonas Santol, Thomas Gruenberger, Alice Assinger, Rory Smoot, J Cell Biochem

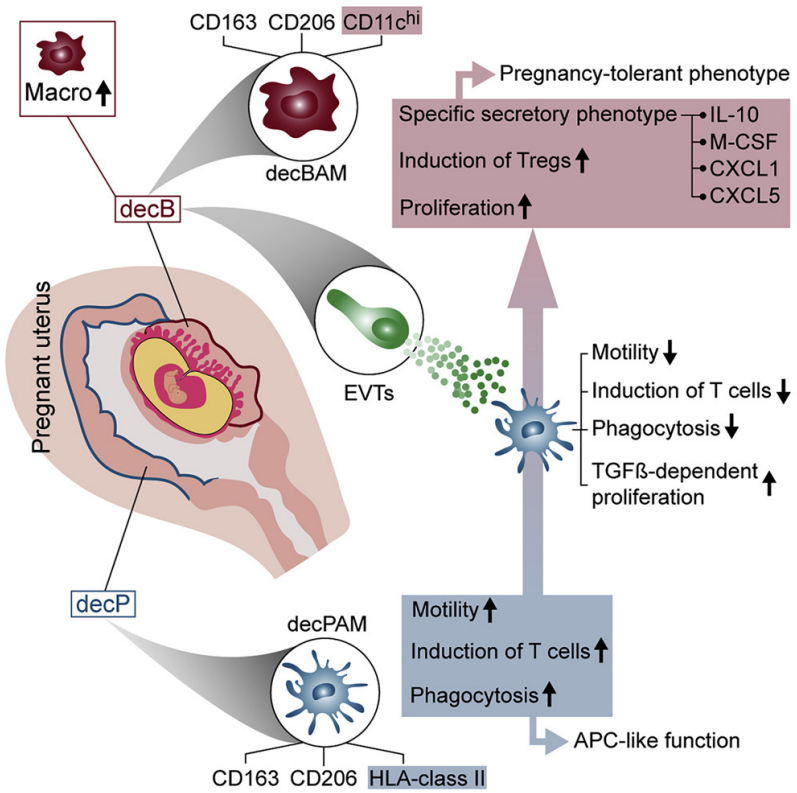
https://doi.org/10.1002/jcb.30398

Elevated plasma complement factor H related 5 protein is associated with venous thromboembolism.

Iglesias MJ, Sanchez-Rivera L, Ibrahim-Kosta M, Naudin C, Munsch G, Goumidi L, Farm M, Smith PM, Thibord F, Kral-Pointner JB, Hong MG, Suchon P, Germain M, Schottmaier W, Dusart P, Boland A, Kotol D, Edfors F, Koprulu M, Pietzner M, Langenberg C, Damrauer SM, Johnson AD, Klarin DM, Smith NL, Smadja DM, Holmström M, Magnusson M, Silveira A, Uhlén M, Renné T, Martinez-Perez A, Emmerich J, Deleuze JF, Antovic J, Soria Fernandez JM, Assinger A, Schwenk JM, Souto Andres JC, Morange PE, Butler LM, Trégouët DA, Odeberg J.

Nat Commun. 2023 Jun 7;14(1):3280. doi: 10.1038/s41467-023-38383-y.

Schabbauer group



The human placenta shapes the phenotype of decidual macrophages.
Vondra S, Höbler AL, Lackner AI, Raffetseder J, Mihalic ZN, Vogel A, Saleh L, Kunihs V, Haslinger P, Wahrmann M, Husslein H, Oberle R, Kargl J, Haider S, Latos P, Schabbauer G, Knöfler M, Ernerudh J, Pollheimer J.
Cell Rep. 2023 Jan 31;42(1):111977.

New funding and grants

Dominika Hromadova - FWF-ESPRIT project

Crosstalk of PI3K signaling & SIGN-R1 in auto-immunity: 345.000€

New team members

Sharif-group:

Hon Lam (PhD student) and Klara Culli (Masters student)

Congress contributions:

Zellner group:

ISTH 2023:

MEDICAL UNIVERSITY OF VIENNA

Platelet glycoprotein IIb- and IIIa levels are altered in persistently lupus anticoagulant positive patients with a history of thrombosis

Anahita Sedighi[1], Theresa Schramm[1], Nazanin Samadi[1], Felicia Hsu[2], Jasmin Rast[1], Cihan Ay[1], Ingrid Pabinger[1], Johanna Gebhart[1], Maria Zellner[2]

[1]Clinical Division of Haematology and Haemostaseology, Department of Medicine I, Medical University of Vienna, Austria

[2]Institute of Vascular Biology and Thrombosis Research, Centre for Physiology and Pharmacology, Medical University of Vienna, Vienna, Austria

Background

Antiphospholipid antibody syndrome (APS) is an autoimmune disorder defined by the presence of antiphospholipid antibodies (aPLAs), like lupus anticoagulant (LA), in combination with the occurrence of venous and/or arterial thromboembolism (TE).

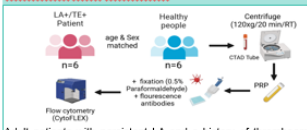
Upon activation the platelet integrins CD41 and CD61 form the glycoprotein IIb/IIIa complex, which acts as an inducible receptor for fibrinogen, essential in thrombus formation.

Prothrombotic diseases such as lung cancer, COVID-19 patients and LA report lower CD41 and CD61 content in their platelets. In addition, the platelets of the latter two also had a reduced ability to bind fibrinogen via this glycoprotein IIb/IIIa complex on their surface, which is currently unknown for LA.

Aim

To quantify the basal and ADP-activated platelet surface levels of integrins CD41 and CD61 and their affinity to bind fibrinogen (via PAC-1) in patients with LA compared to matched healthy controls.

Patients and Methods



Adult patients with persistent LA and a history of thromboembolism (LA/TE+) and healthy controls from the Vienna Lupus Anticoagulant Thrombosis cohort (EC 068/2001 and 1268/2014) were analysed.

Flow Cytometry:

- Surface levels of CD41 (Pacific Blue™;Cat# 303714 Biolegend) and CD61 (AF647; Cat# 336408 Biolegend) were measured in platelet-rich plasma (PRP) by fluorescence conjugated antibodies
- Activated CD41/CD61 complex (PAC-1 FITC; 362804 Biolegend) levels in PRP were measured at baseline and after stimulation with ADP [15 M]

Table 1: Demographic, clinical and laboratory data of the study cohort

	LA/TE+ (n=6)	Healthy Controls (n=6)
Female, n (%)	3 (50)	3 (50)
Age, years, mean ± SD	58.7 ± 10.8	57.2 ± 10.3
Platelet Count, x10⁹/L, median (IQR)	204.0 (168.0-210.0)	273.0 (258.0-311.0)
aPLAs, n (%)		
LA alone[a]	1 (16.7)	-
LA+ anti-β2GPI	1 (16.7)	-
LA+ aCL[b]	1 (16.7)	-
LA+ a(Anti-β2GPI+aCL (triple positivity)[b]	3 (50)	-
Thrombosis history, n(%)	6 (100)	0 (0)
Arterial TE, n(%)	2 (33.3)	-
Venous TE, n(%)	4 (66.7)	-
Disease specific treatment, n (%)	5 (83.3)	-
Phenprocoumon, n(%)	5 (100)	-

Note: n, number; SD, standard deviation; IQR, interquartile range; LA, lupus anticoagulant, TE, thromboembolism; β2GPI, beta-2 glycoprotein; aCL, anti-cardiolipin antibodies; na, not applicable

[a]LA alone defined as the absence of IgG/IgM anti-β2GPI and aCL

[b]Cutoff: anti-β2GPI >8 GPL/MPL U/mL, aCL >40 GPL/MPL U/mL

Results

- Table 1 shows demographic, clinical and laboratory data of LA/TE+ (n=6) patients and matched healthy controls (n=6)
- Basal levels of CD41 (+1.31; P=0.041) and CD61 (+1.38; P=0.008) were increased in LA/TE+ patients compared to healthy controls (Figure 1B).
- The increase in platelet surface levels of CD61 and CD41 after ADP activation was significant stronger in healthy controls than in LA/TE+ patients (Figure 1A-1B).
- Healthy controls showed an upregulation of ADP-induced binding affinity to fibrinogen (+1,42, p=0.031) than LA/TE+ patients (+1.21, p=0.063) (Figure 1C).

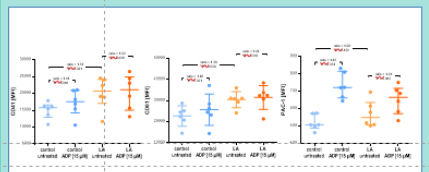


Figure 1. Basal and ADP-induced platelet surface expression of CD41, CD61, and the activated GPIIb/IIIa complex of LA patients and matched healthy controls. Flow cytometric analysis and activation were performed from platelet rich-plasma (PRP) derived from centrifugation of CTAD blood. The ADP [15 µM] activation was made in PRP for 5 minutes at room temperature. The abundance of these platelet surface receptors is indicated by median fluorescence intensity (MFI) from (A) CD41, (B) CD61 and (C) the activated GPIIb/IIIa complex by PAC-1 binding from LA patients (n = 6) and healthy controls (n = 6). Median values are indicated with a horizontal line ± 95% confidence interval. The P values within a study group are calculated by the Wilcoxon test and between different study groups by Mann Whitney test.

Conclusion

- The elevated basal platelet surface levels of the integrins CD41 and CD61 indicate a higher activation state of platelets in LA/TE+ patients.
- Reduced ADP-induced platelet upregulation in LA/TE+ patients, may be due to the lower total available amount of CD41 and CD61.
- **Our observations support the assumption that persistently activated and thus "exhausted" platelets may contribute to the prothrombotic phenotype in patients with persistent LA.**

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