A vérlemezkék szerepe az immunválaszban

Kappelmayer János

Debreceni Egyetem,

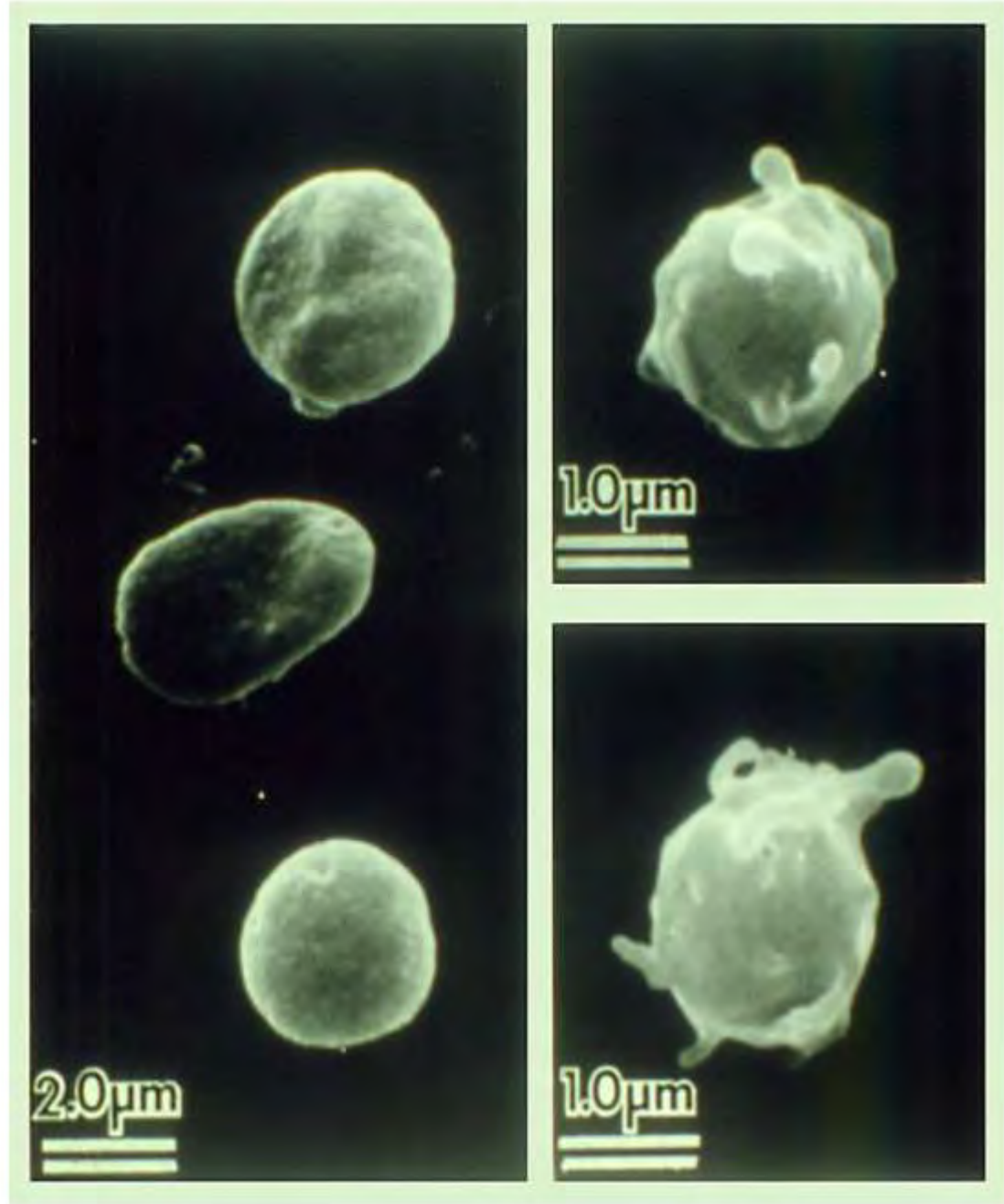
Laboratóriumi Medicina Intézet

SE PhD kurzus,
2025 április 4.

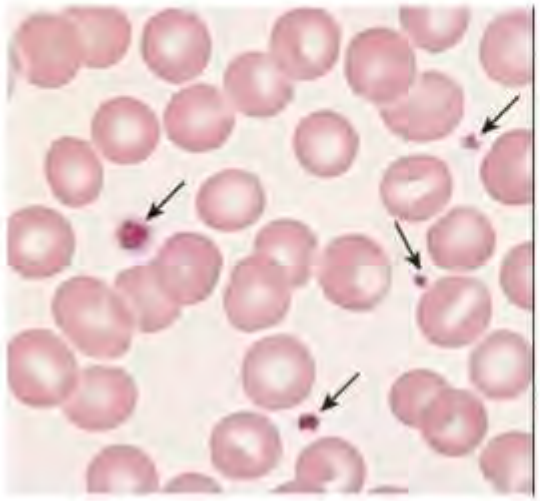
Immunsejtek versus alvadást elősegítő sejtek

Hemocyta:
alsóbb rendű szervezetek közös alvadást és immunválaszt generáló sejtek

		Szolublis elemek
Thrombocyta:	Mag nélküli sejt	Alvadási faktorok
Veleszületett immunválasz sejtjei:	Granulocyta, macrophag	Komplement


1.0μm
2.0μm
1.0μm

Kóros thrombocyta morfológia



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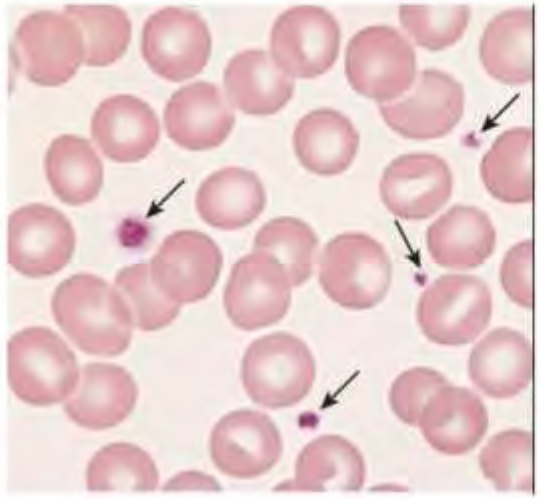
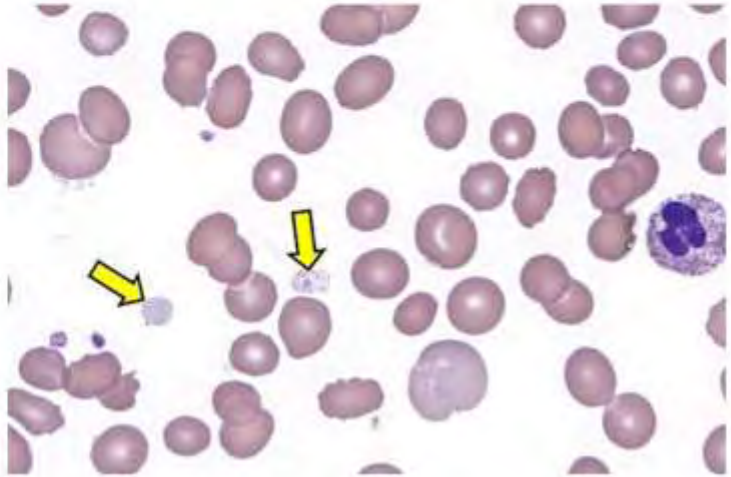
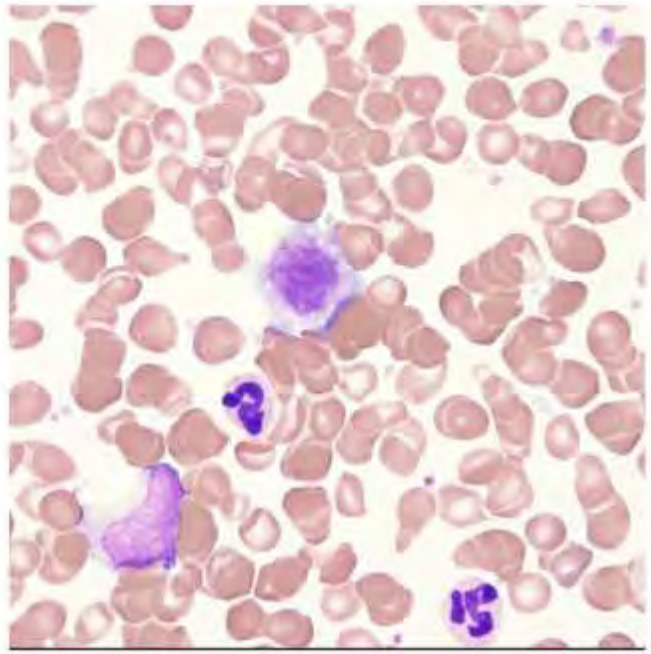
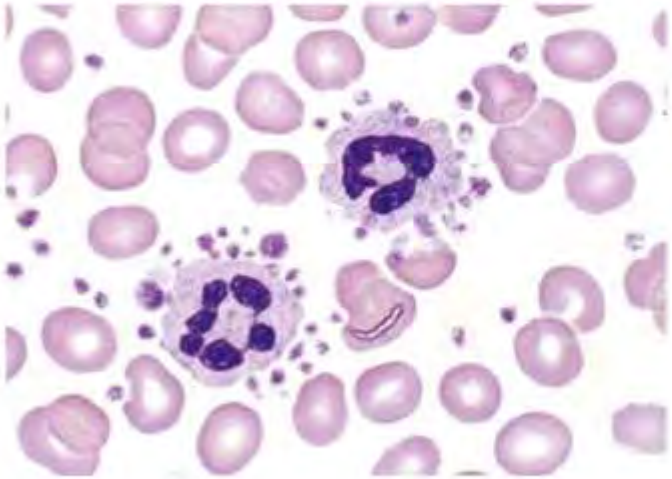
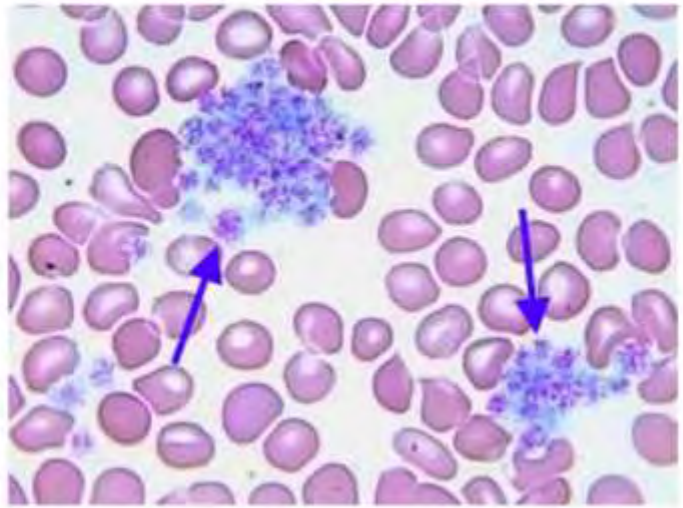
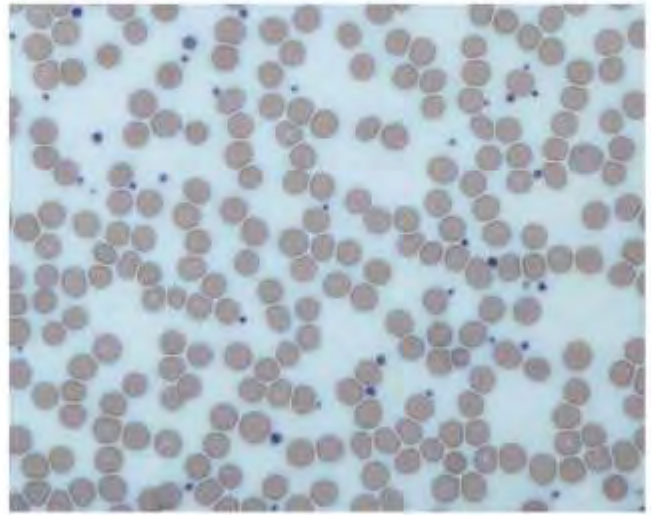


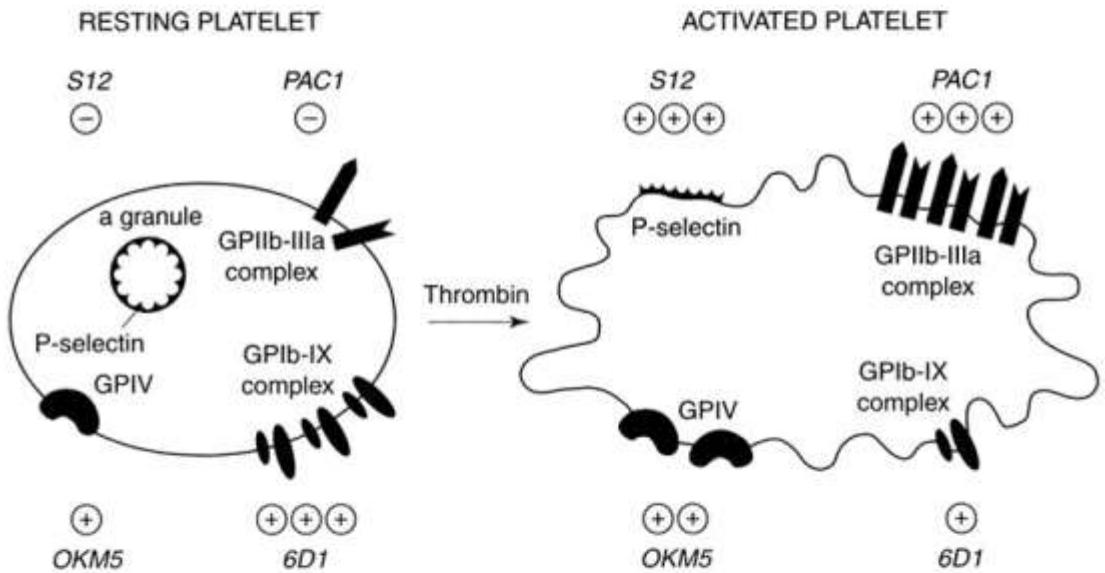


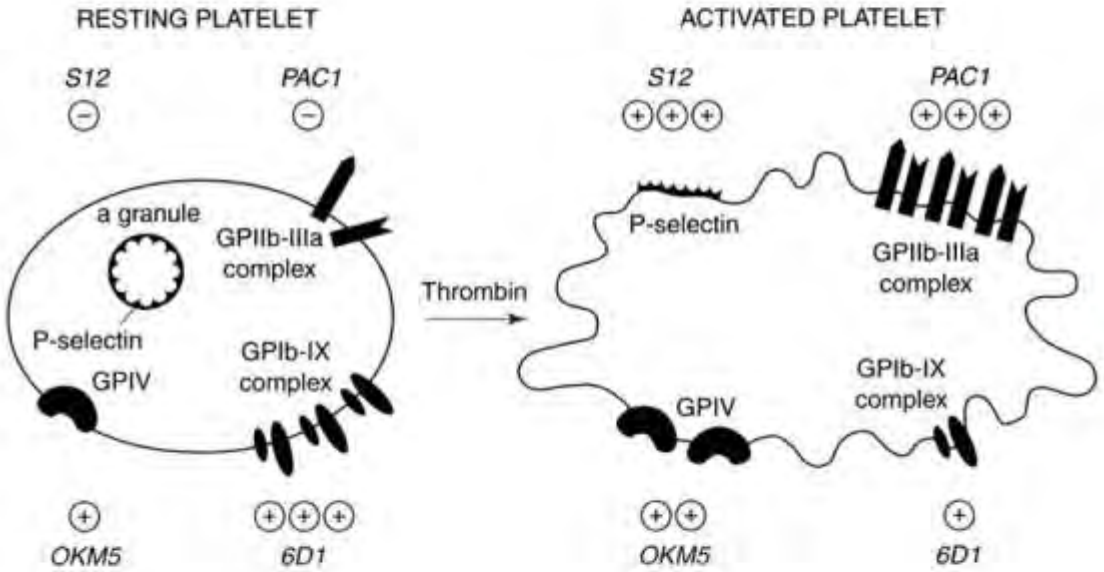


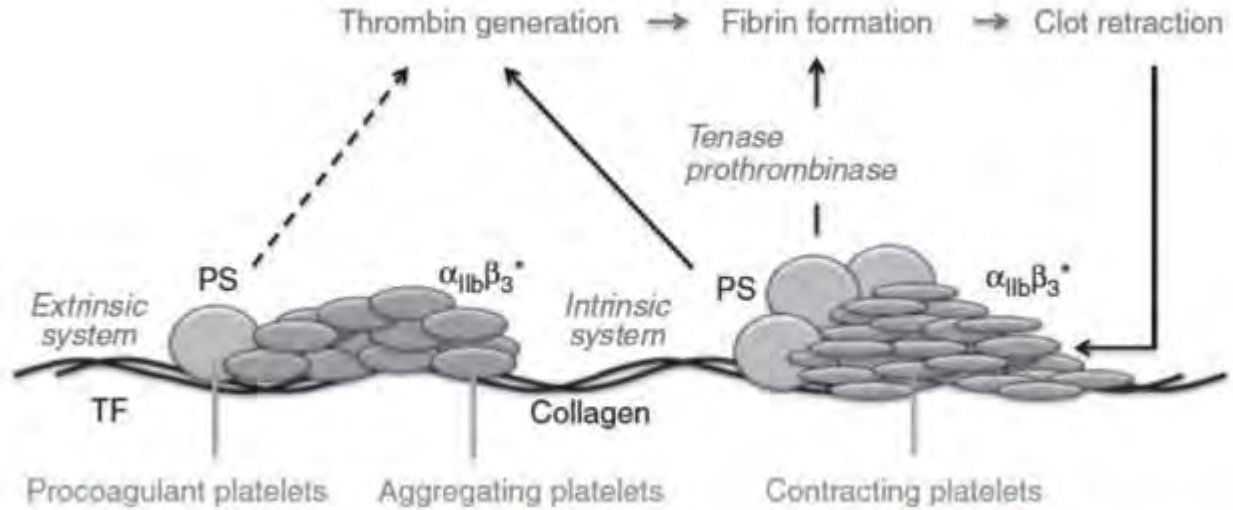




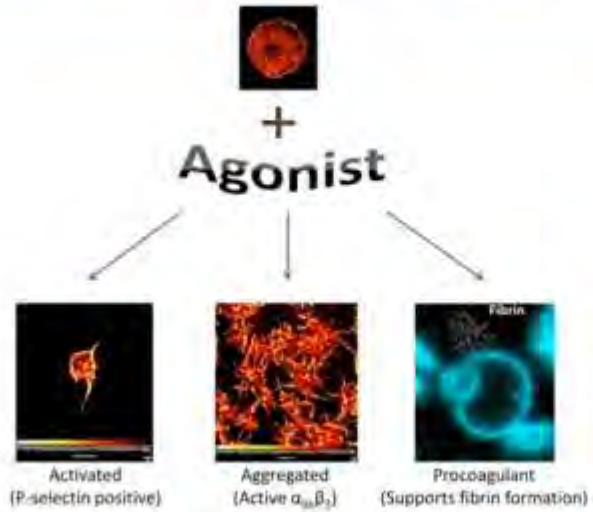



RESTING PLATELET
ACTIVATED PLATELET
S12
PAC1
S12
PAC1
a granule
GPIIb-IIIa complex
P-selectin
GPIV
GPIb-IX complex
Thrombin
P-selectin
GPIIb-IIIa complex
GPIb-IX complex
GPIV
OKM5
6D1
OKM5
6D1





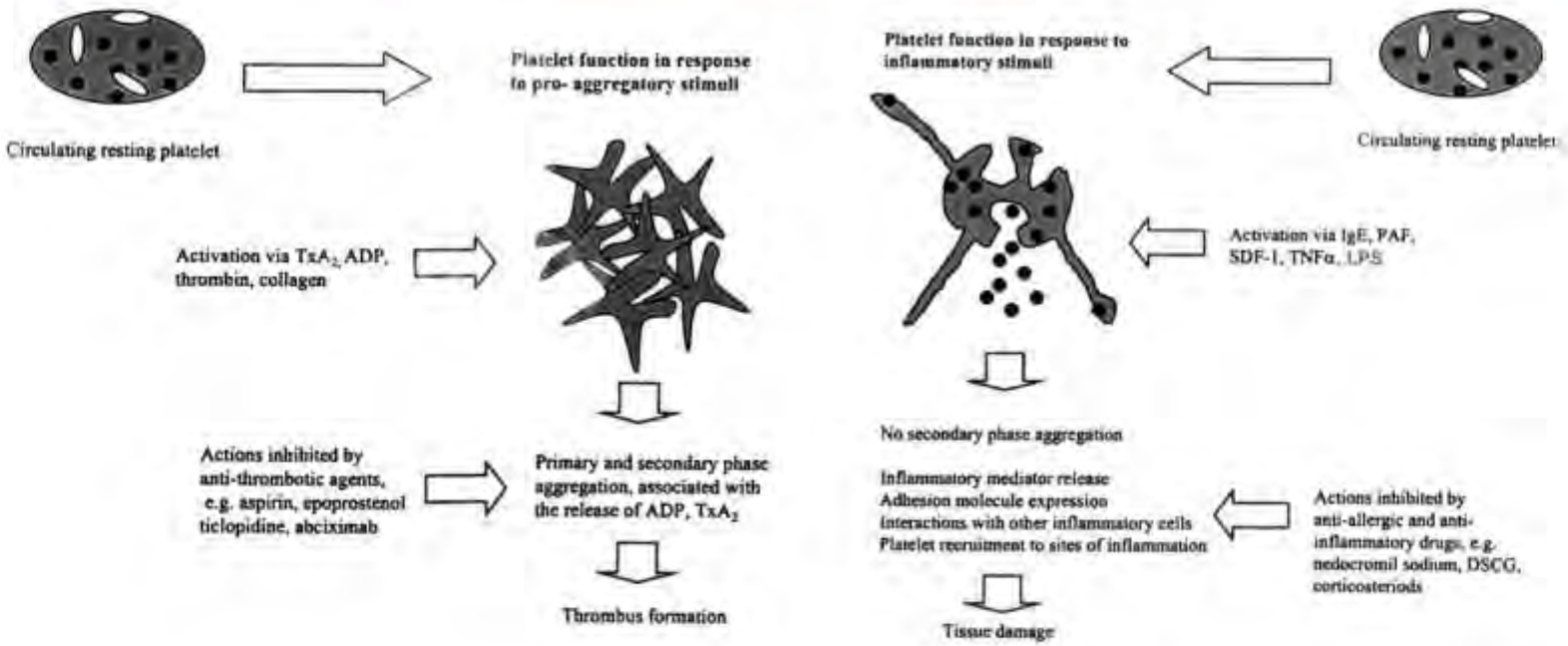
Different activated platelet subpopulations form with the same agonist stimulation



Adapted from Tohidi-Esfahani et al, IJLH 2020

A thrombocyta aktiváció útvonalai

Klasszikus	"Alternatív"
Thrombin	Komplement
Kollagén	PAF
ADP	LPS



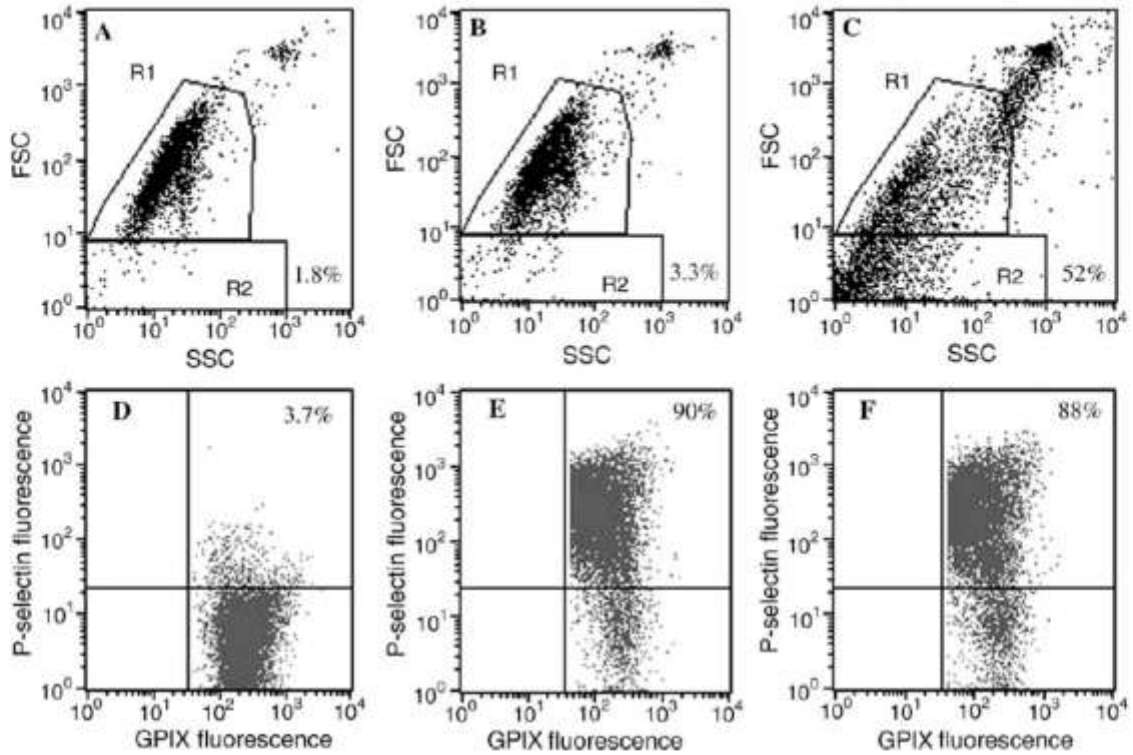
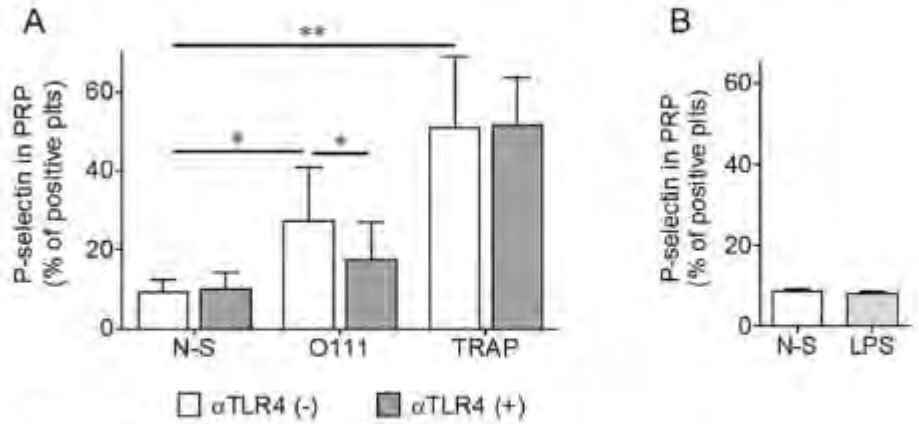


Table 2 Different sensitivity of direct platelet activation markers.

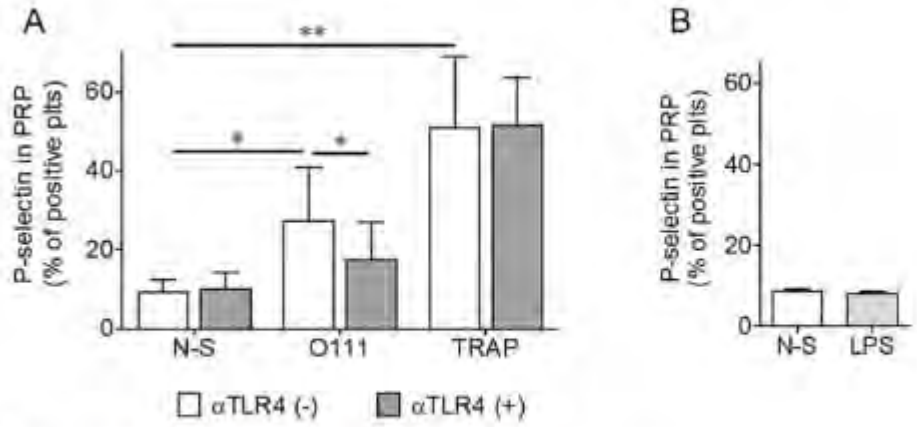
Thrombin, U/ml	P-selectin, %	P-selectin MFI	GPIX MFI	Microparticle, %
0	2	60	182	2
0.01	8	65	163	2
0.02	20	69	171	2
0.03	48	116	109	2
0.05	66	142	124	3
0.1	85	168	110	9

Citrated whole blood sample was stimulated with increasing thrombin concentrations. P-selectin expression, the mean fluorescence intensity (MFI) of P-selectin staining, GPIX fluorescence and the percentage of events in the microparticle gate were registered. P-selectin expression was sensitive to even miniscule amounts of thrombin.



Matus et al.

PLOS ONE | https://doi.org/10.1371/journal.pone.0185431 September 28, 2017



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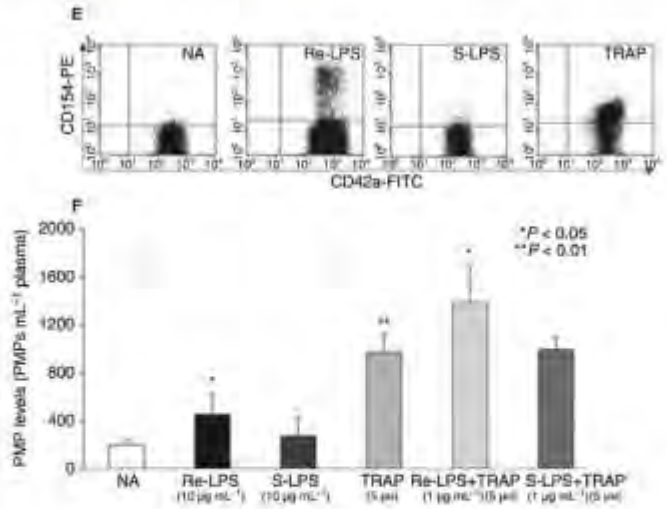
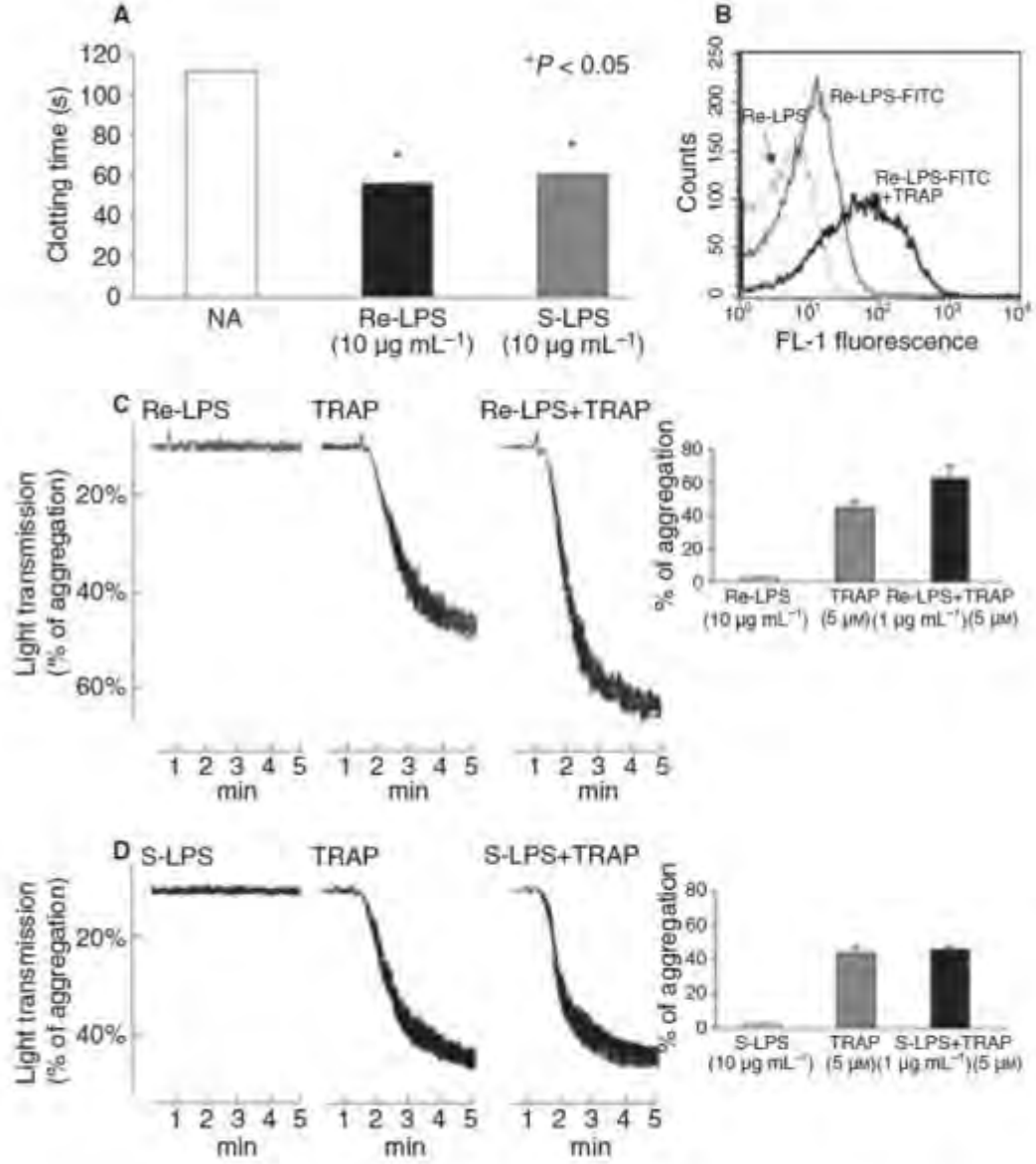




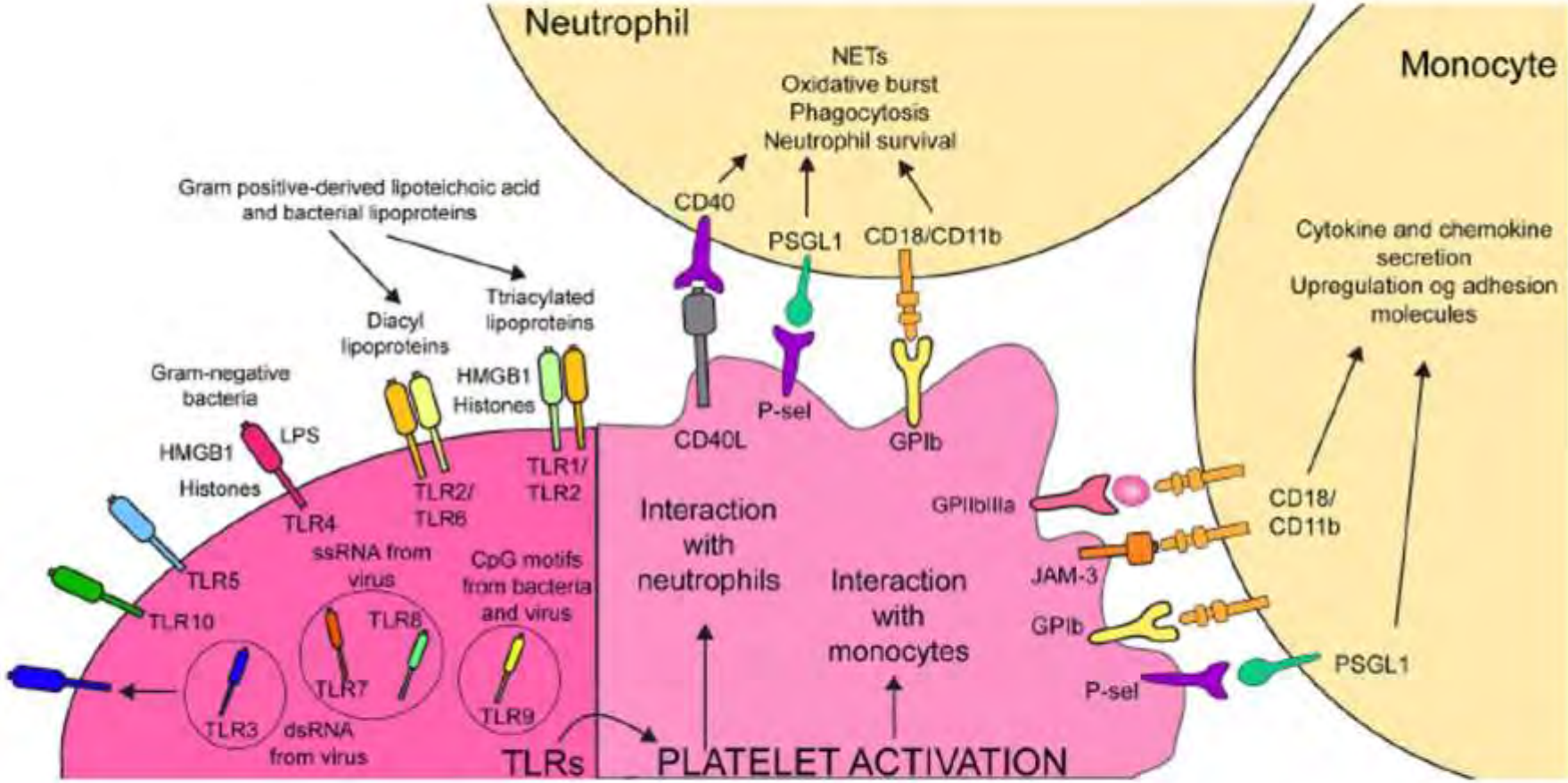
Kappelmayer et al. J *Thromb Haemost 2013; 11: 775-778.*

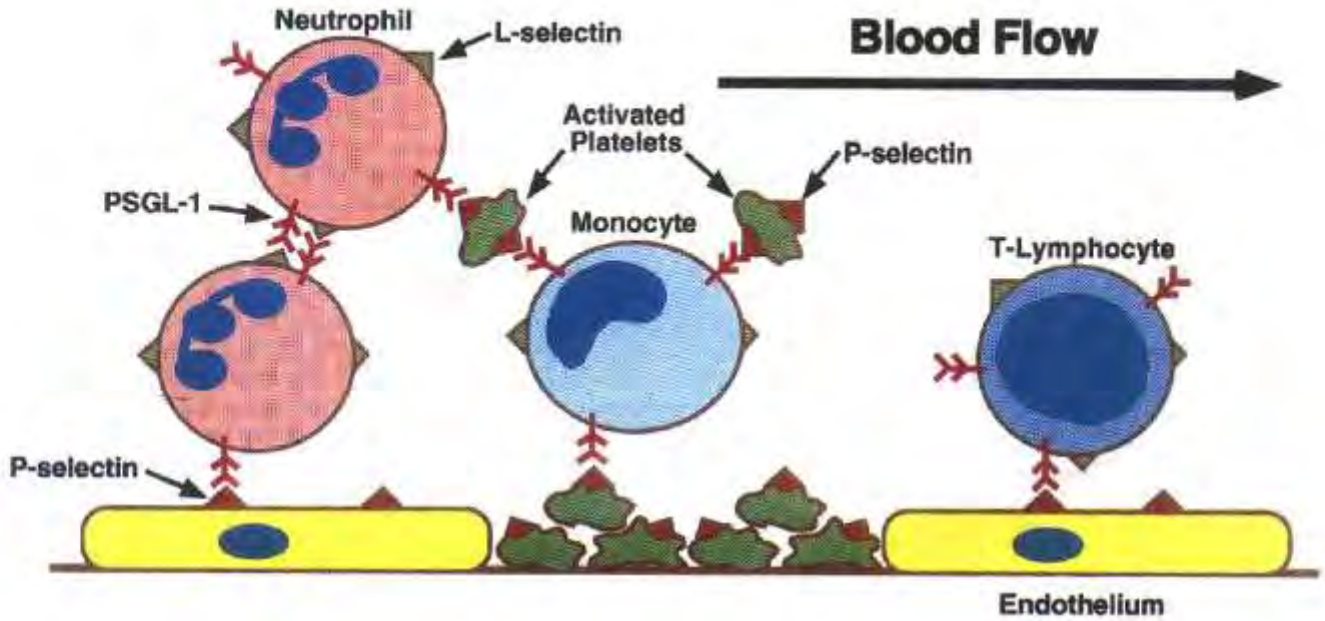
Pattern Recognition Receptor

TLR

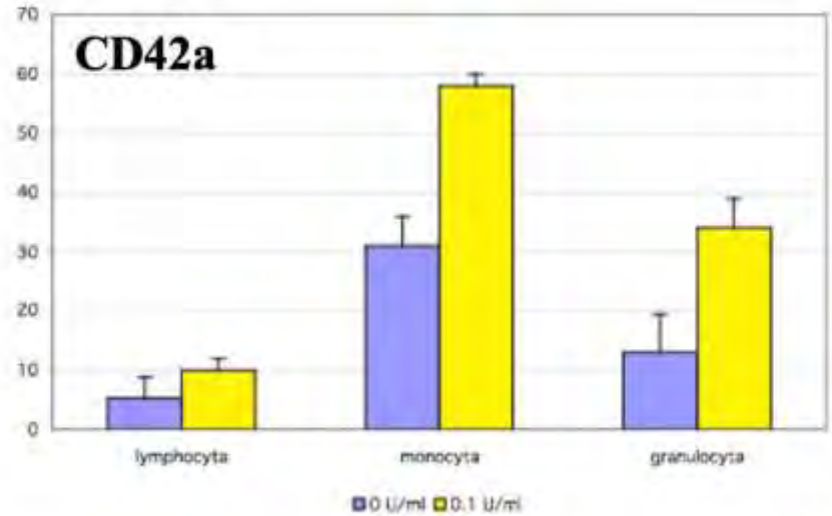
PAMP

DAMP




Neutrophil
L-selectin
Blood Flow
Activated Platelets
P-selectin
PSGL-1
Monocyte
T-Lymphocyte
P-selectin
Endothelium

(%)


CD42a
70
60
50
40
30
20
10
0
lymphocyta
monocyta
granulocyta
0 U/ml
0.1 U/ml

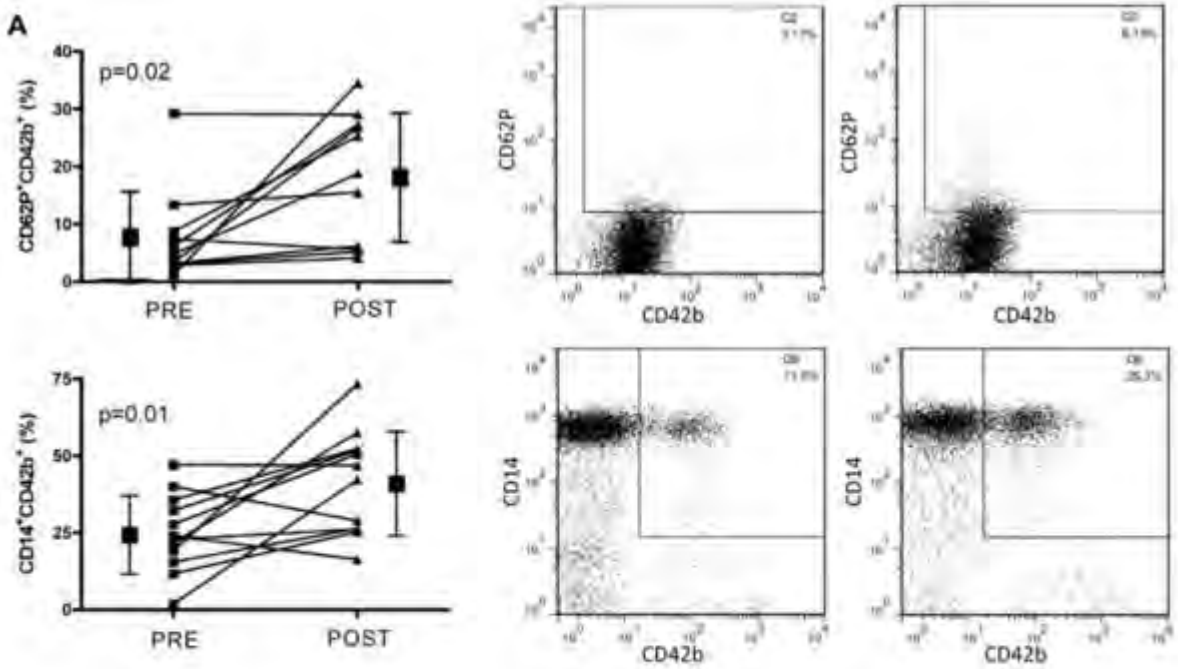
OPEN ACCESS Freely available online

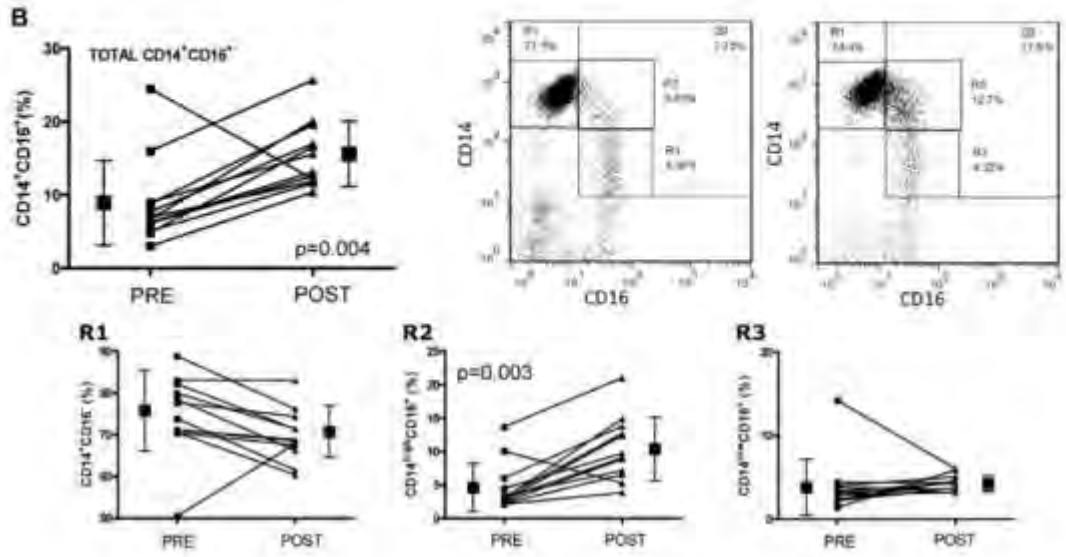
PLoS one

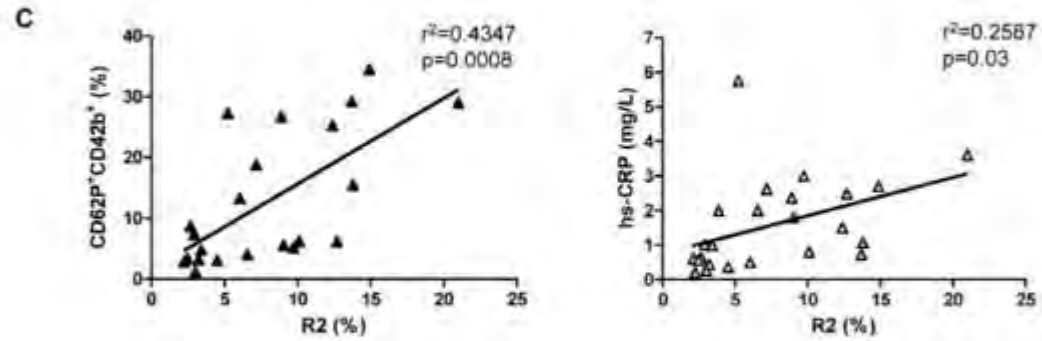
Monocyte-Platelet Interaction Induces a Pro-Inflammatory Phenotype in Circulating Monocytes

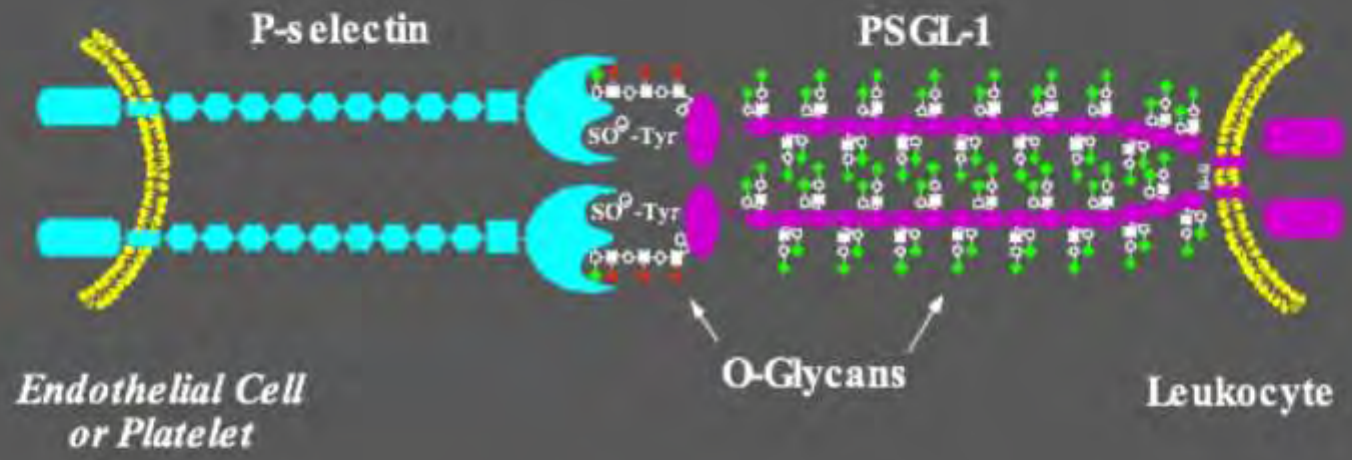
Gabriella Passacquale[1], Padman Vamadevan[1], Luis Pereira[1], Colleen Hamid[1], Valerie Corrigall[2], Albert Ferro[1]*

1 Cardiovascular Division, Department of Clinical Pharmacology, King's College London, London, United Kingdom, 2 Academic Department of Rheumatology, King's College London, London, United Kingdom





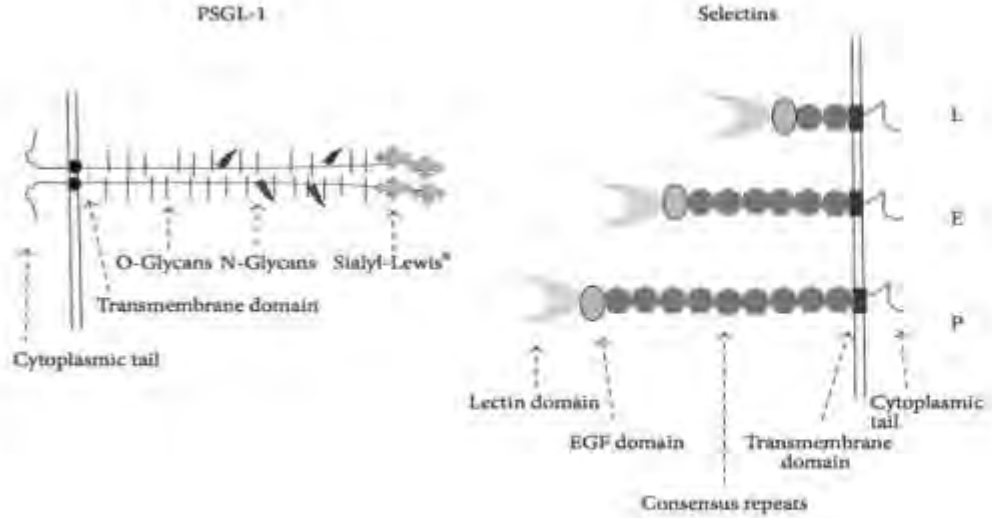



P-selectin
PSGL-1
SO3-Tyr
SO3-Tyr
Endothelial Cell
or Platelet
O-Glycans
Leukocyte

Review Article

The Interaction of Selectins and PSGL-1 as a Key Component in Thrombus Formation and Cancer Progression

János Kappelmayer and Béla Nagy Jr.



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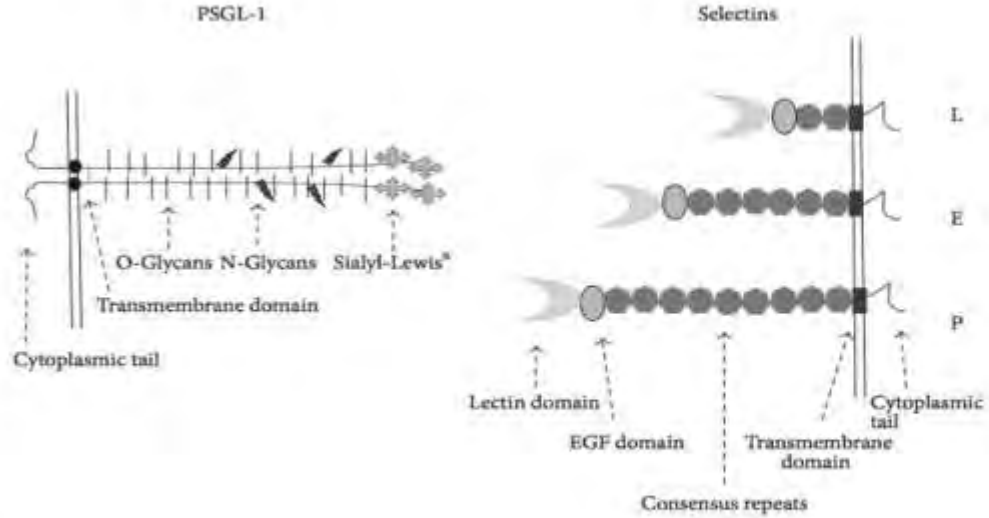
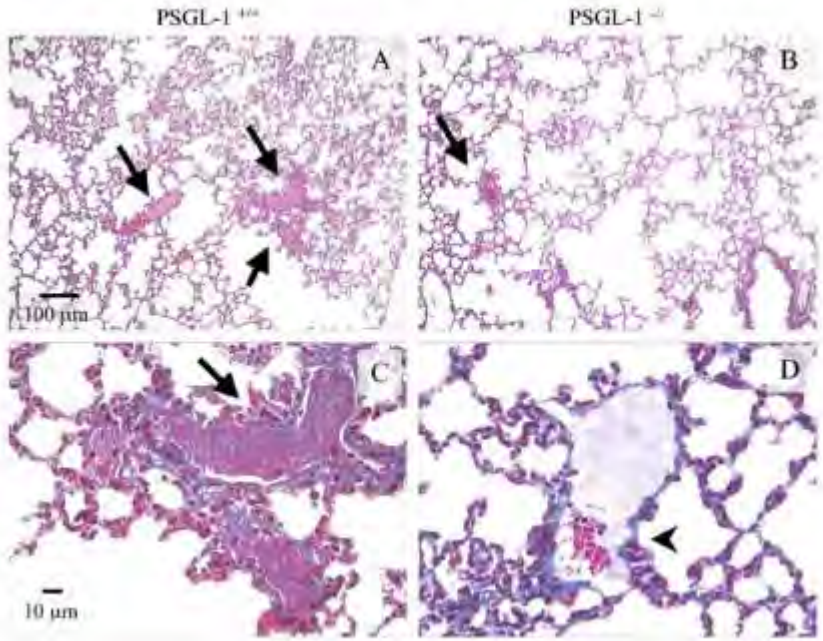
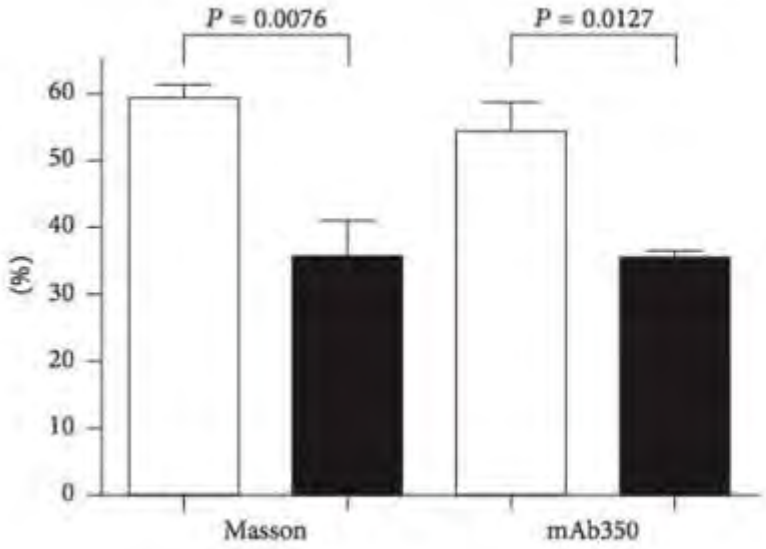
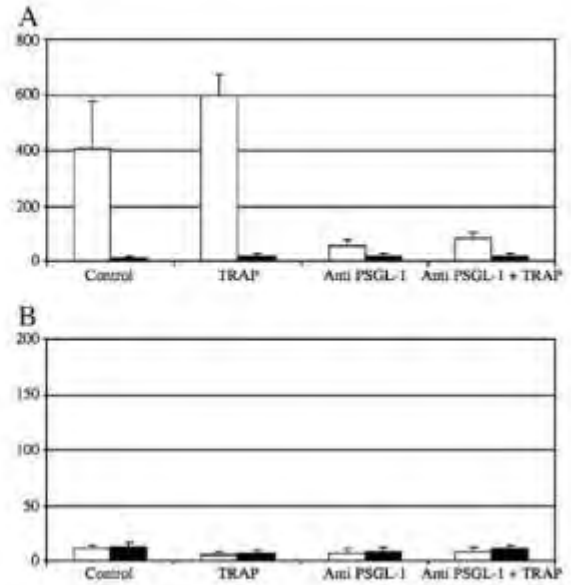


Lack of P-selectin glycoprotein ligand-1 protects mice from thrombosis after collagen/epinephrine challenge

Kornél Miszti-Blasius [a], Ildikó Beke Debreceni [a], Szabolcs Felszeghy [b], Balázs Dezső [c], János Kappelmayer [a,*]

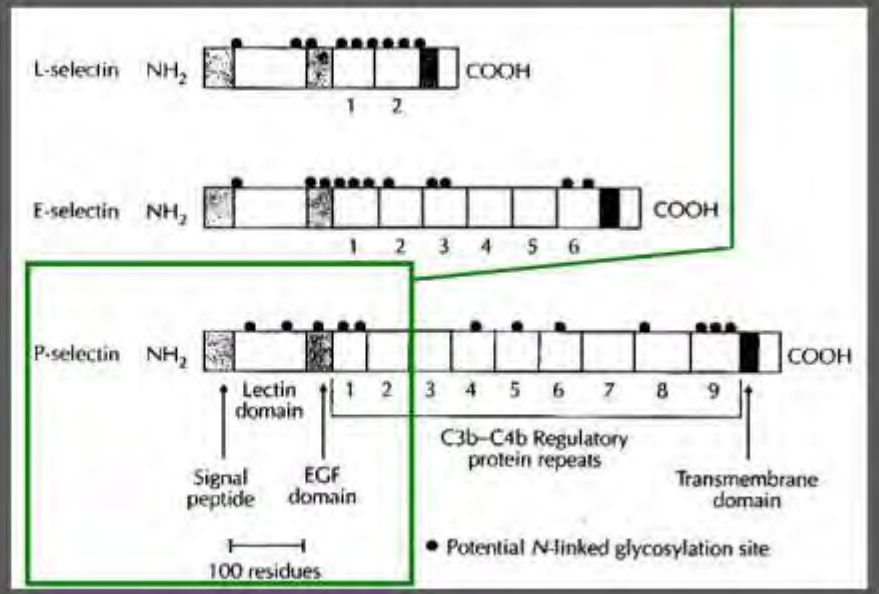


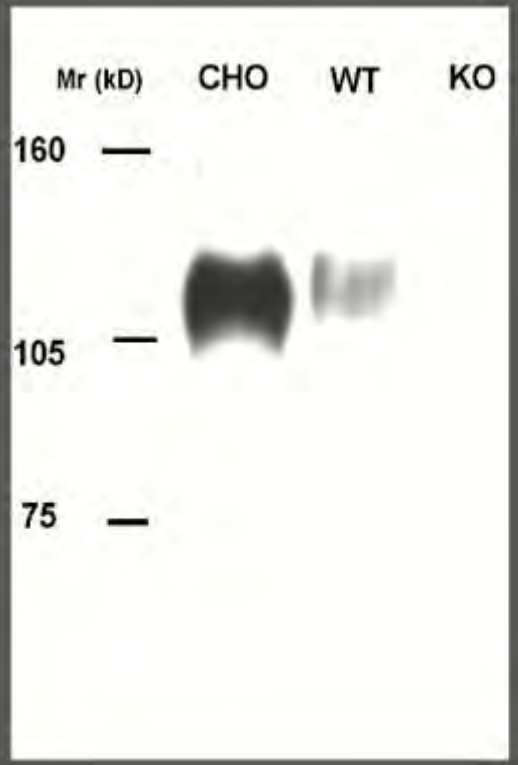




Thrombosis Research 127 (2011) 228–234

	PSGL-1 +/+	PSGL-1 -/-
Psel-Ig chimera	+	+
Control IgG	+	+
	H + M	M

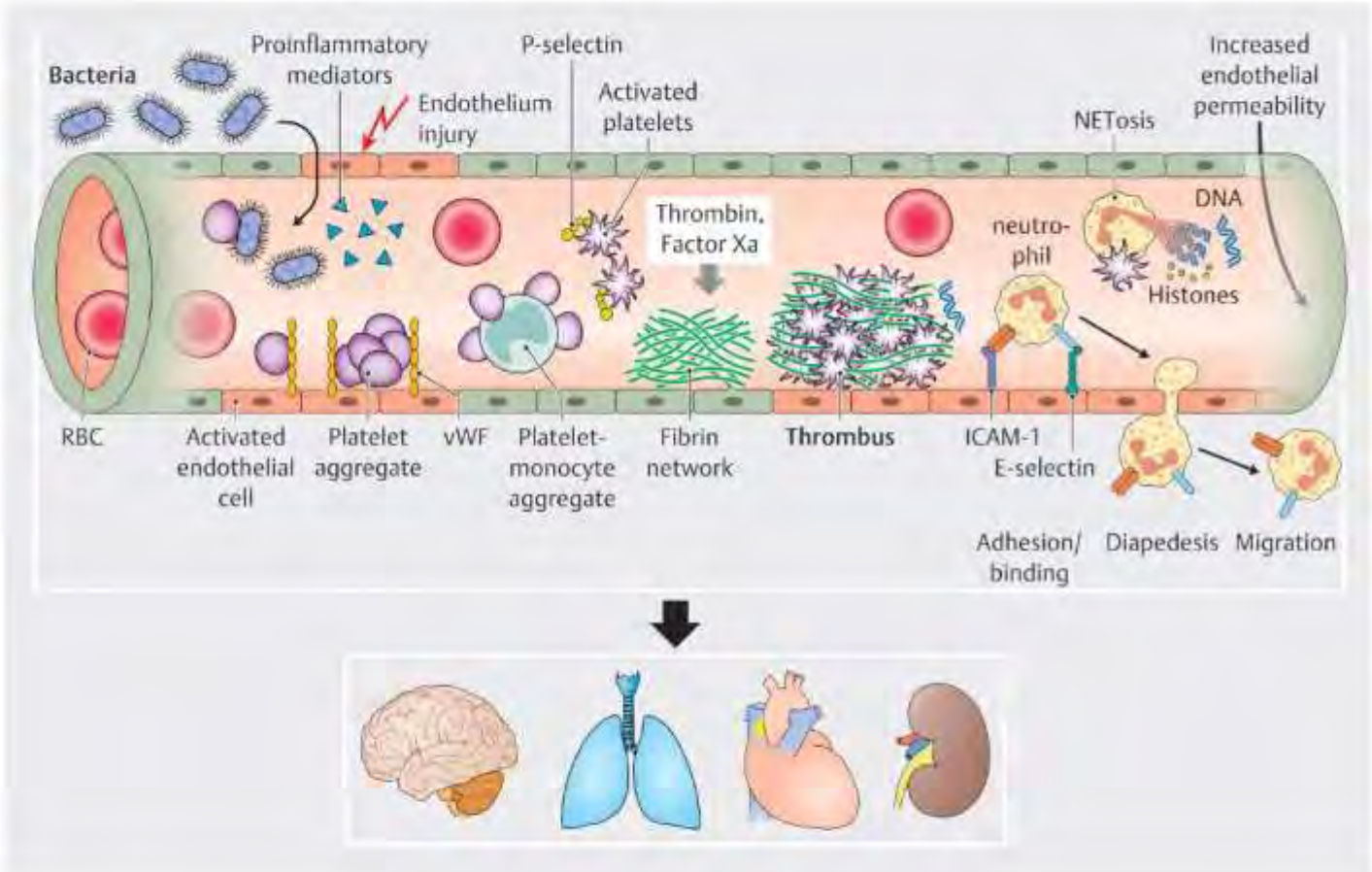




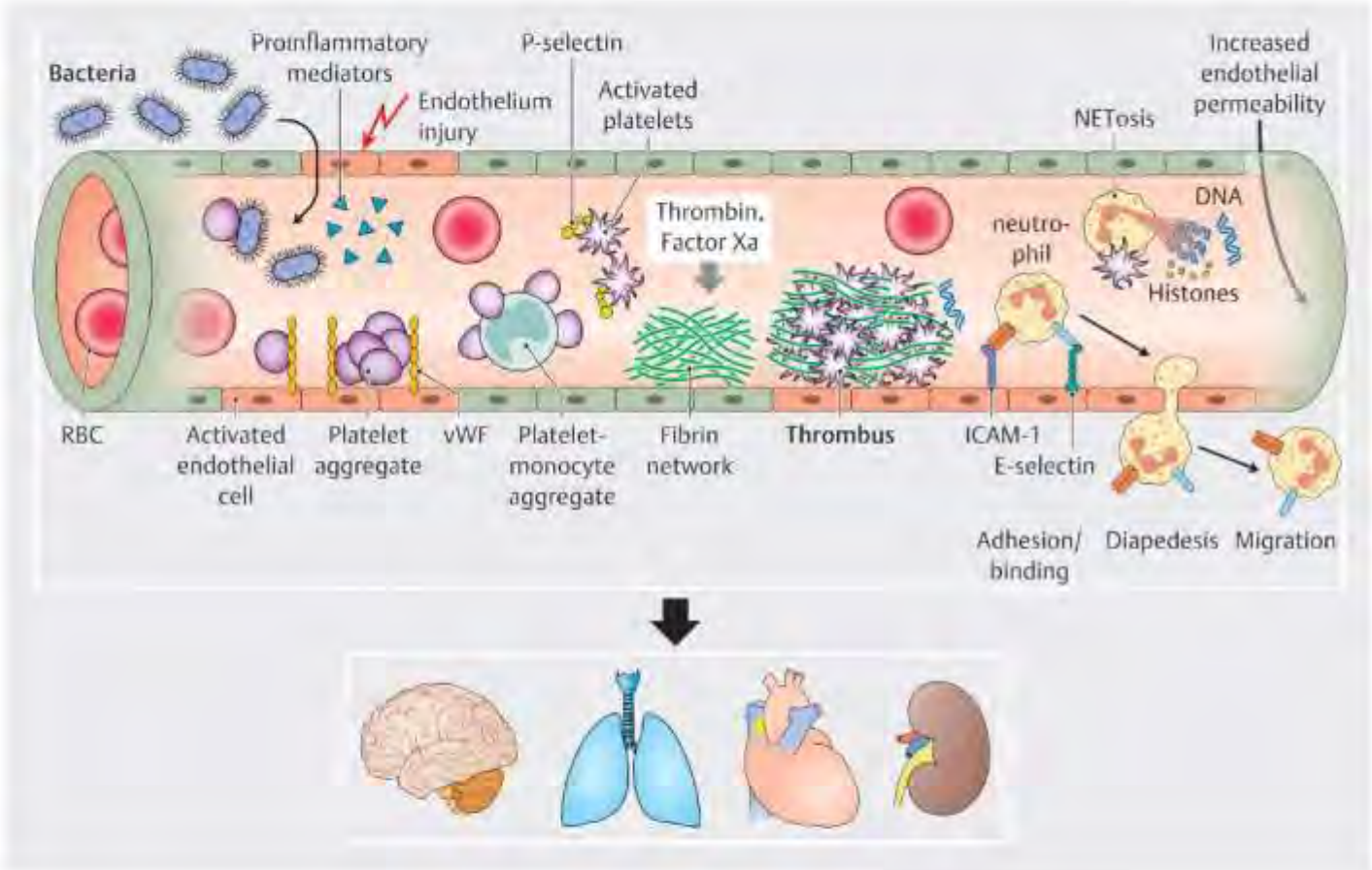
Role of age and PSGL-1 in MP formation

MP number	PSGL-1 +/+	PSGL-1 -/-	p value
9-12 weeks	12 173 ± 2243	14 399 ± 2746	0.54
17-20 weeks	29 404 ± 2941	18 183 ± 1 532	< 0.001
After administration of Psel-Ig			
MP number/ml	833 ± 137	382 ± 101	< 0.03
TF (%)	7.3 ± 1.5	2.9 ± 0.3	< 0.02

Hrachovinová et al. Nature Medicine 2003



Kappelmayer et al. *Haemostaseologie*
2024, 44(4): 268-276



Kappelmayer et al. *Haemostaseologie* 2024, 44(4): 268-276

A klinikai mintákban a betegek számos egyidejű kórállapota és a szedett gyógyszerek jelentősen befolyásolhatják az eredményeket.

Experimentális körülmények között, a kórokozó kontrollált beadásával a stimulus standardizálható és a fenti körülmények kizárhatóak.

Point of Care Testing:

- Core temperature, heart rate, mean arterial pressure (PiCCO device)

Citrated whole blood:

- Blood cell count (Siemens ADVIA 120, „Pig" software)
- Blood smear examinations – platelet morphology

PRP:

- **Platelet PS expression (Beckman Coulter FC 500 flow cytometer)**
- Thrombin generation (TS Fluoroskan Thrombinoscop)

- PPP:
- Coagulation screening tests: PT, APTT, TT, fibrinogen (Siemens BCS)
- Thrombin generation (Fluoroskan) – double centrifugation!
  - in the presence of phospholipid and exogenous TF
  - in the absence of any added reagent
  - in the presence of phospholipid but without exogenous TF

- **In vitro experiments**
  Effect of the plasma samples on washed human RBCs

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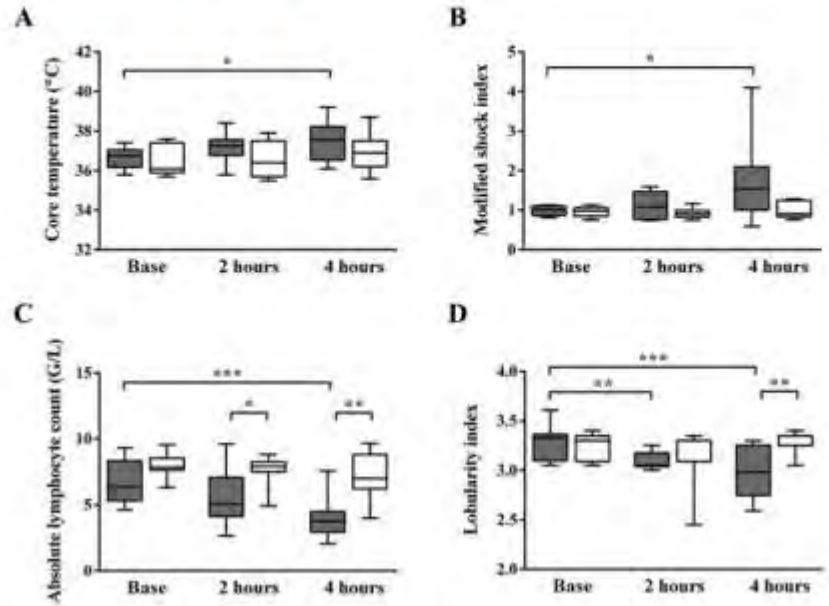
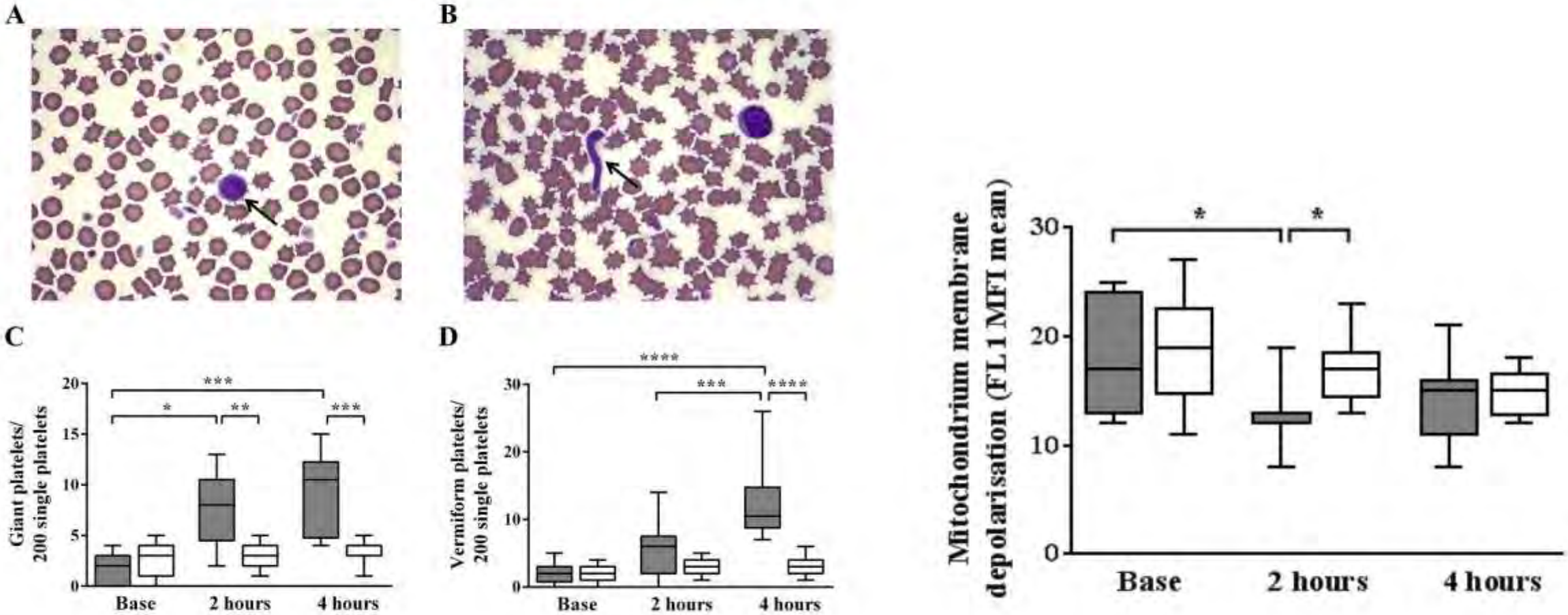
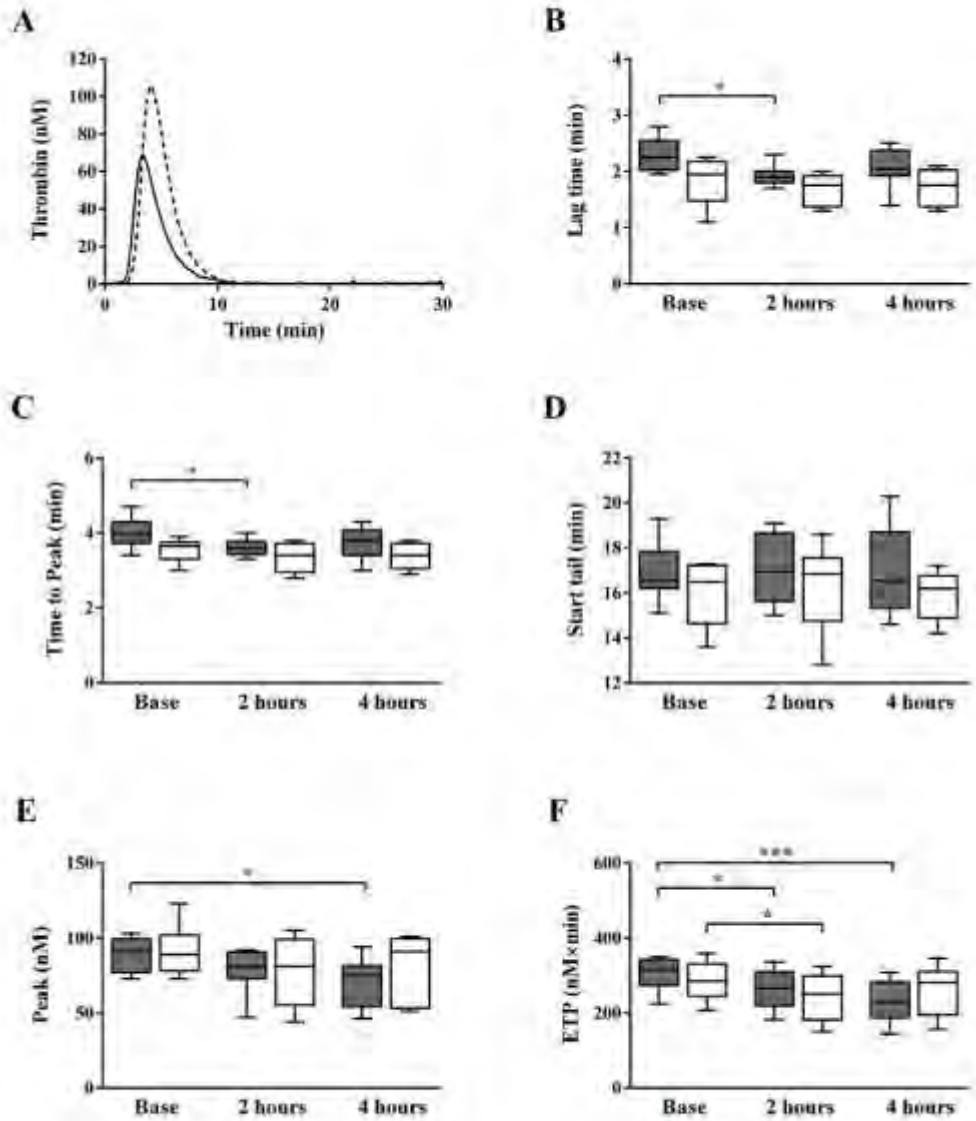
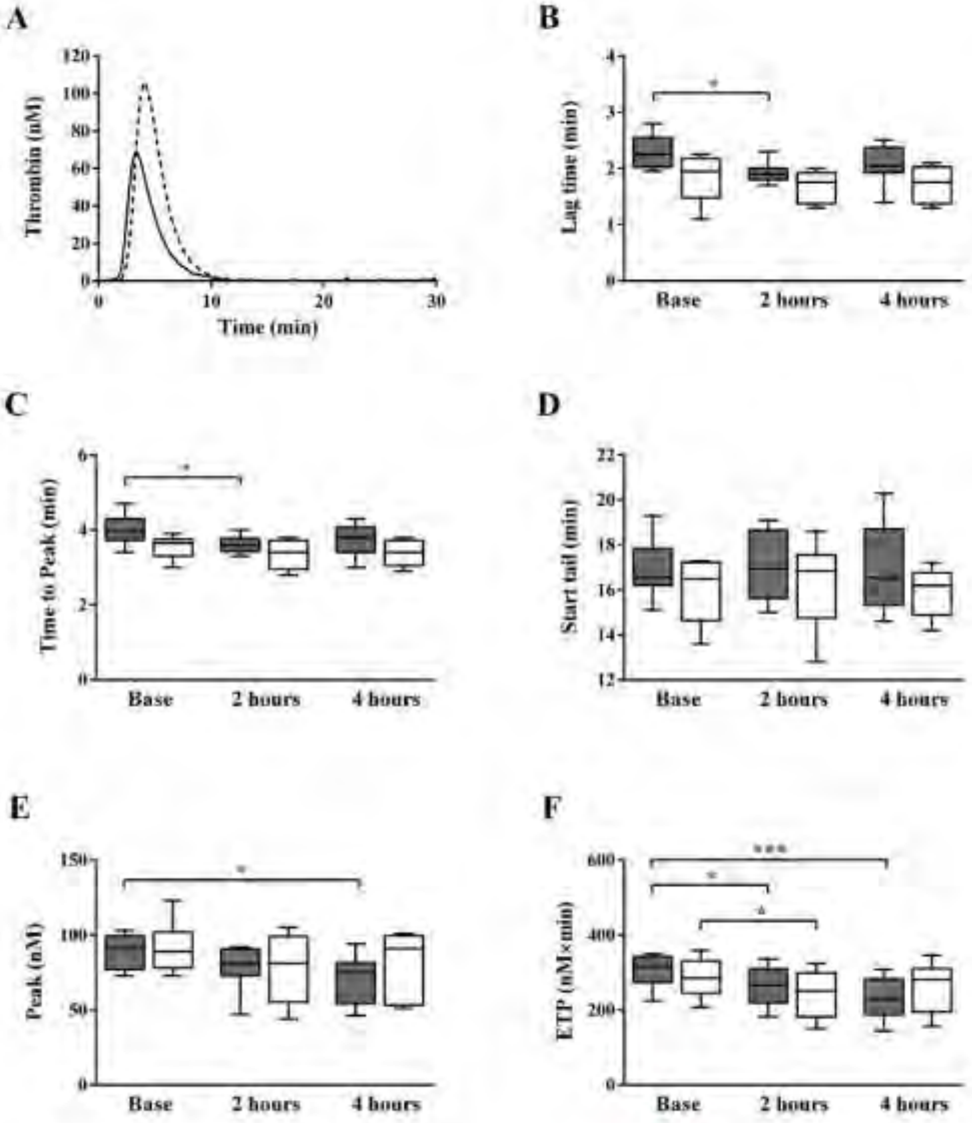


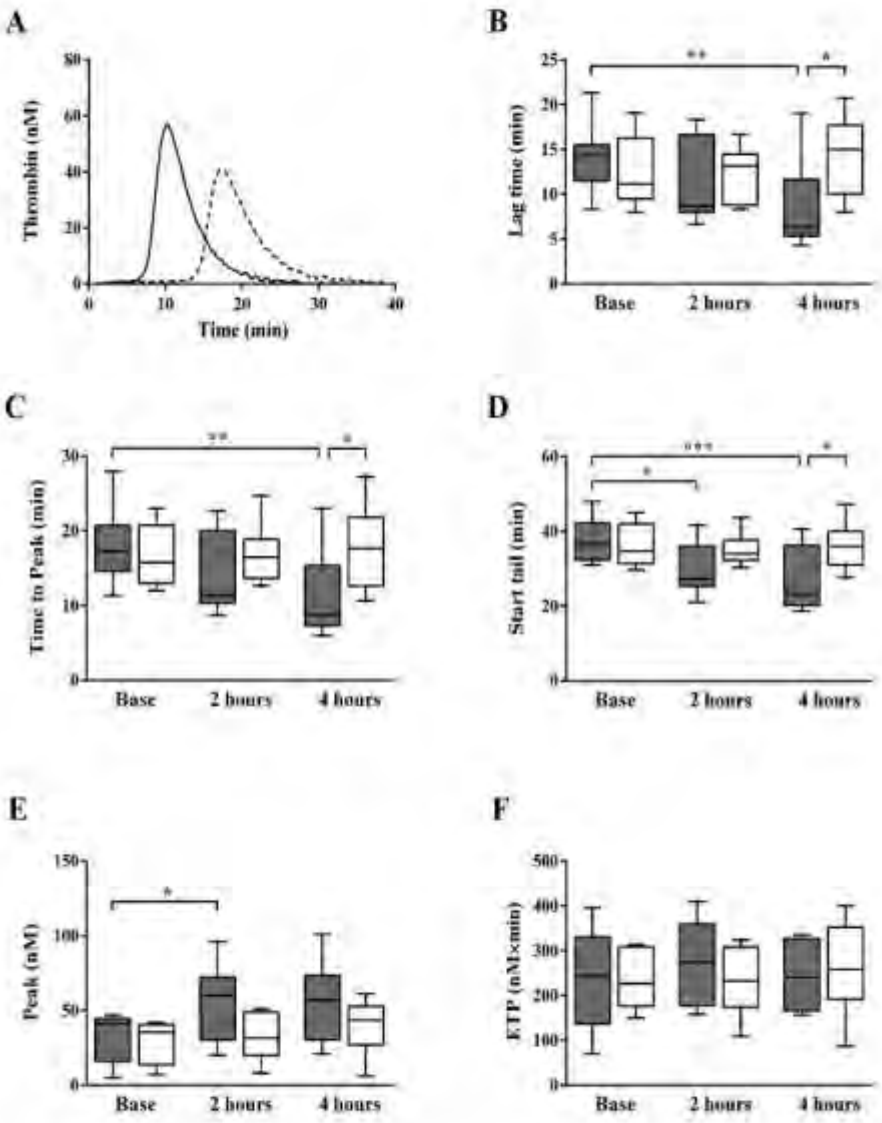

A
B
C
D
Giant platelets/
200 single platelets
Vermiform platelets/
200 single platelets
Base
2 hours
4 hours
Mitochondrium membrane
depolarisation (FL1 MFI mean)



Characteristics of thrombin generation in a fulminant porcine sepsis model

Judit Tóth [a], Ildikó Beke Debreceni [a,*], Ádám Deák [a], Katalin Pető [b], Mariann Berhés [c], Endre Hajdú [c], Judit Szabó [b], Norbert Németh [b], Béla Fülesdi [c], János Kappelmayer [a,c]





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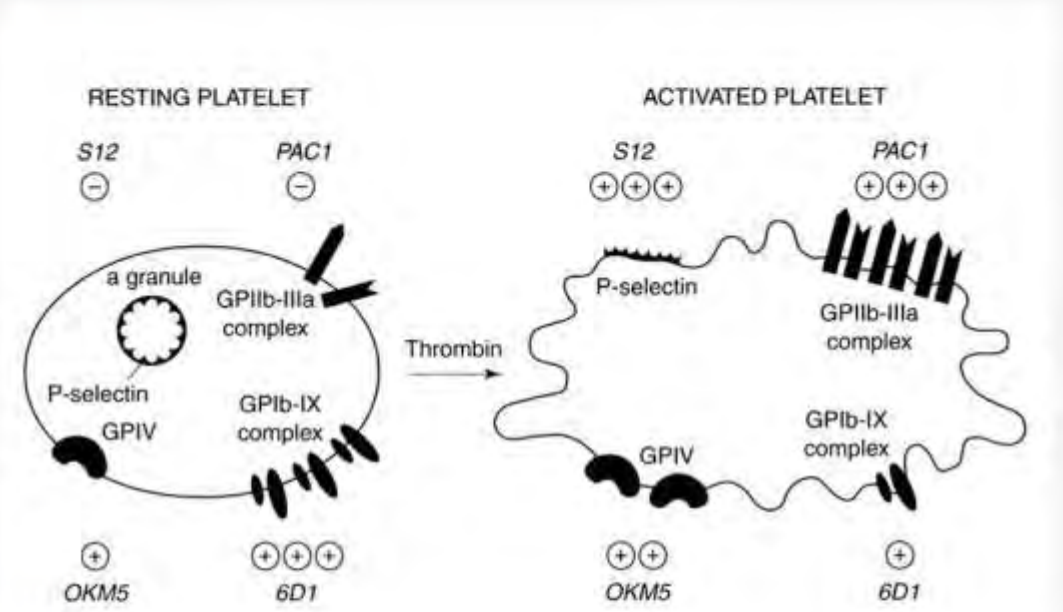
A thrombocyták aktiváltsági állapotának jellemzői (Platelet Activation Status=PAS)



Direkt tesztek:

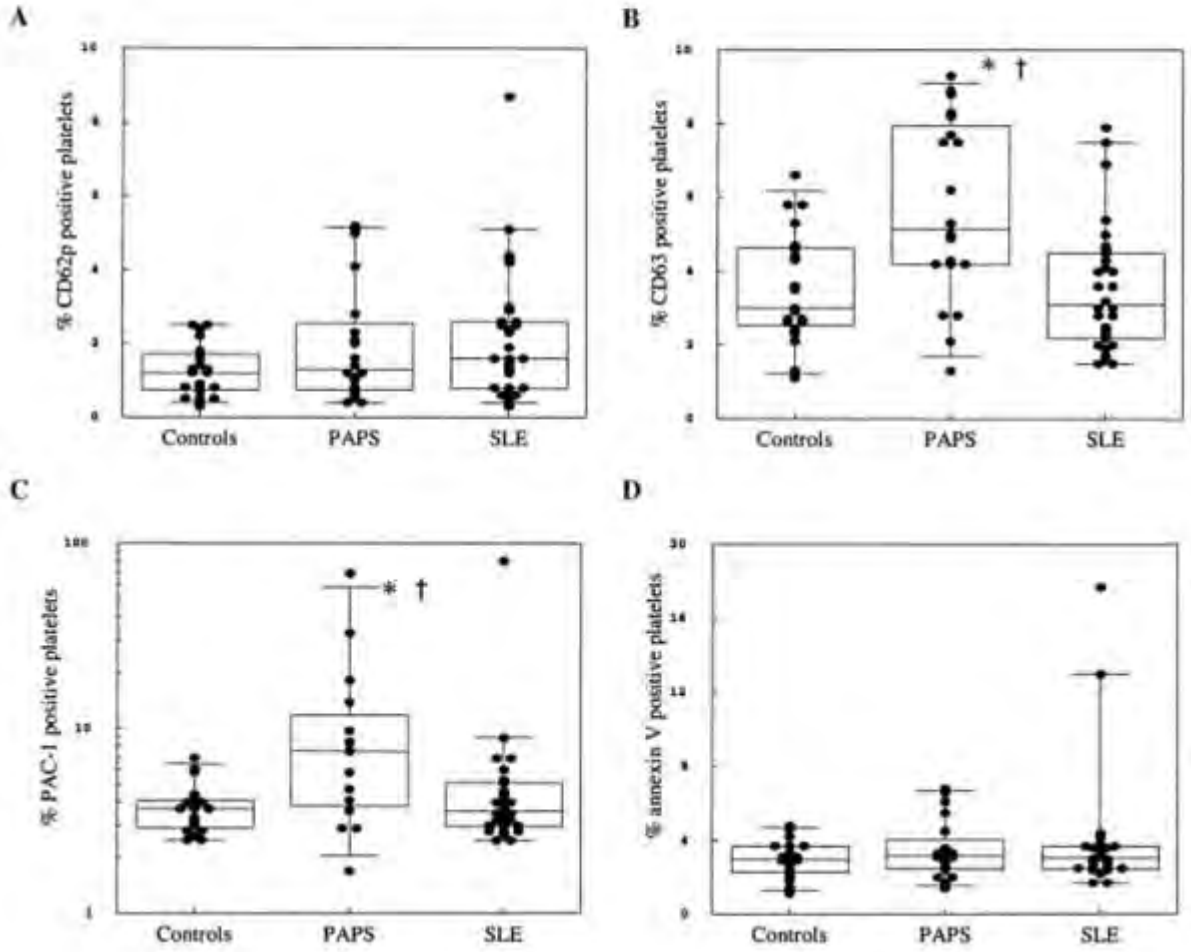
- a P-selectin (CD62) expresszió
- a GPIX (CD42a) expresszió
- LAMP-3 (CD63) expresszió
- PS expozíció (annexin kötés)
- ligandkötés és konformáció
- a mikropartikula arány emelkedése
- Szolubilis markerek analízise (b-TG, PF4, sPsel)

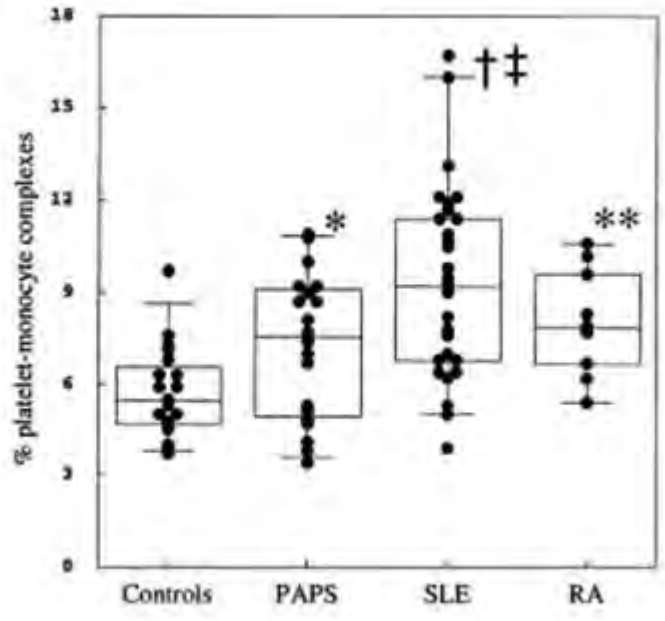
Indirekt tesztek:

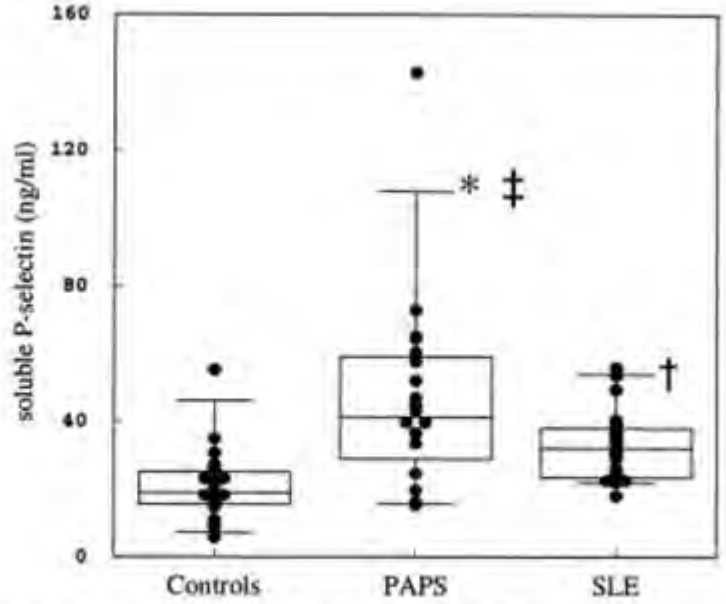
- a thrombocyta-leukocyta heterotypikus aggregátumok mennyiségének változása
- monocyta szöveti faktor (TF) expresszió vizsgálata

Increased circulating platelet–leucocyte complexes and platelet activation in patients with antiphospholipid syndrome, systemic lupus erythematosus and rheumatoid arthritis

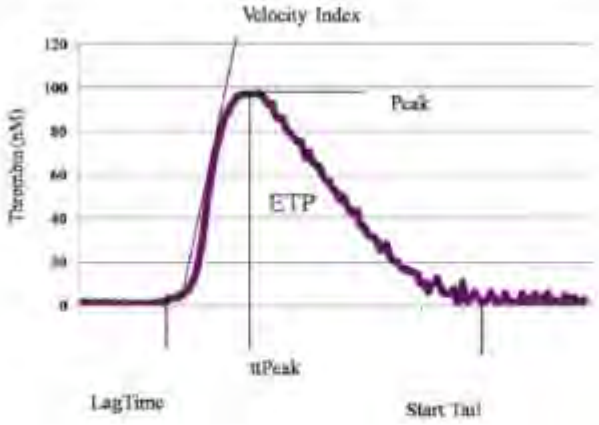
JOANNE E. JOSEPH,[1] PAUL HARRISON[1], IAN J. MACKIE,[1] DAVID A. ISENBERG[2] AND SAMUEL J. MACHIN[1] [1]*Haemostasis Research Unit and* [2]*Centre for Rheumatology, Department of Medicine, University College London, UK*

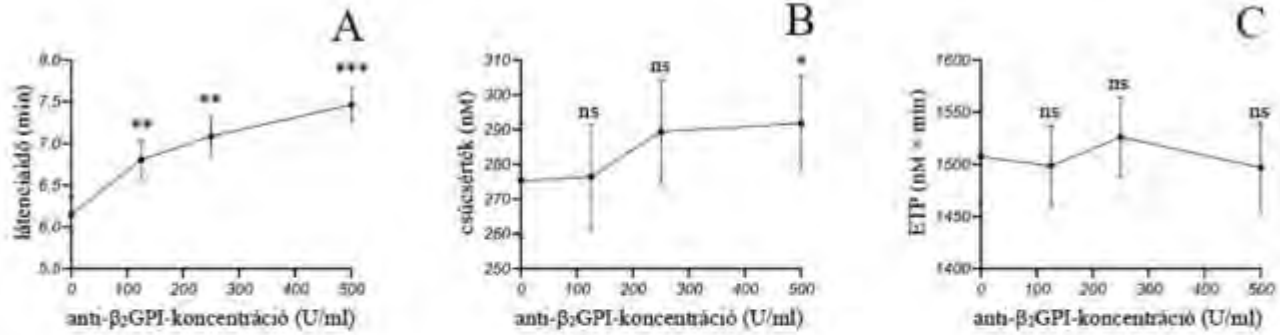






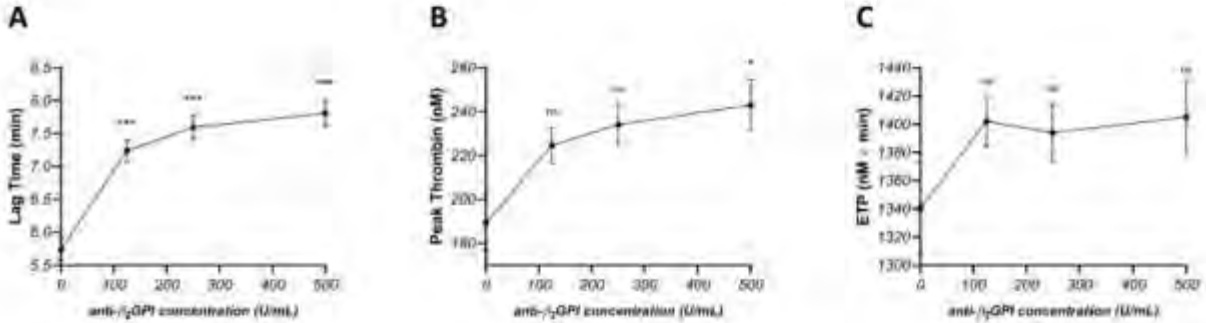
British Journal of Haematology, 2001, 115, 451-459

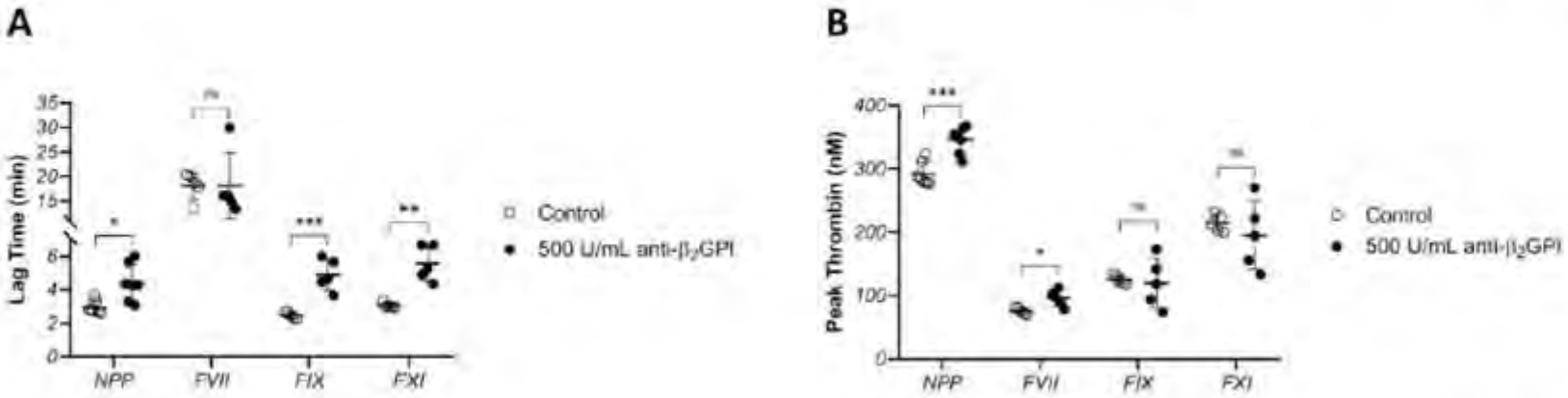




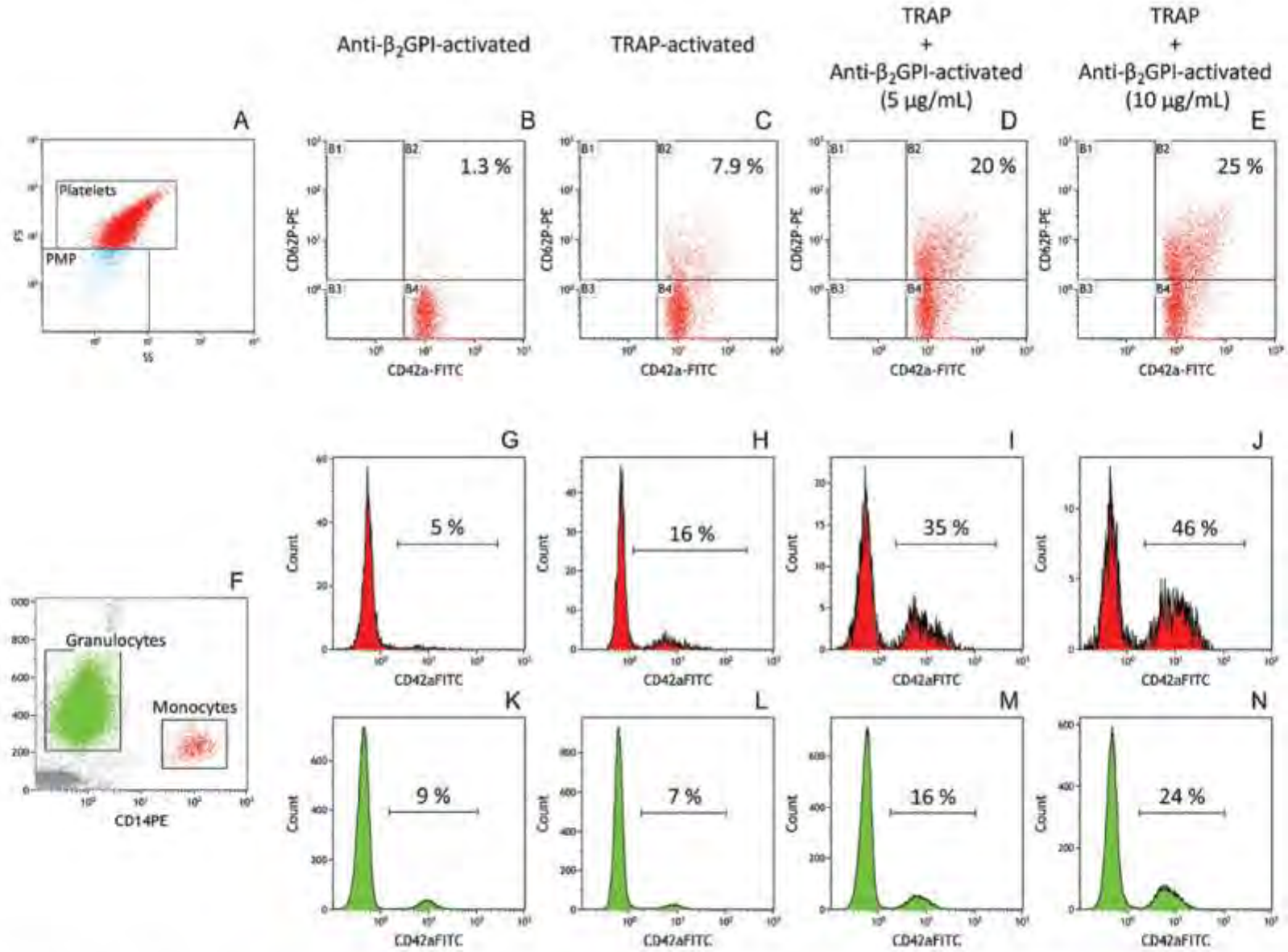
Anti-β_2-glycoprotein I autoantibodies influence thrombin generation parameters via various mechanisms

Gábor Szabó [a,b], Ildikó Beke Debreceni [a], Tünde Tarr [c], Pál Soltész [d], Bjarne Østerud [e], János Kappelmayer [a,*]

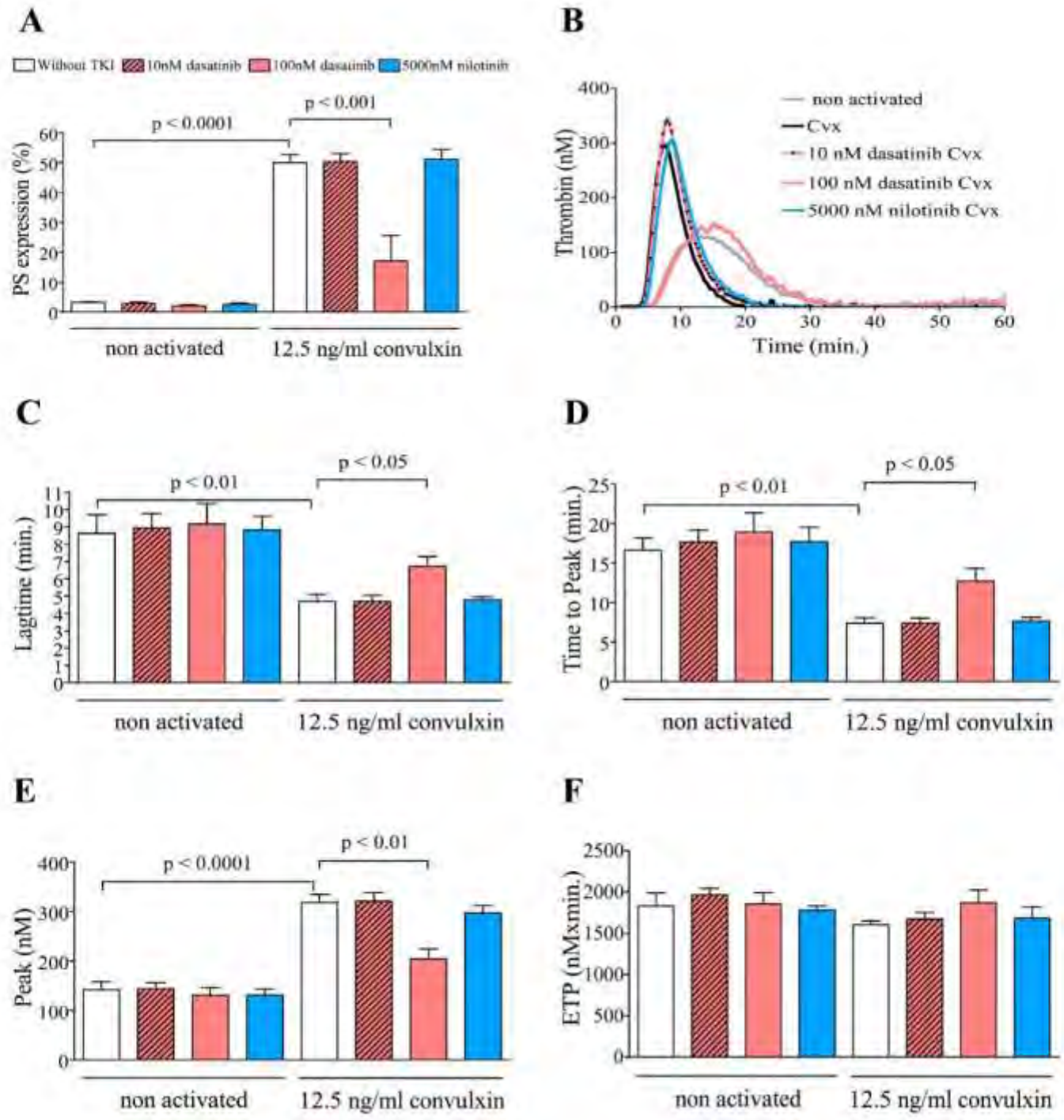


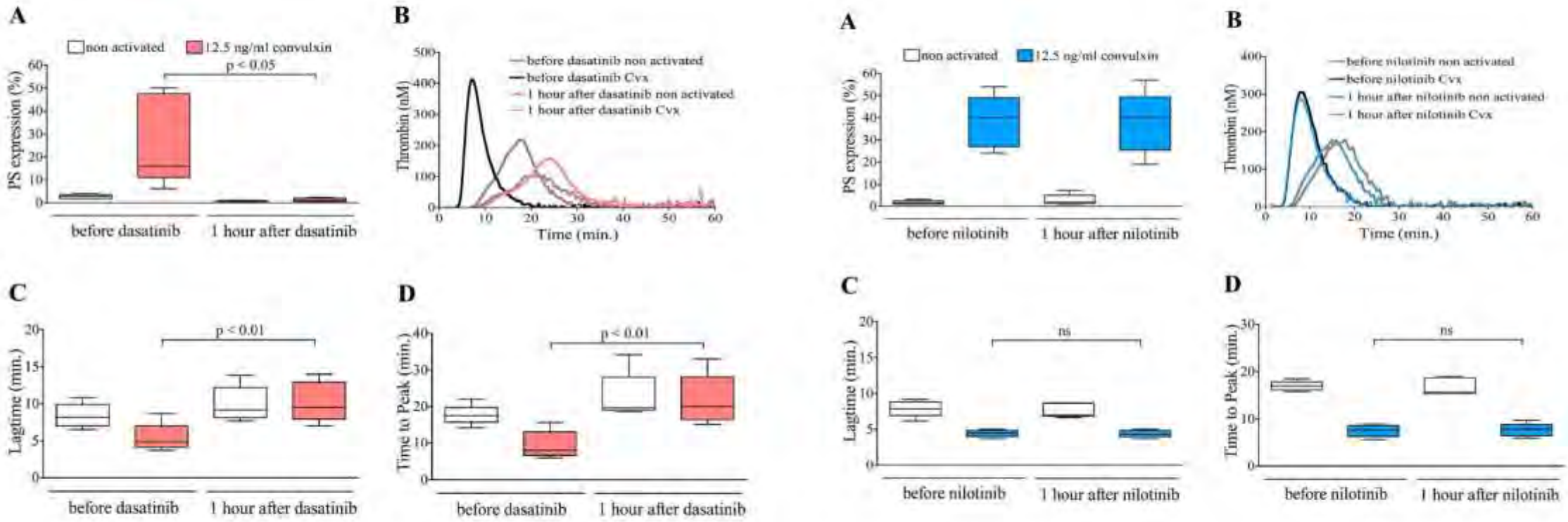


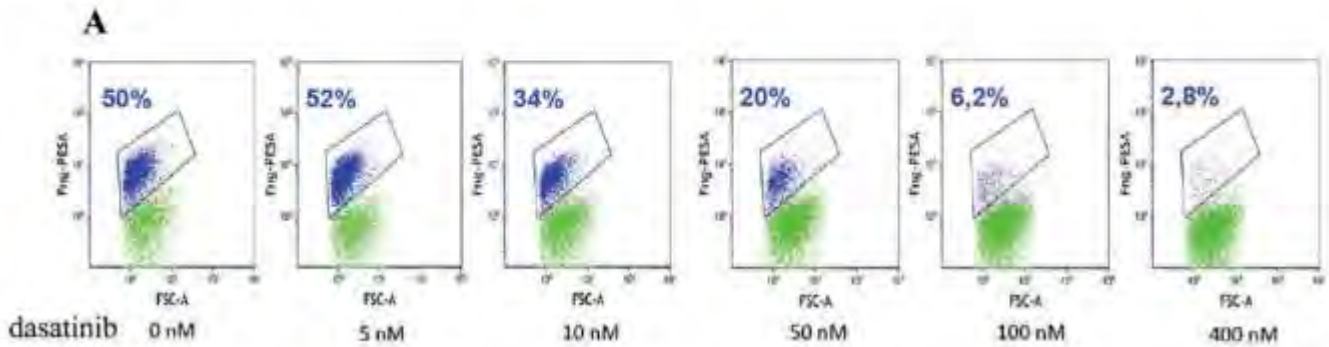
Thrombosis Research 2021;197:124-131.

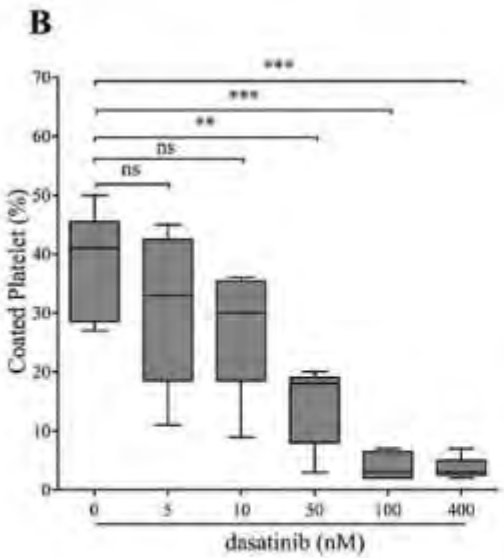


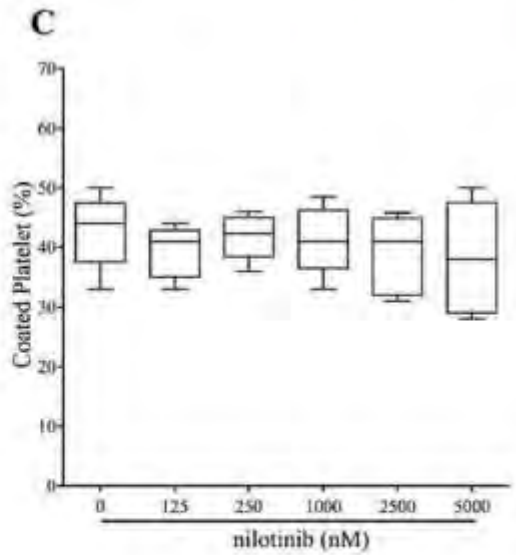
Laboratory Approaches to Test the Function of Antiphospholipid Antibodies.
Szabó G, Antal-Szalmás P, Kerényi A, Pénzes K, Bécsi B, Kappelmayer J.
Semin Thromb Hemost. 2022 Mar;48(2):132-144.

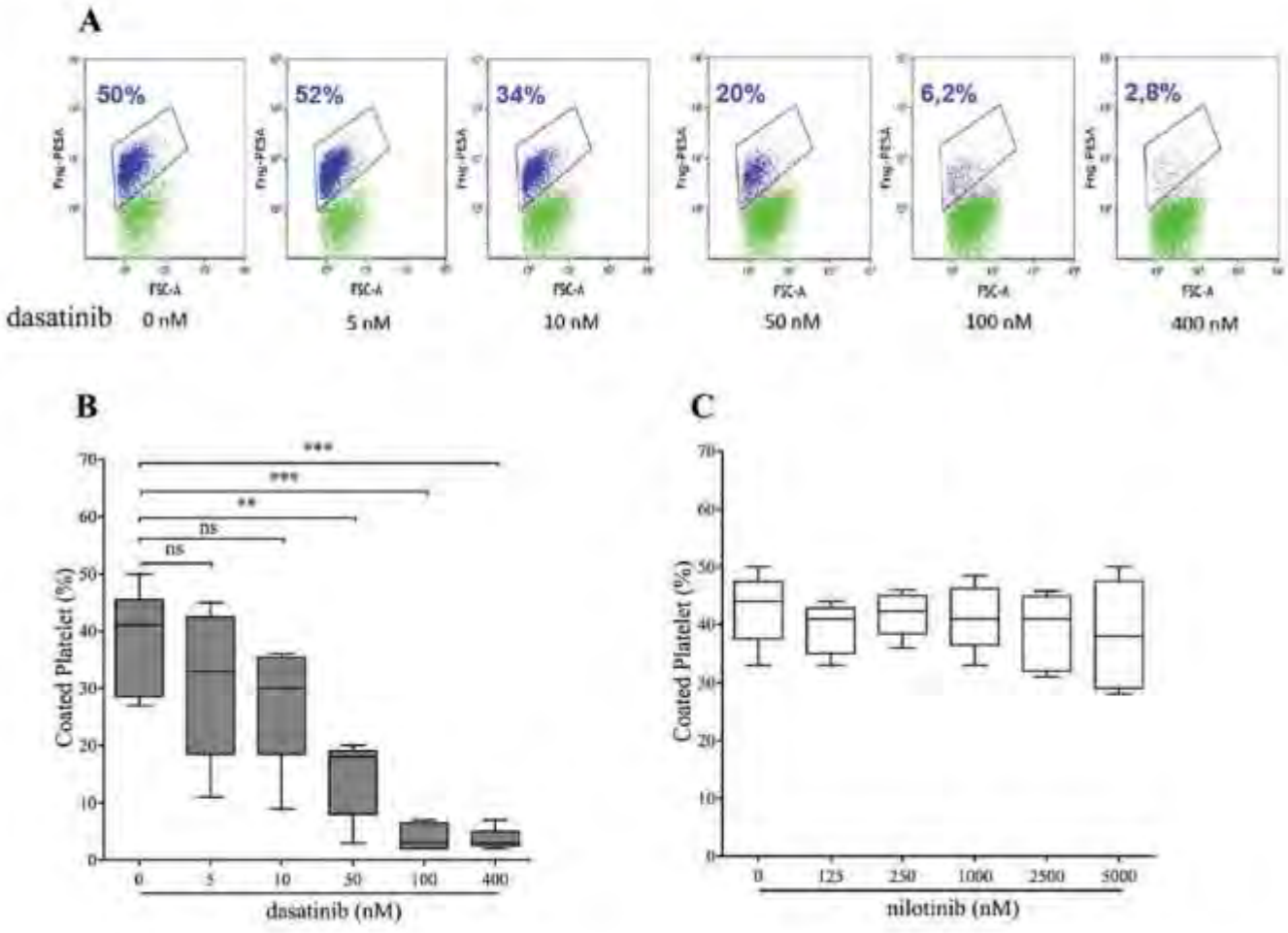

A
Without TKI
10nM dasatinib
100nM dasatinib
5000nM nilotinib
p < 0.0001
p < 0.001
PS expression (%)
non activated
12.5 ng/ml convulxin
B
non activated
Cvx
10 nM dasatinib Cvx
100 nM dasatinib Cvx
5000 nM nilotinib Cvx
Thrombin (nM)
Time (min.)
C
p < 0.01
p < 0.05
Lagtime (min.)
non activated
12.5 ng/ml convulxin
D
p < 0.01
p < 0.05
Time to Peak (min.)
non activated
12.5 ng/ml convulxin
E
p < 0.0001
p < 0.01
Peak (nM)
non activated
12.5 ng/ml convulxin
F
ETP (nMxmin.)
non activated
12.5 ng/ml convulxin

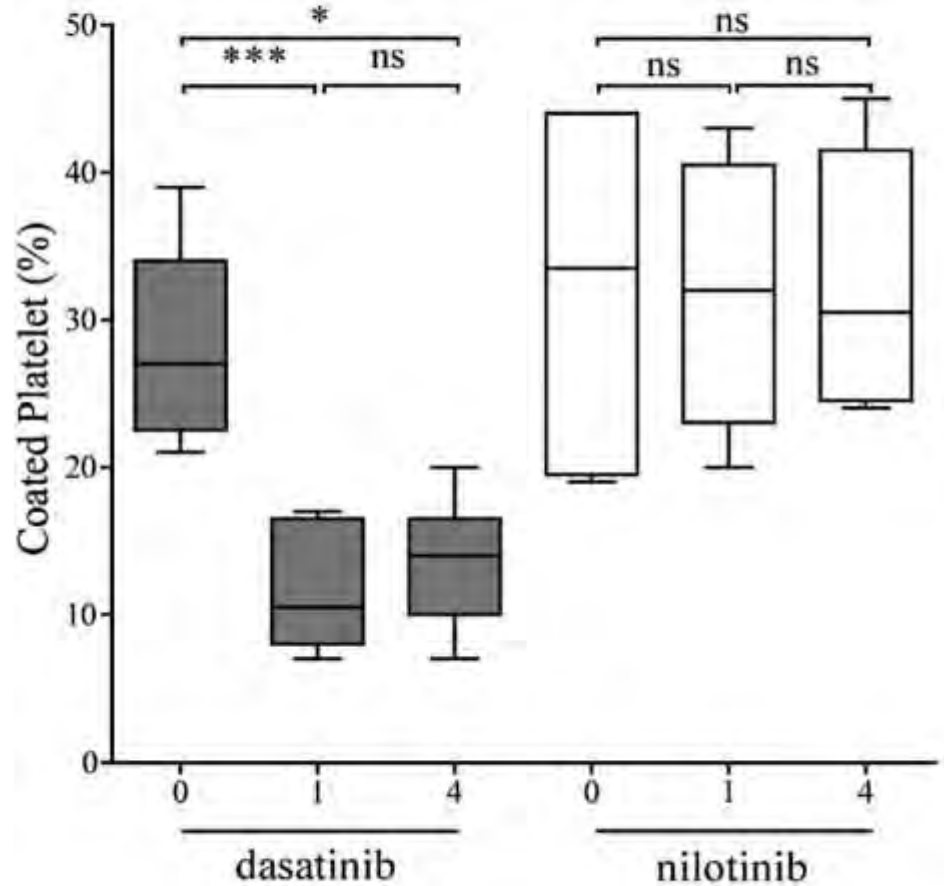

A
non activated
12.5 ng/ml convulxin
p < 0.05
PS expression (%)
before dasatinib
1 hour after dasatinib
B
before dasatinib non activated
before dasatinib Cvx
1 hour after dasatinib non activated
1 hour after dasatinib Cvx
Thrombin (nM)
Time (min.)
C
p < 0.01
Lagtime (min.)
before dasatinib
1 hour after dasatinib
D
p < 0.01
Time to Peak (min.)
before dasatinib
1 hour after dasatinib
A
non activated
12.5 ng/ml convulxin
PS expression (%)
before nilotinib
1 hour after nilotinib
B
before nilotinib non activated
before nilotinib Cvx
1 hour after nilotinib non activated
1 hour after nilotinib Cvx
Thrombin (nM)
Time (min.)
C
ns
Lagtime (min.)
before nilotinib
1 hour after nilotinib
D
ns
Time to Peak (min.)
before nilotinib
1 hour after nilotinib

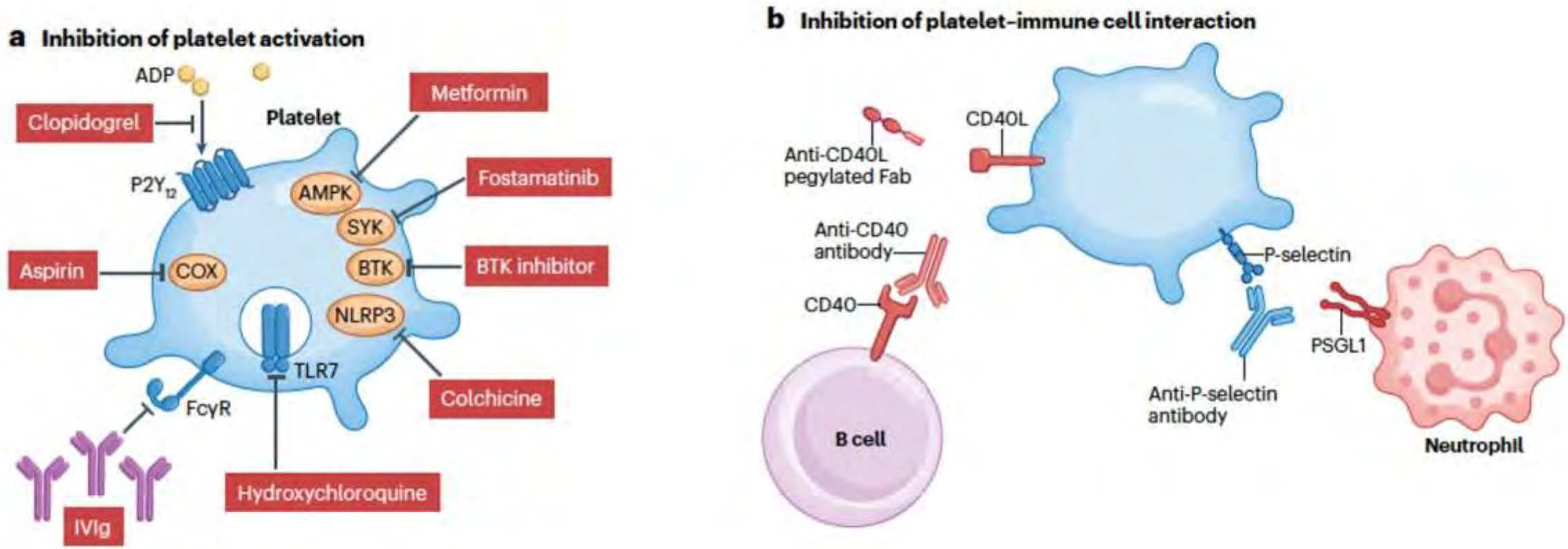

A
50%
52%
34%
20%
6,2%
2,8%
FSC-A
dasatinib 0 nM
5 nM
10 nM
50 nM
100 nM
400 nM


B
***
***
**
ns
ns
Coated Platelet (%)
0
10
20
30
40
50
60
70
0
5
10
50
100
400
dasatinib (nM)


C
Coated Platelet (%)
0
10
20
30
40
50
60
70
0
125
250
1000
2500
5000
nilotinib (nM)


A
50%
52%
34%
20%
6,2%
2,8%
FSC-A
dasatinib 0 nM
5 nM
10 nM
50 nM
100 nM
400 nM
B
Coated Platelet (%)
dasatinib (nM)
C
Coated Platelet (%)
nilotinib (nM)


Coated Platelet (%)
dasatinib
nilotinib
ns
***
*


a Inhibition of platelet activation
ADP
Clopidogrel
Platelet
Metformin
P2Y12
AMPK
Fostamatinib
SYK
Aspirin
COX
BTK
BTK inhibitor
NLRP3
TLR7
FcγR
Colchicine
Hydroxychloroquine
IVIg
b Inhibition of platelet–immune cell interaction
Anti-CD40L
pegylated Fab
CD40L
Anti-CD40
antibody
CD40
P-selectin
PSGL1
Anti-P-selectin
antibody
B cell
Neutrophil

nature reviews immunology

Review article

The role of platelets in immune-mediated inflammatory diseases

Marc Scherlinger, Christophe Richez, George C. Tsokos, Eric Boilard & Patrick Blanco

nature reviews immunology

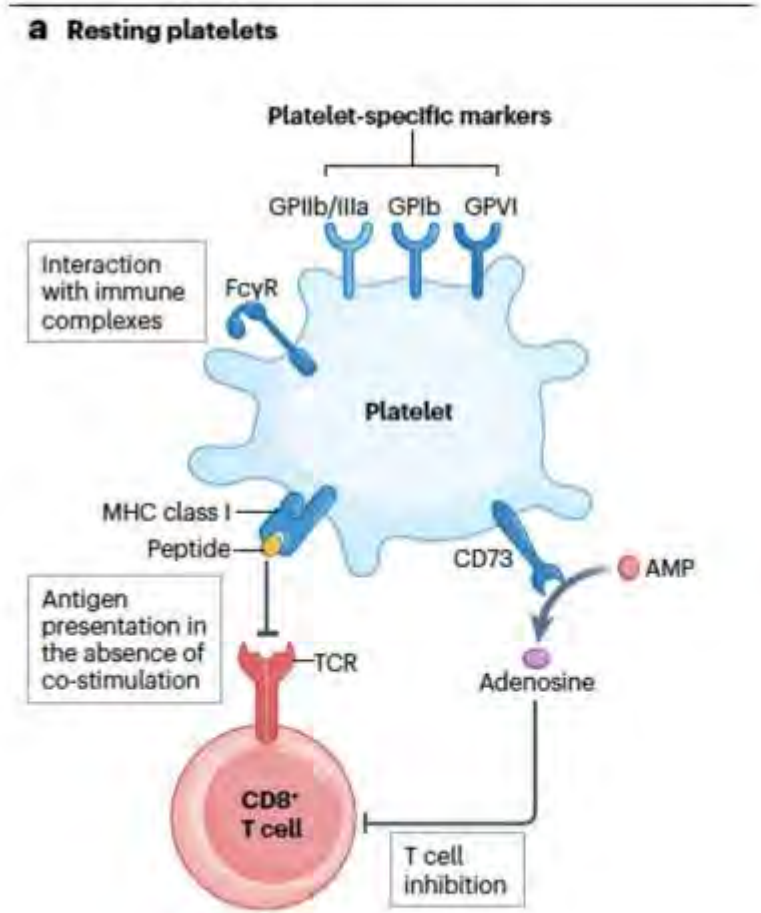
https://doi.org/10.1038/s41577-025-00834-4

Review article

Check for updates

The role of platelets in immune-mediated inflammatory diseases

Marc Scherlinger[1,2,3], Christophe Richez[4,5], George C. Tsokos[6], Eric Boilard[4,7] & Patrick Blanco[3,8]



nature reviews immunology

Review article

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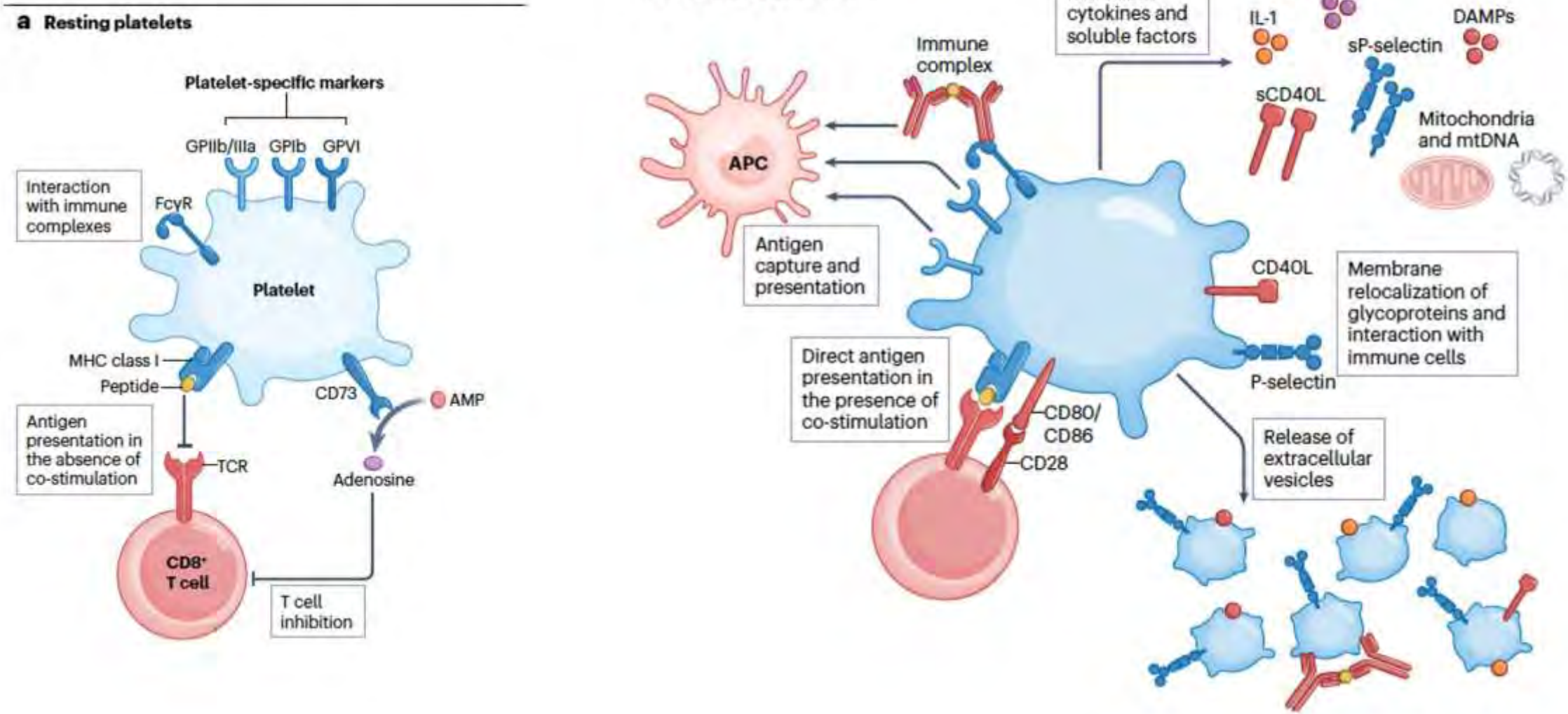

Platelet-Rich Plasma for Rheumatoid Arthritis: A Case Series

Dana Shively [1], Neel Amin [2]

A Platelet's Guide to Synovitis

Giacomo Cafaro MD, Elena Bartoloni MD, Alessia Alunno MD PhD, Onelia Bistoni BSc, Sabrina Cipriani PhD, Fabiana Topini PhD and Roberto Gerli MD

Rheumatology Unit, Department of Medicine, University of Perugia, Perugia, Italy

Case Series

Platelet Rich Plasma for Treatment of Rheumatoid Arthritis: Case Series and Review of Literature

Humeira Badsha, [1] Ghita Harifi, [1] and William D. Murrell[2,3,4,5]

Table 1. Overview of active ingredients of PRP

Growth factors	Origins	Physiological effects
PDGF	Neuronal cells, astrocytes, oligodendrocytes, and vascular cells[9]	Induces stem cell differentiation, participates in neuroprotection, and promotes cell proliferation and migration[9,10]
TGF-β	B cells, T cells, dendritic cells, macrophages[11]	Promoting cell proliferation and differentiation, participating in tissue repair and fibrosis, and inhibiting the activation of immune cells[12,13]
VEGF	Production by endothelial cells, smooth muscle cells, platelets, neutrophils and macrophages[14]	In charge of angiogenesis and vascular repair, indirectly promoting tissue repair and neuroprotection[15]
IGF-1	Hepatic stellate cells, osteoblasts, fibroblasts, macrophages[16]	Promotes growth, cell differentiation and cell proliferation[16]
bFGF	Endothelial cells, bone cells[17,18]	Induction of neovascularization and neurotrophy[18–20]
EGF	Endothelial cells, vascular smooth muscle cells, neutrophils, macrophages[21]	Promoting wound healing and anti-inflammatory[22]

Table 3. The current status of PRP applications across various clinical departments

Departments	Diseases
Orthopedic	Osteoarthritis, tendinopathy of Achilles tendon, rotator cuff tear, peripheral nerve injury, fracture, etc.[80–82]
Pain medicine	Radiculopathy, lumbago, phantom limb pain, etc.[83–86]
Plastic surgery	Skin healing, autologous fat transplantation, cartilage rebuilding, etc.[86,87]
Urology	Erectile dysfunction, urethral stricture, hypospadias, prostatic hyperplasia, bladder contracture, peyronie disease, etc.[58–60]
Dermatology	Androgenetic alopecia, alopecia areata, alopecia cicatrisata, chronic vitiligo, chloasma, psoriasis, paronychia, acne scarring, skin aging, etc.[91–94]
Ophthalmology	Xerophthalmia, corneal ulcers, etc.[95,96]
Otorhinolaryngology, Head and Neck Surgery	Tympanic membrane perforation, sensorineural hearing loss, perforation of nasal septum, leakage of cerebrospinal, dyssomnia, atrophic rhinitis, cicatricial stenosis of larynx, tracheal stenosis, tonsillectomy, etc.[97,98]
Oral and maxillofacial surgery	Alveolar osteitis, gingivitis, periodontitis, osteonecrosis of jaw, oral implant, etc.[99,100]
Respiratory medicine	COPD, asthma, interstitial pulmonary fibrosis, etc.[101]
Gynecology	Intrauterine adhesion, premature ovarian failure, genital tract fistula, pelvic floor dysfunction, thin endometrium, repeated Implantation Failure, etc.[102–104]
General surgery	Anal fistula, etc.[105]
Cardiothoracic surgery	Coronary artery bypass grafting, sternotomy complications, bronchial fistula, myocardial injury, etc.[106–108]

The role of platelet-rich plasma in biomedicine: A comprehensive overview.

Zhang Z, Liu P, Xue X, Zhang Z, Wang L, Jiang Y, Zhang C, Zhou H, Lv S, Shen W, Yang S, Wang F. iScience. 2025 Jan 3;28(2):111705. doi: 10.1016/j.isci.2024.111705.

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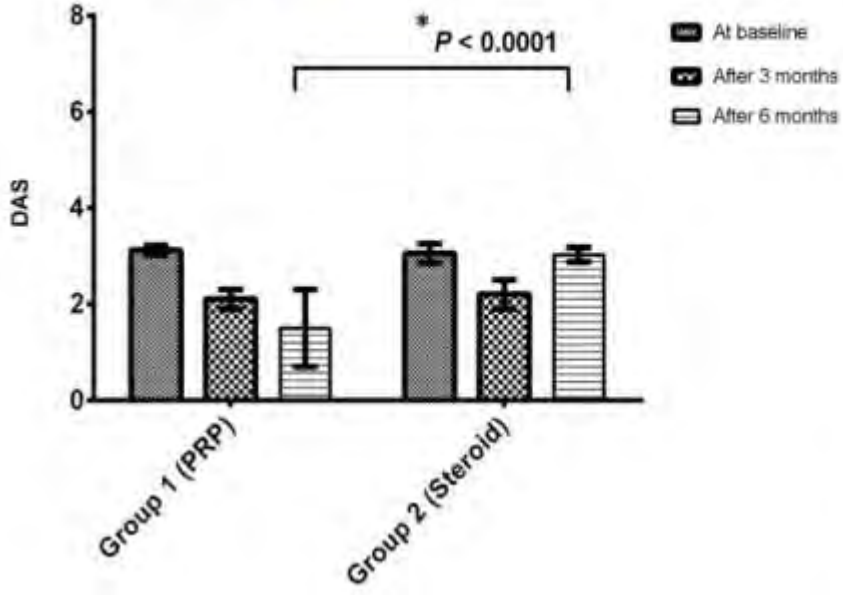

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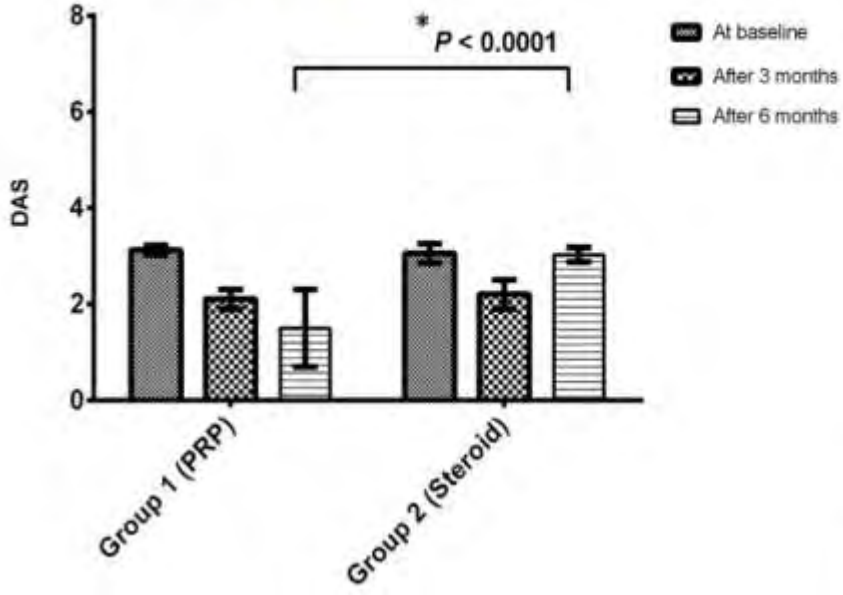

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A PRP egyfajta csodaszernek tűnhet
Amitől nekem rögtön gyanússá válik

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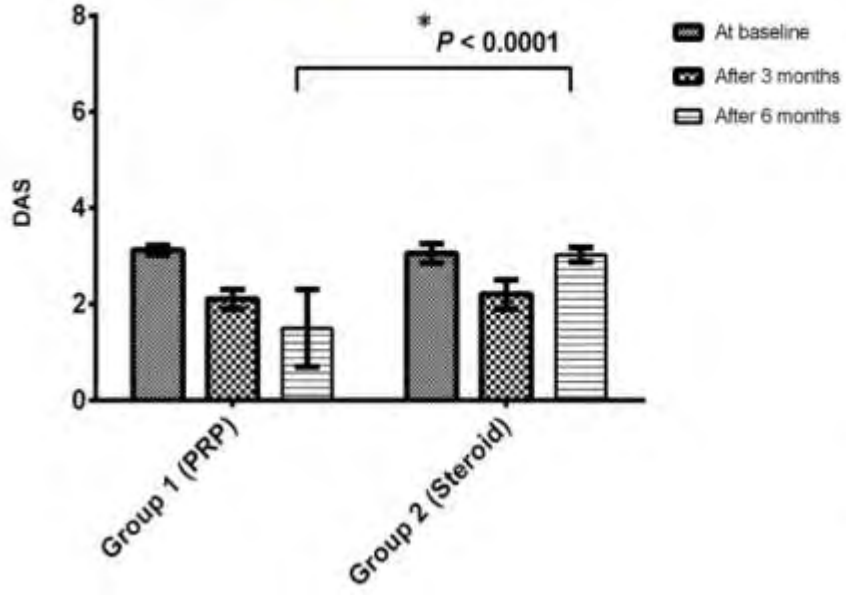

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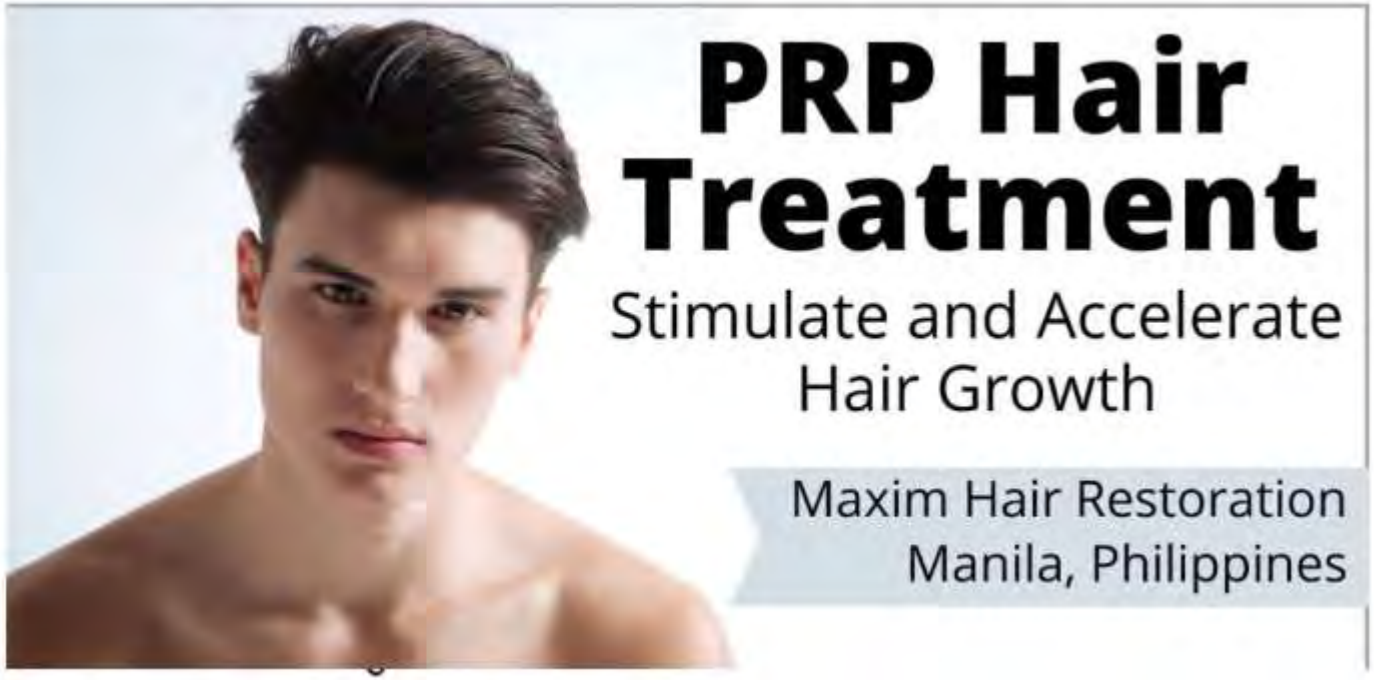

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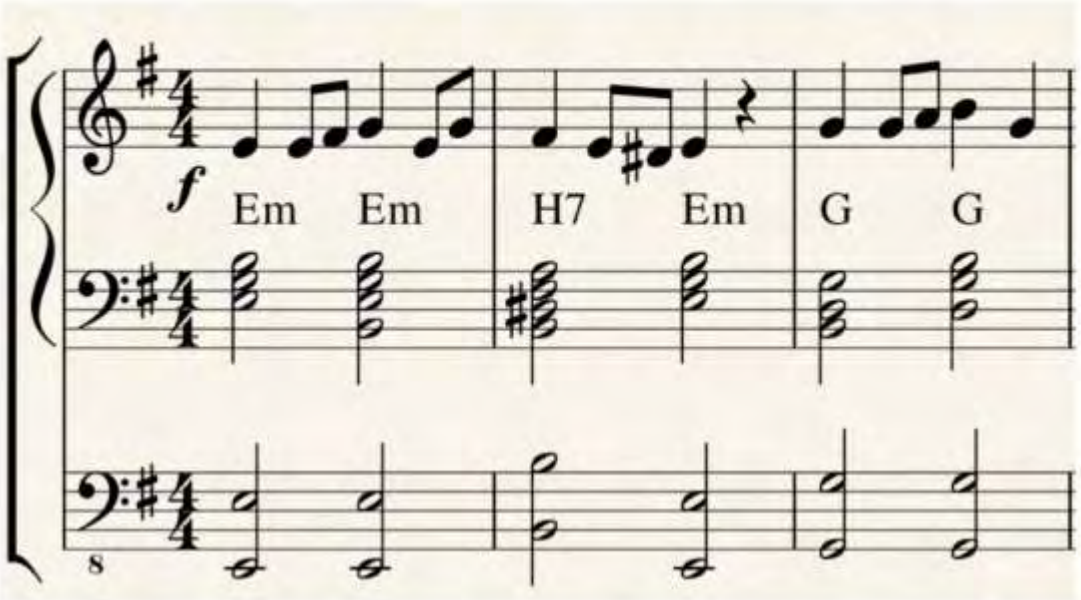
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SZÓLJON AZ ÉNEK...
ÁPRILIS 4-RŐL