

A vérlemezkek szerepe az immunválaszban

Kappelmayer János

Debreceni Egyetem,

Laboratóriumi Medicina Intézet



Immunsejtek versus alvadást elősegítő sejtek

Hemocytta:

alsóbb rendű szervezetek közös alvadást és immunválaszt generáló sejtek

Szolublis elemek

Thrombocytta:

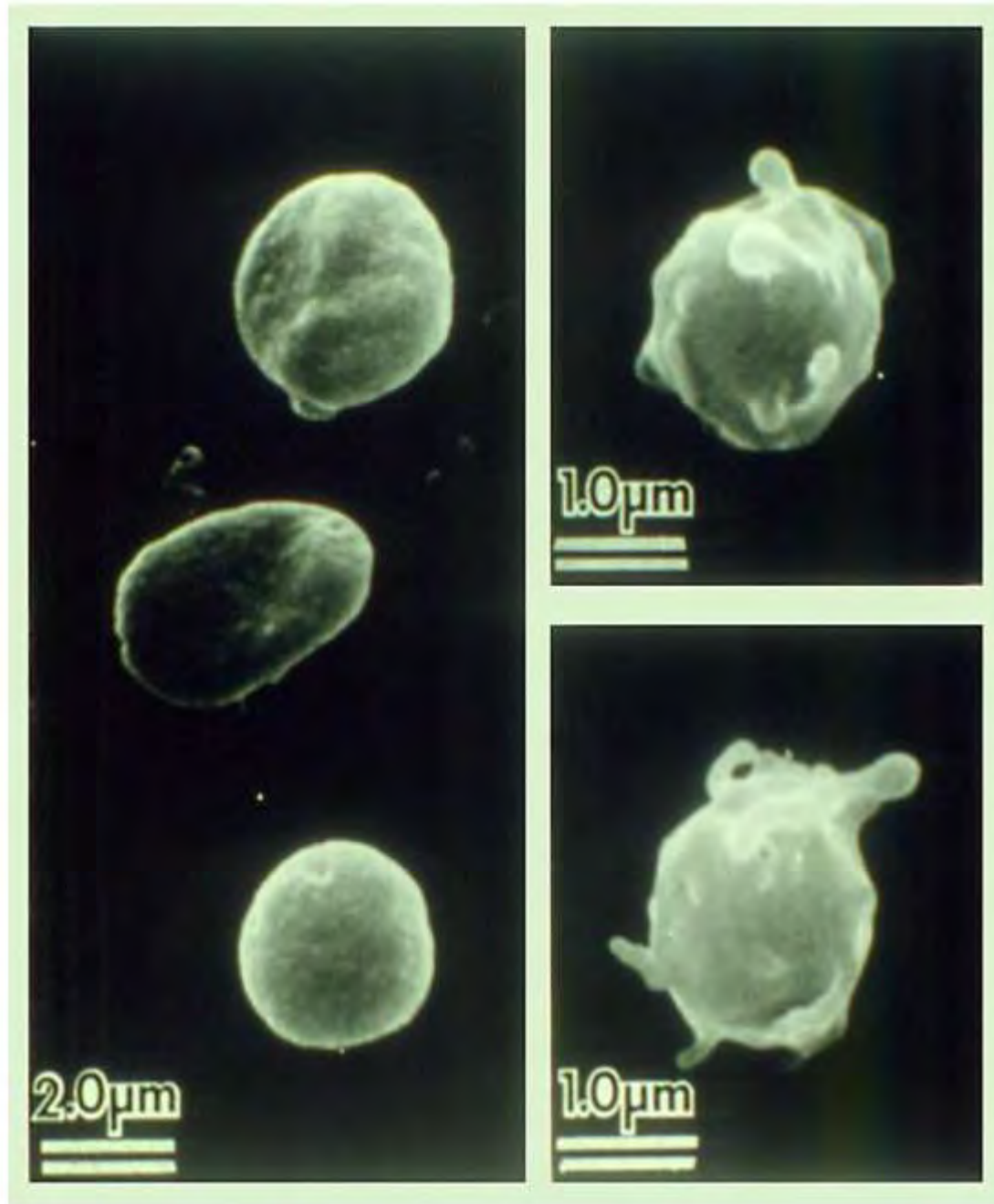
Mag nélküli sejt

Alvadási faktorok

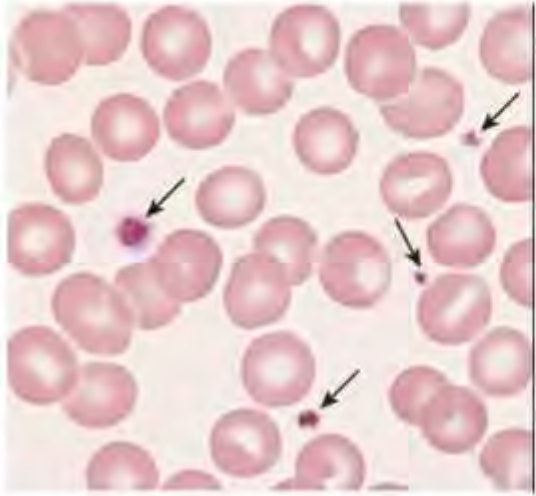
Veleszületett
immunválasz sejtjei:

Granulocytta, macrophag

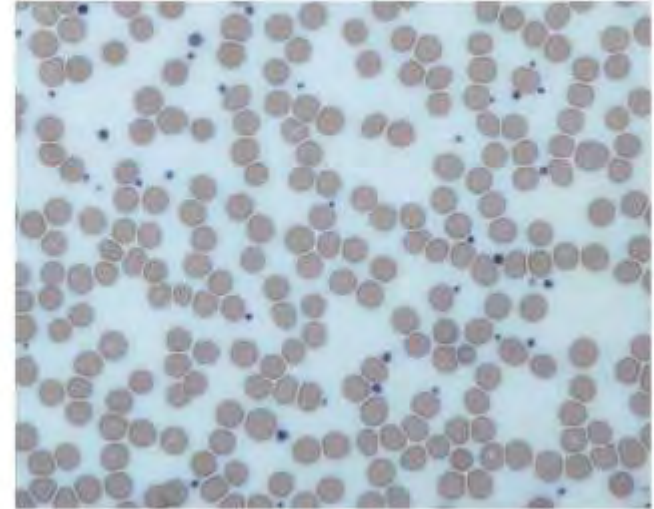
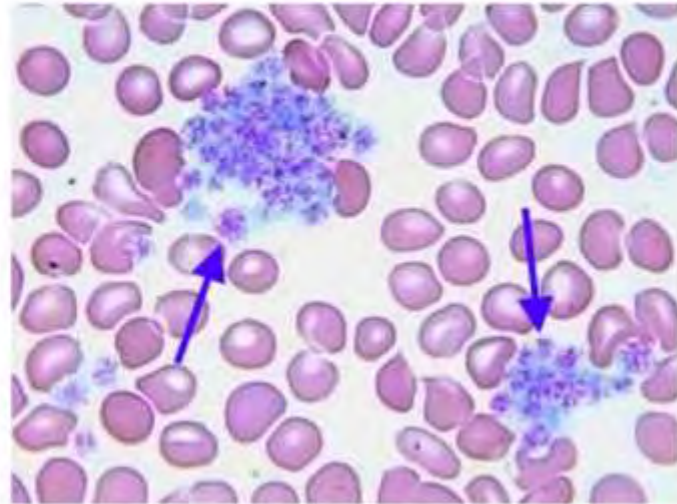
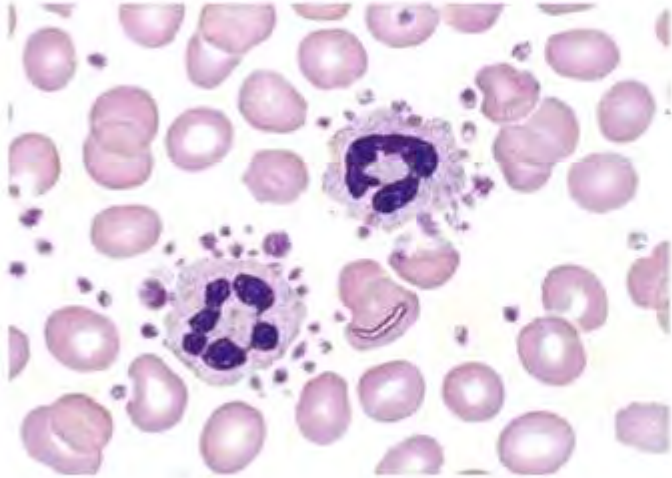
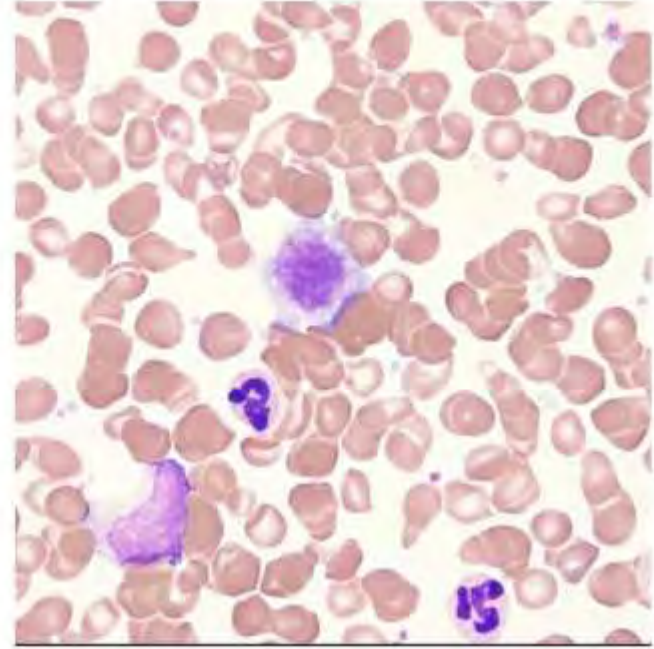
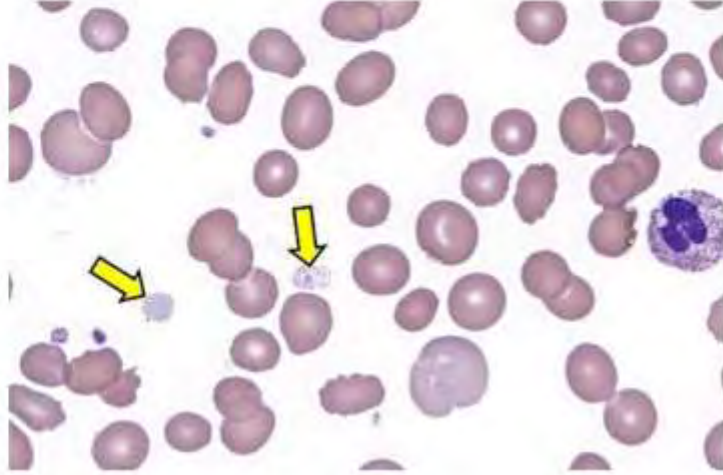
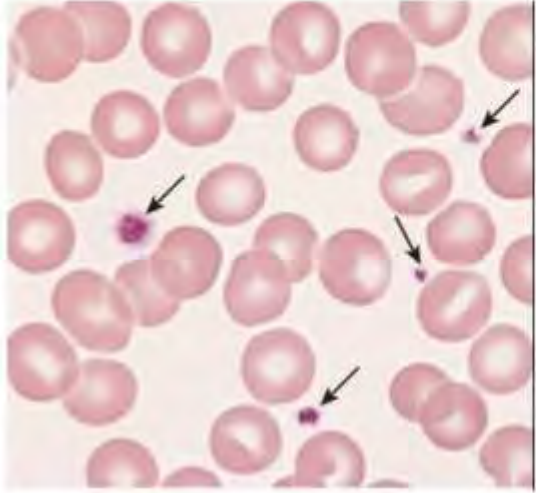
Komplement

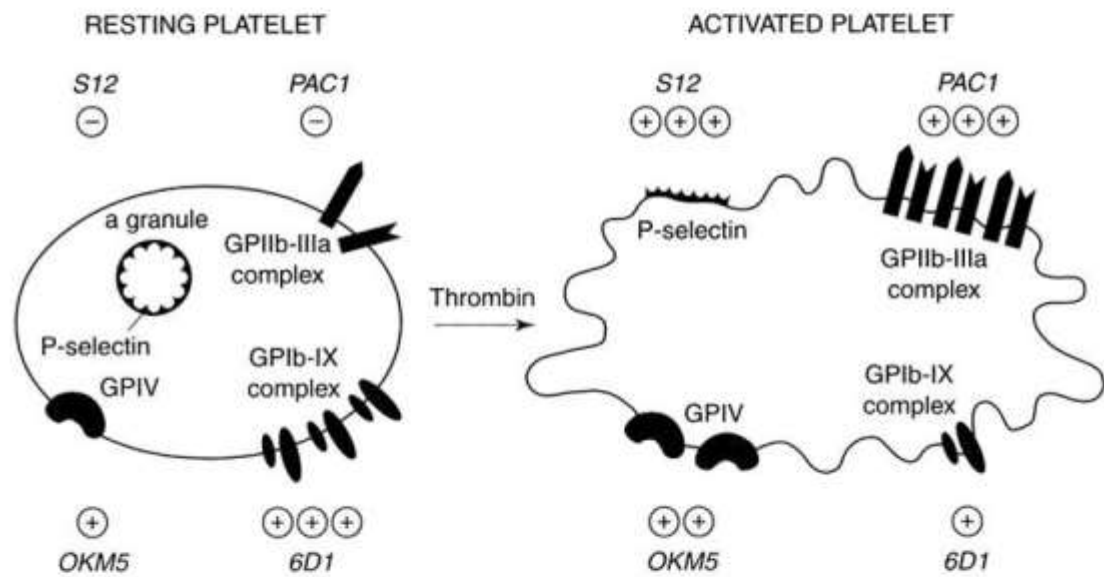


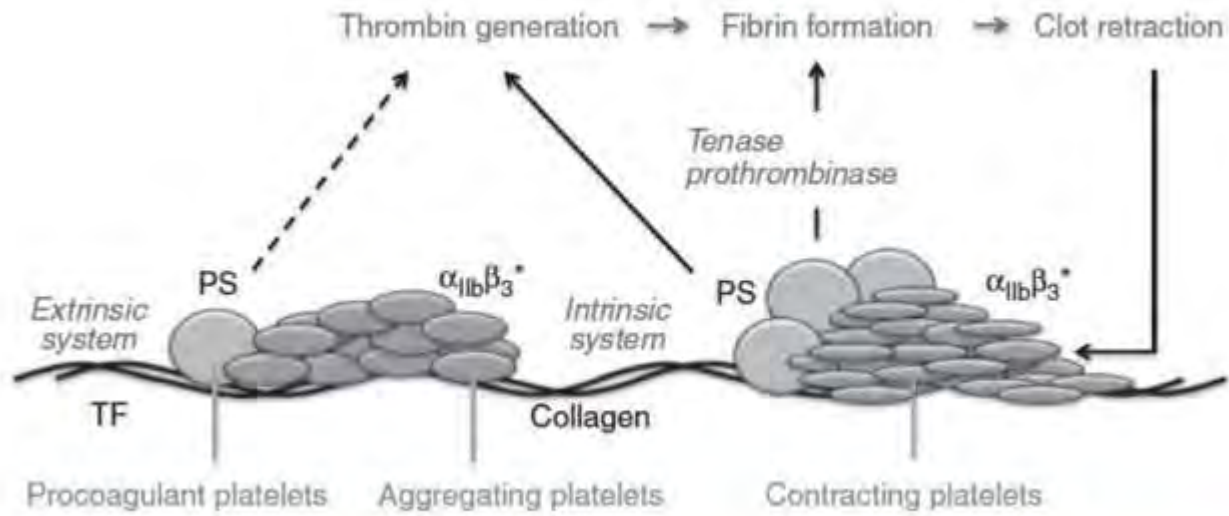
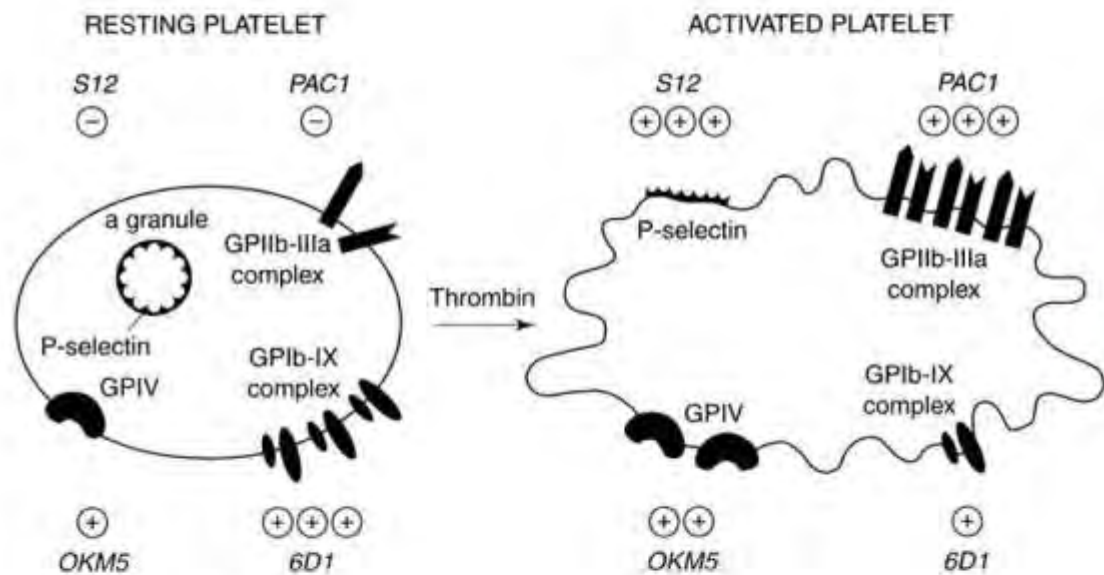
Kóros thrombocyta morfológia



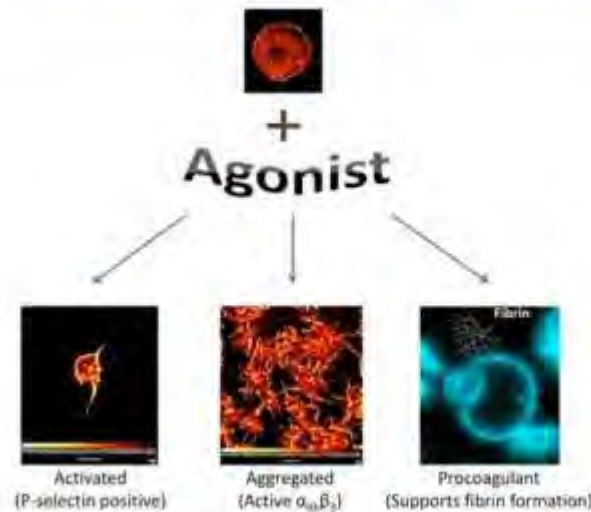
Kóros thrombocyta morfológia







Different activated platelet subpopulations form with the same agonist stimulation



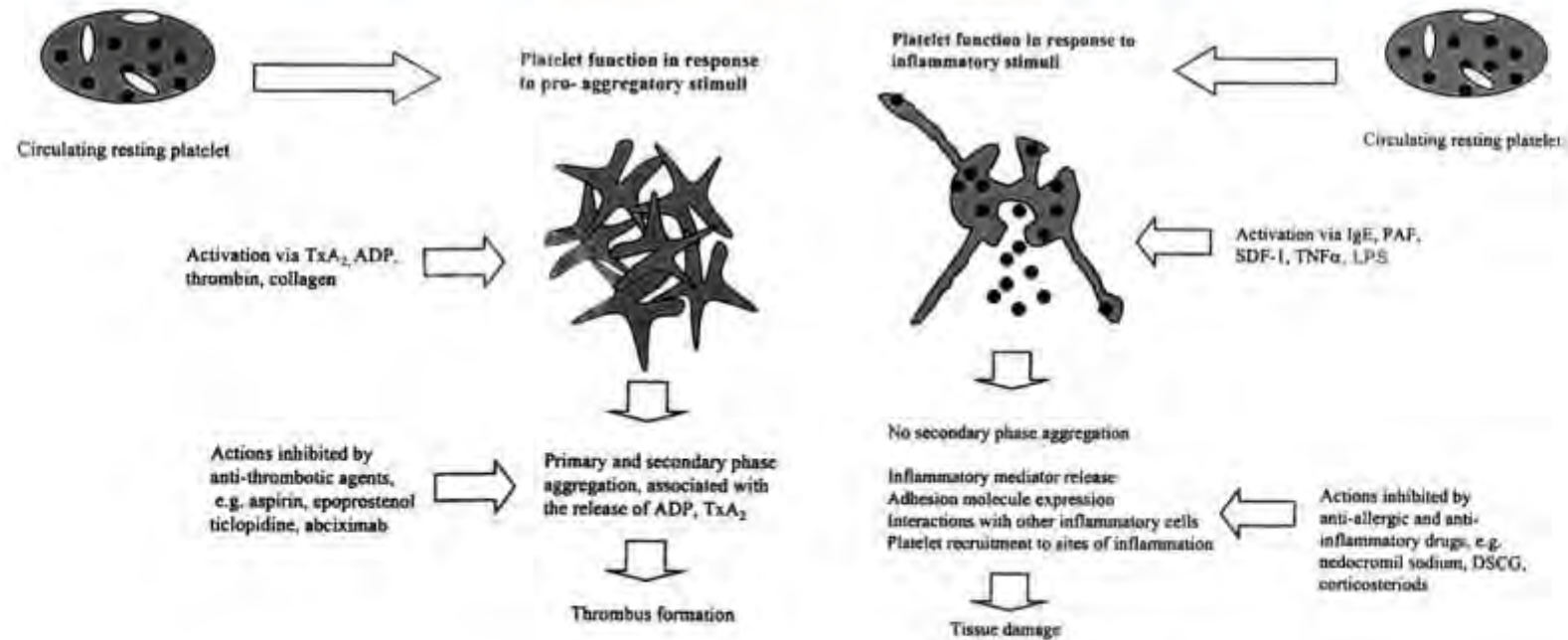
A thrombocytá aktiváció útvonalai

Klasszikus

Thrombin
Kollagén
ADP

“Alternatív”

Komplement
PAF
LPS



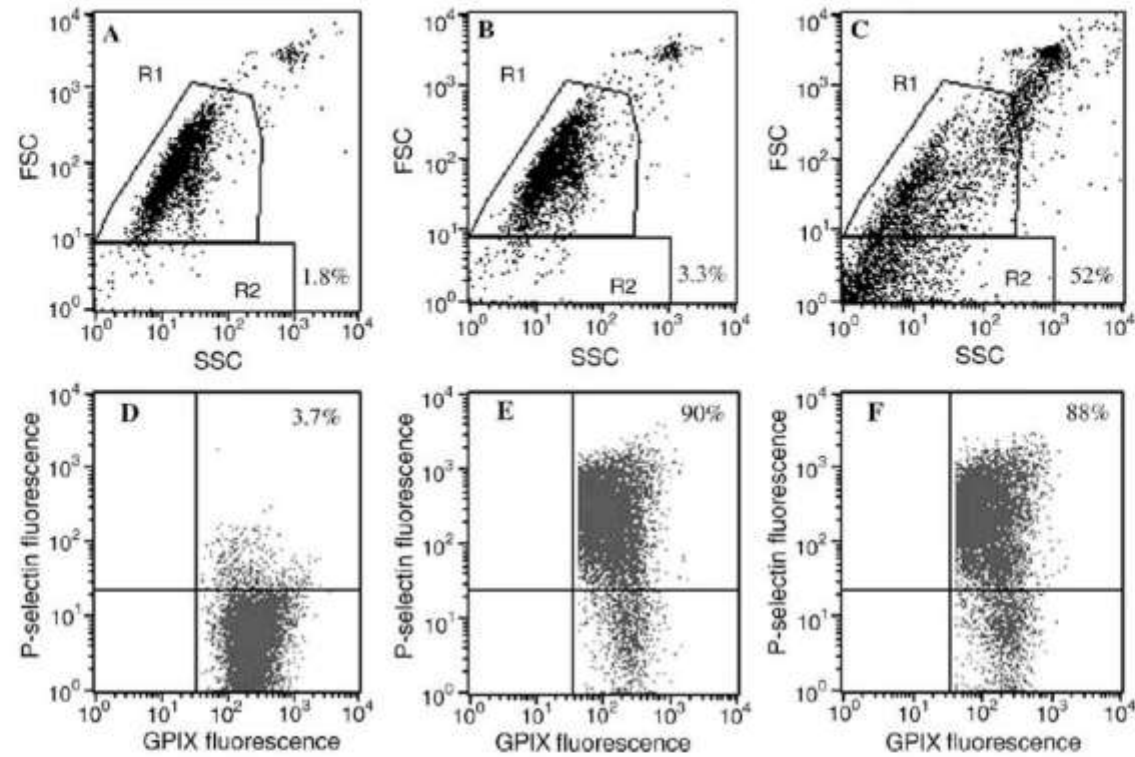
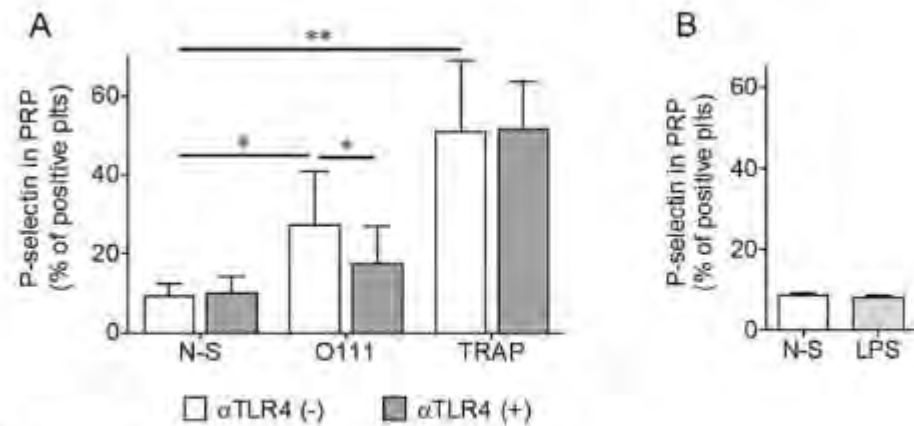


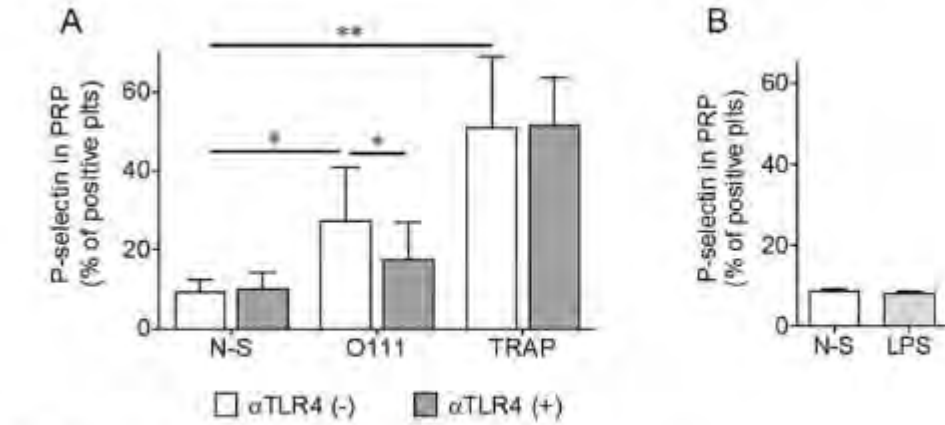
Table 2 Different sensitivity of direct platelet activation markers.

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.

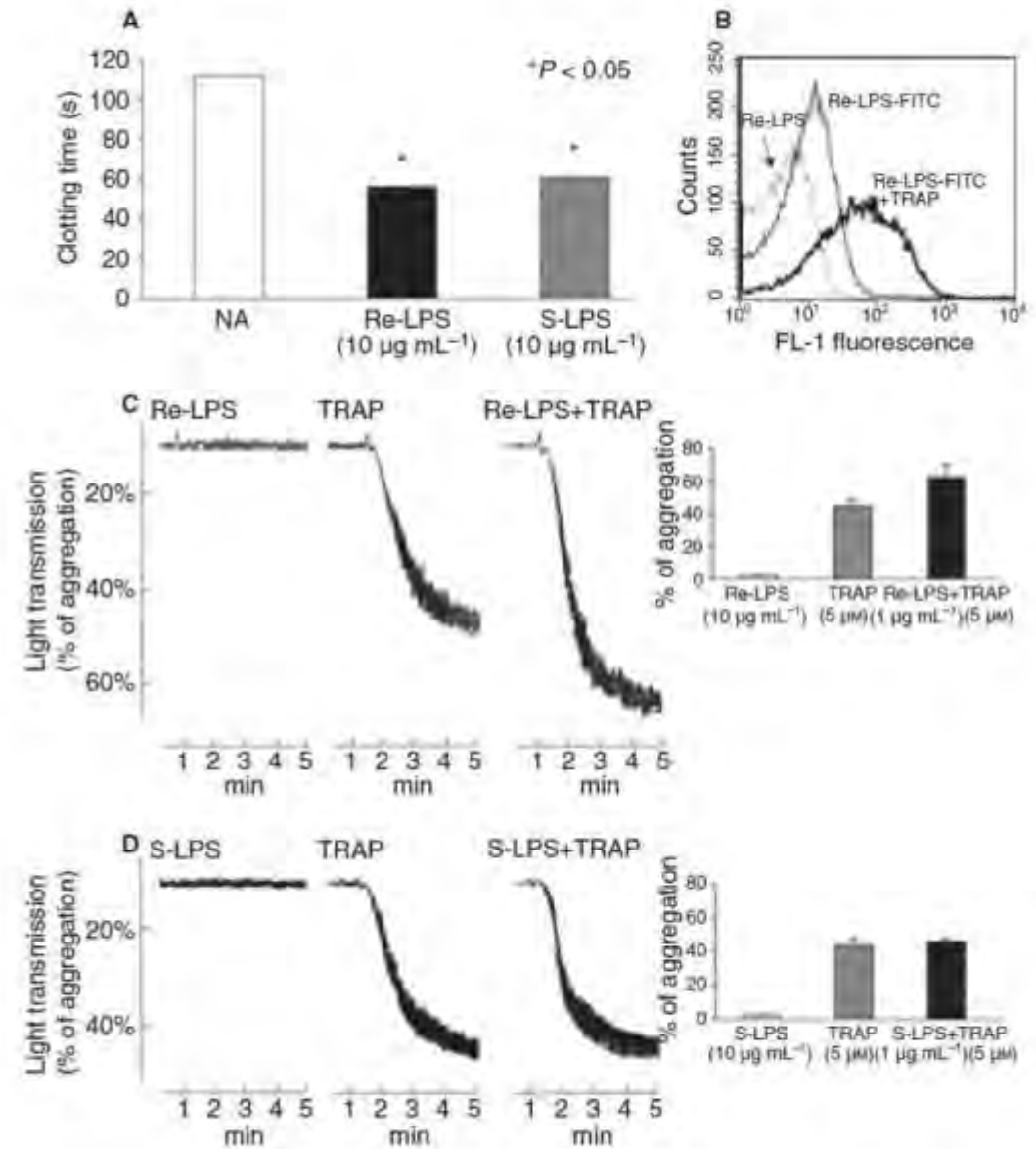
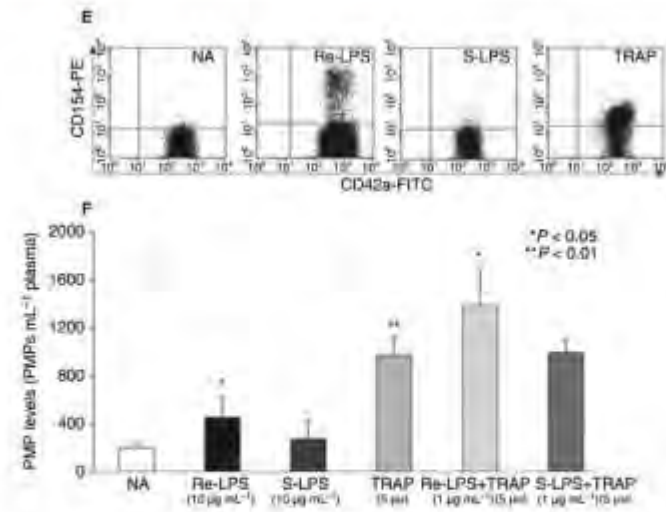


Matus et al.



Matus et al.

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



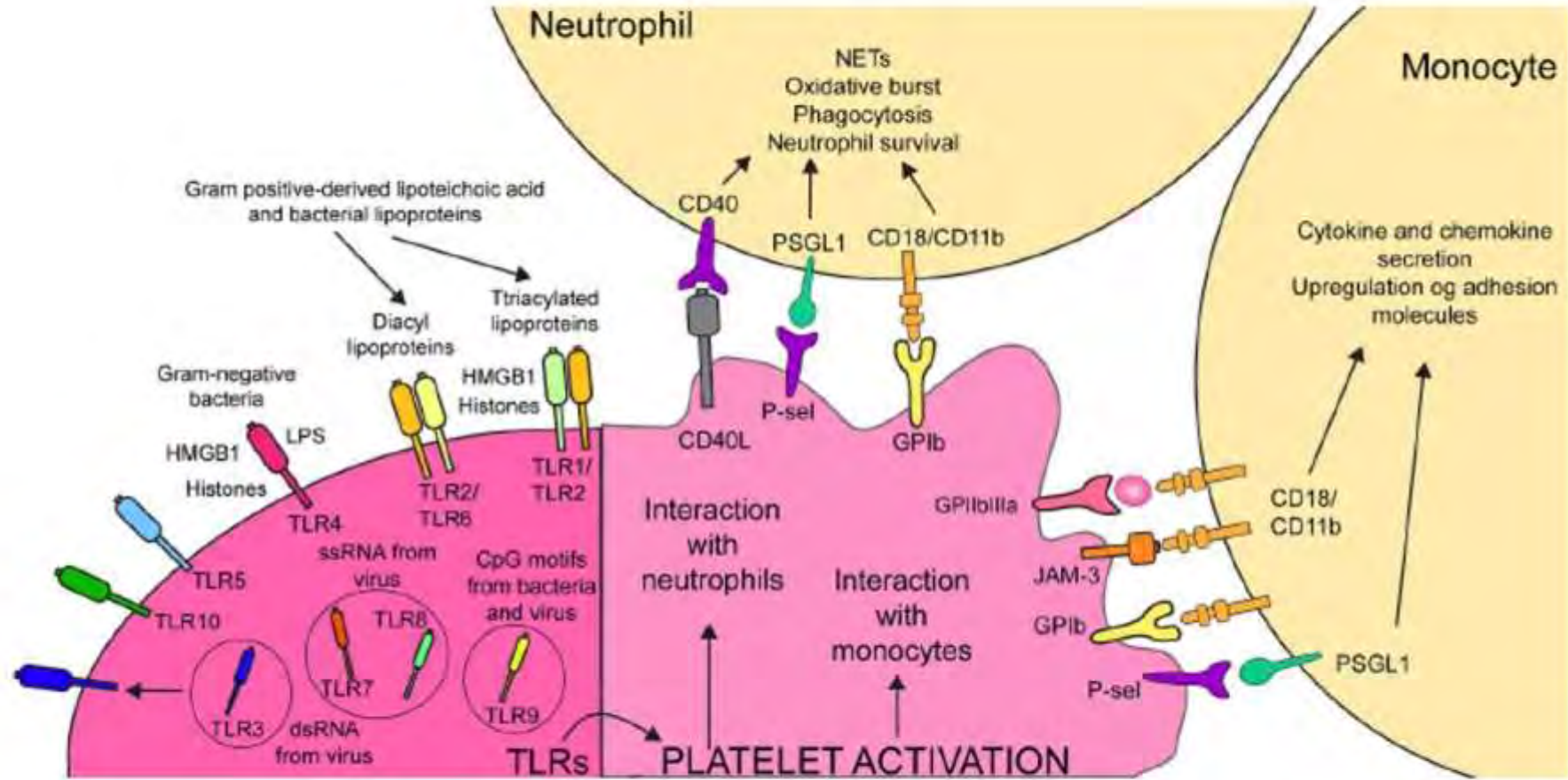
Pattern Recognition Receptor

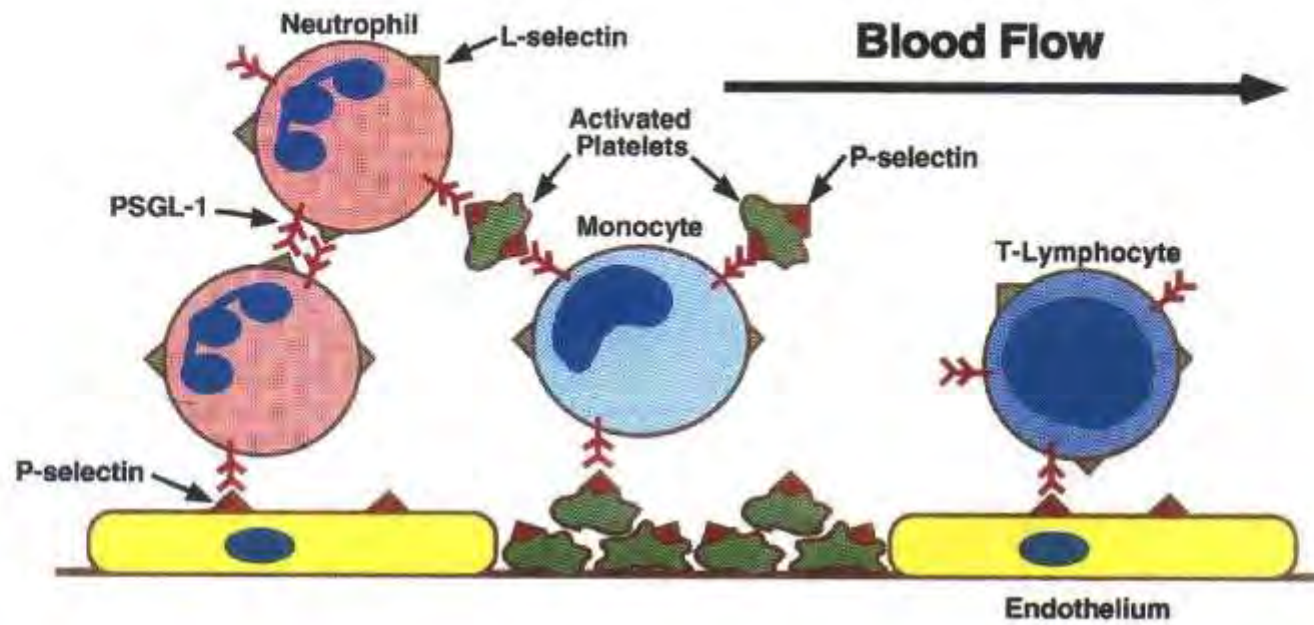


TLR

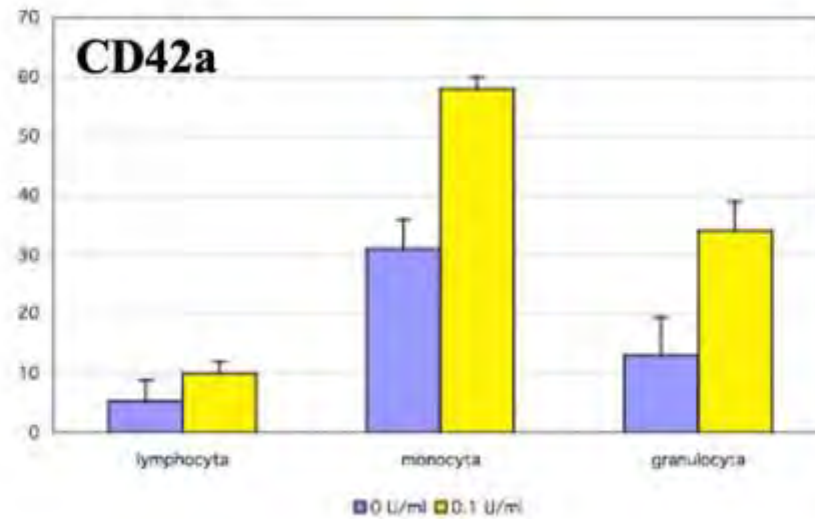
PAMP

DAMP





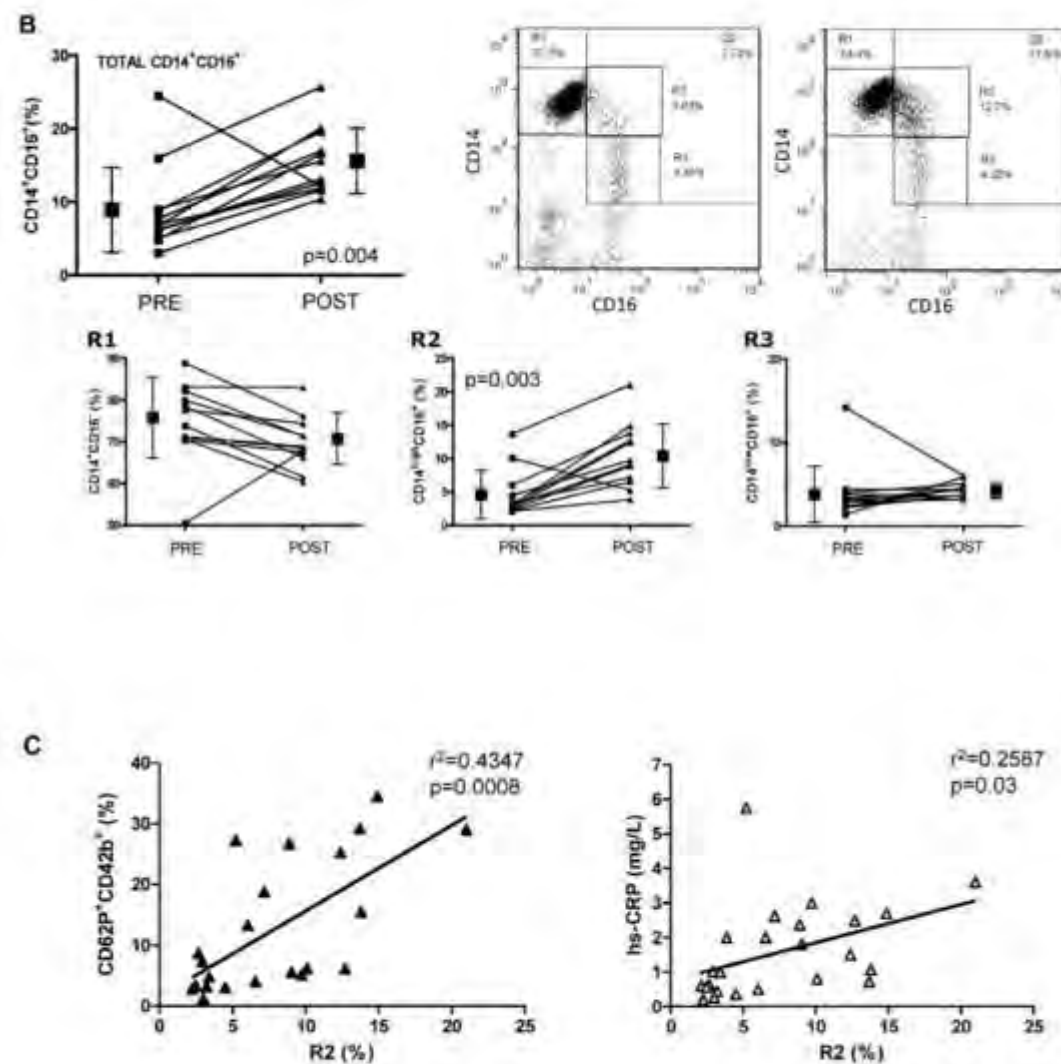
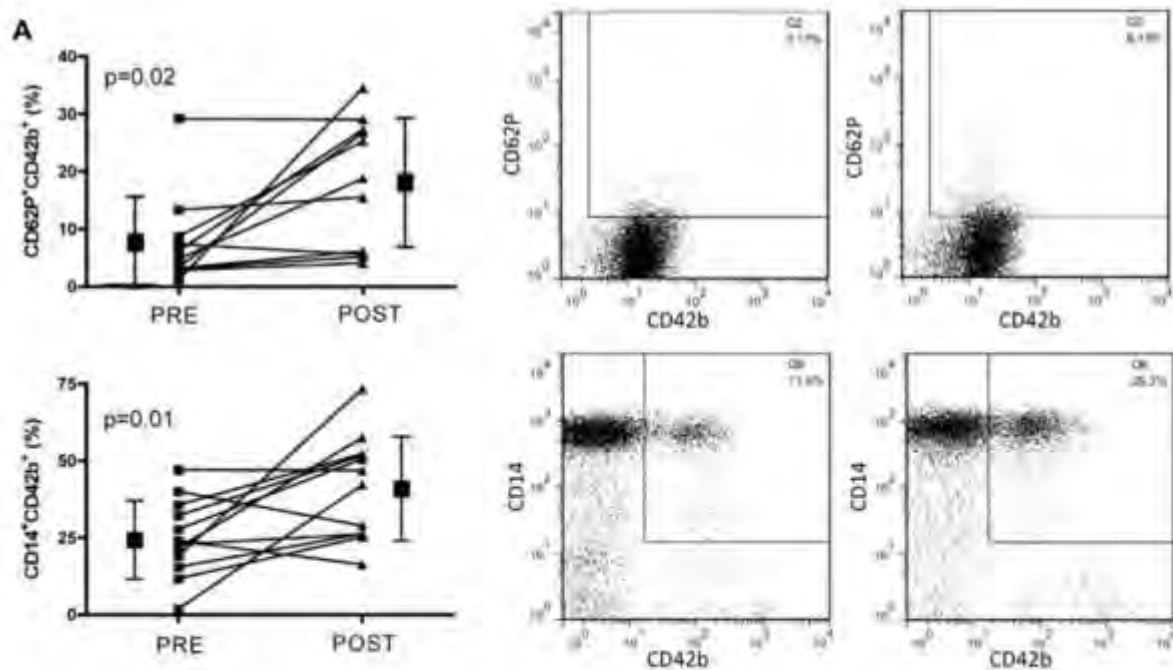
(%)

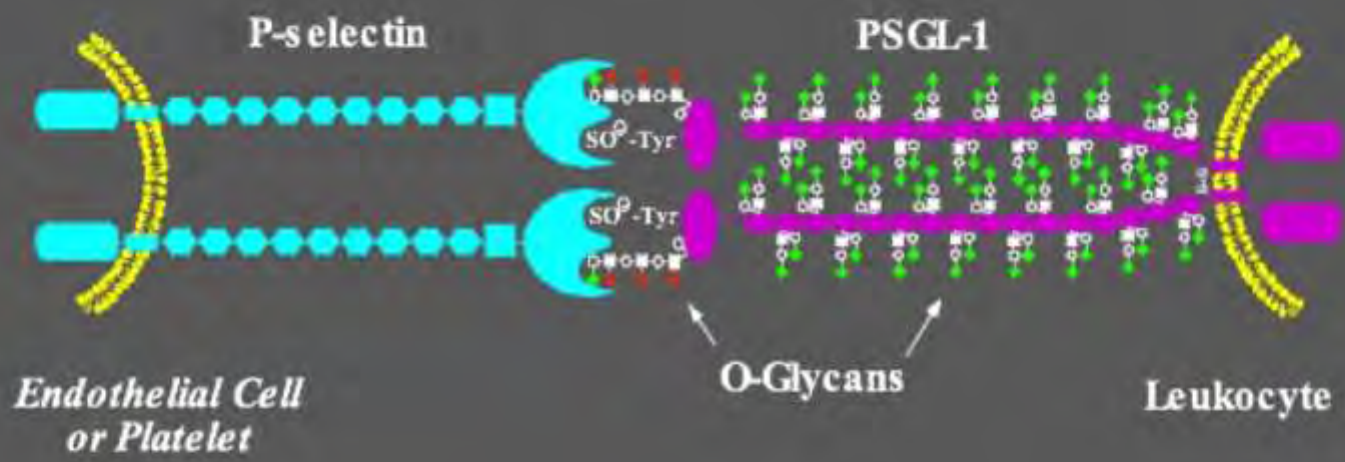


Monocyte-Platelet Interaction Induces a Pro-Inflammatory Phenotype in Circulating Monocytes

Gabriella Passacuale¹, Padman Vamadevan¹, Luis Pereira¹, Colleen Hamid¹, Valerie Corrigan², Albert Ferro^{1*}

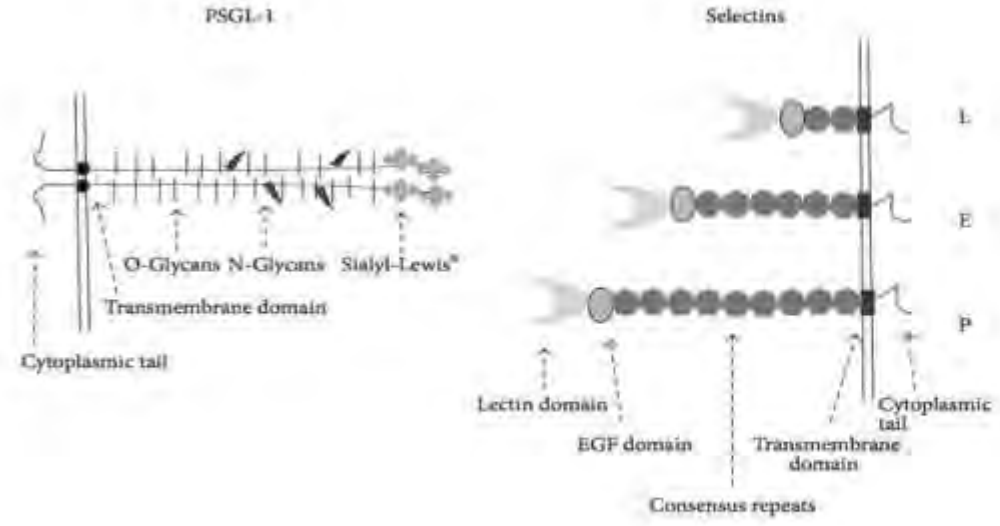
¹Cardiovascular Division, Department of Clinical Pharmacology, King's College London, London, United Kingdom, ²Academic Department of Rheumatology, King's College London, London, United Kingdom





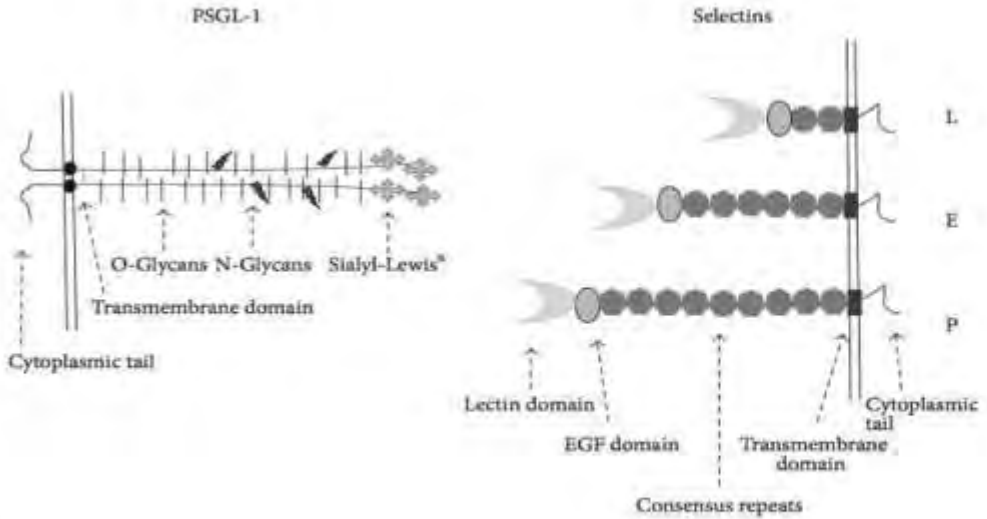
The Interaction of Selectins and PSGL-1 as a Key Component in Thrombus Formation and Cancer Progression

János Kappelmayr and Béla Nagy Jr.



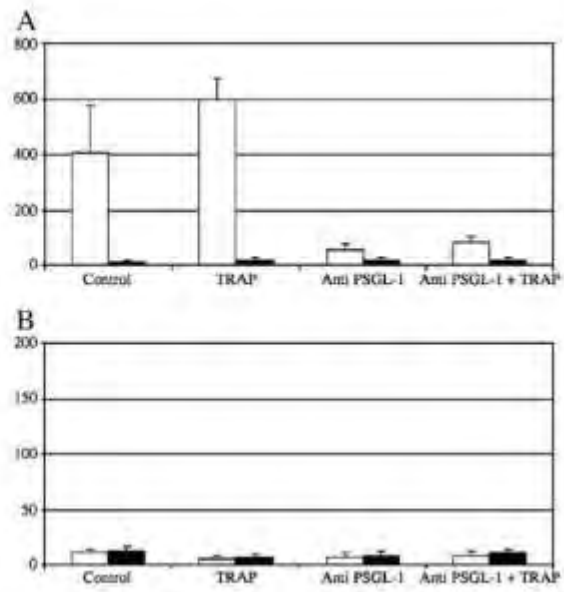
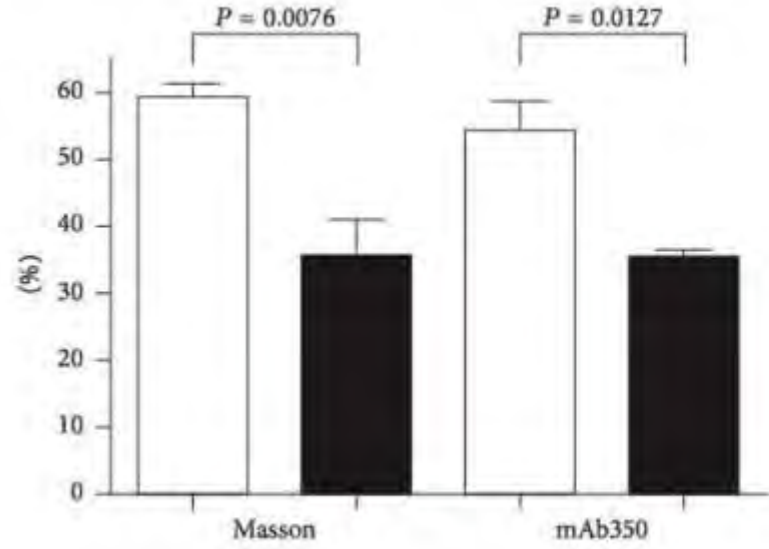
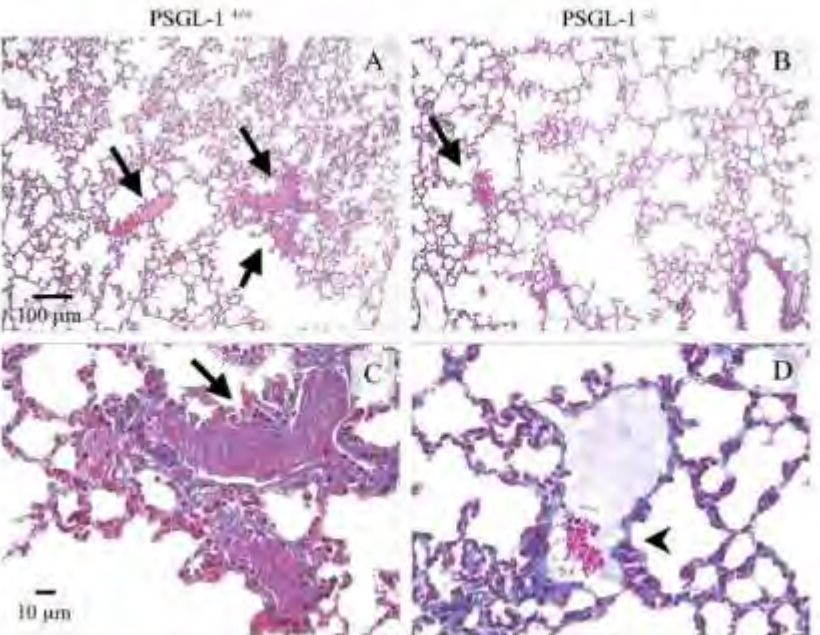
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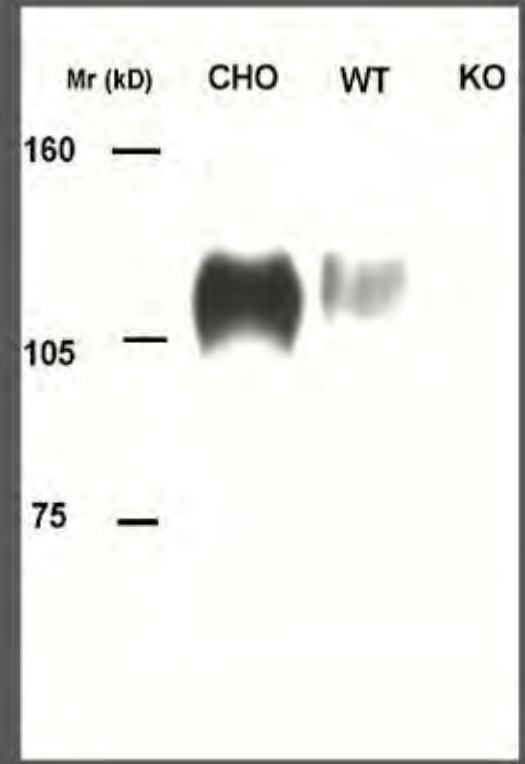
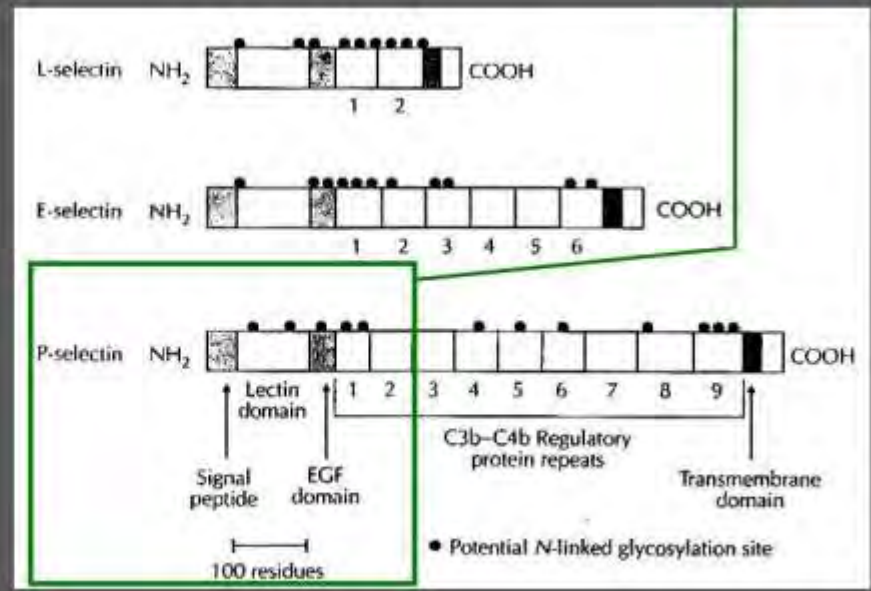


Lack of P-selectin glycoprotein ligand-1 protects mice from thrombosis after collagen/epinephrine challenge

Kornél Miszti-Blasius^a, Ildikó Beke Debreceni^a, Szabolcs Felszeghy^b, Balázs Dezső^c, János Kappelmeier^{a,*}

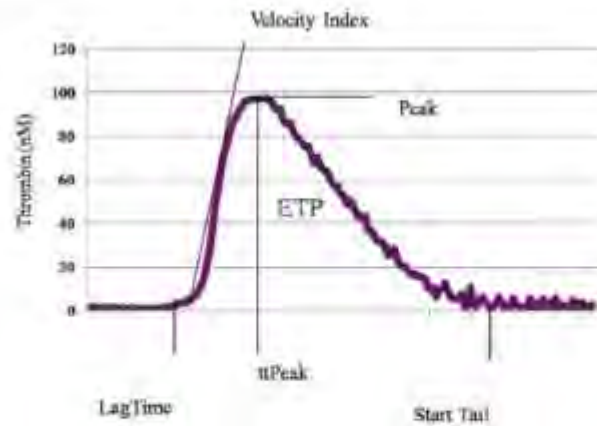


	PSGL-1 +/+	PSGL-1 -/-
Psel-Ig chimera	+	+
Control IgG	+	+
	H + M	M



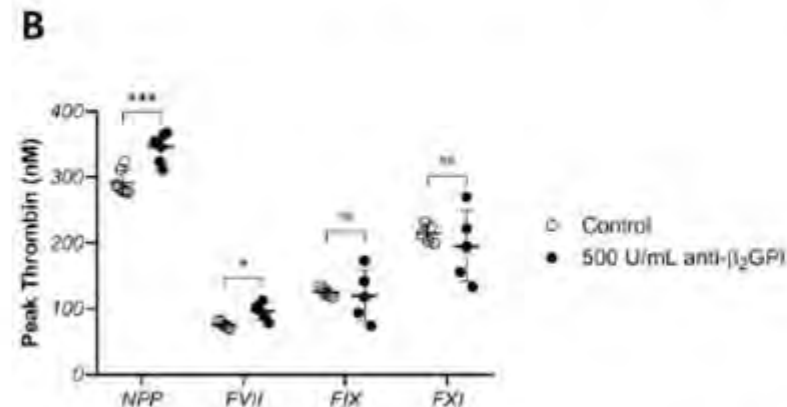
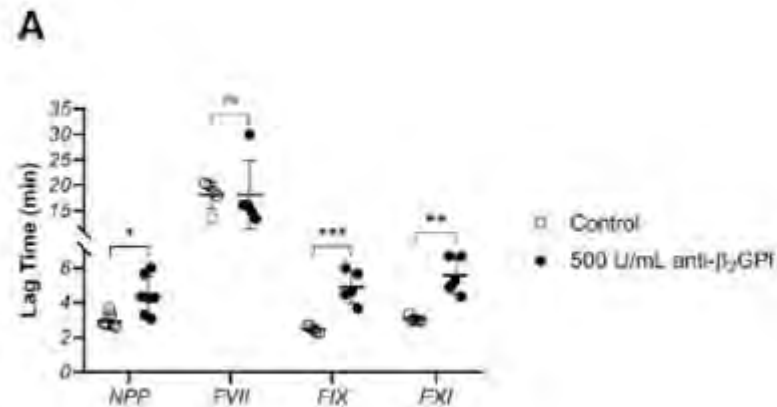
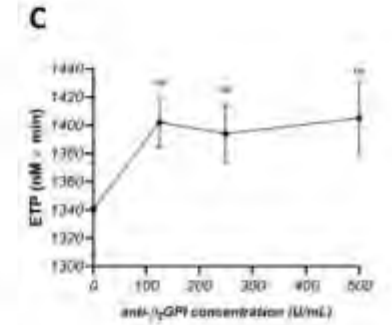
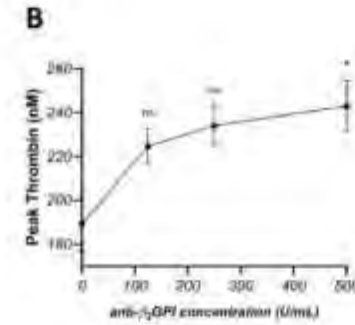
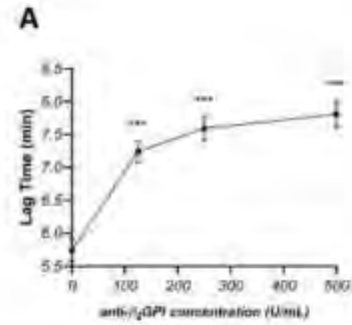
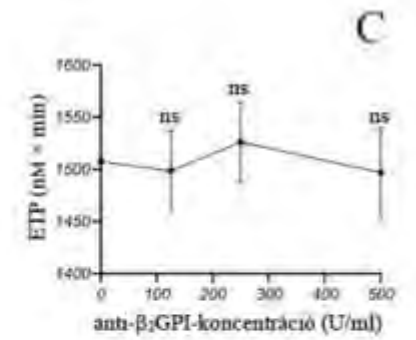
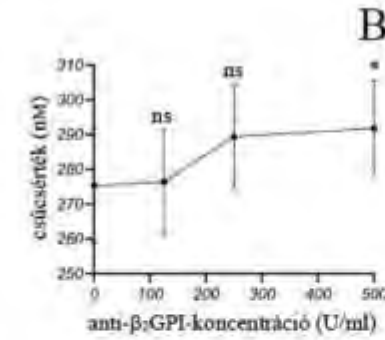
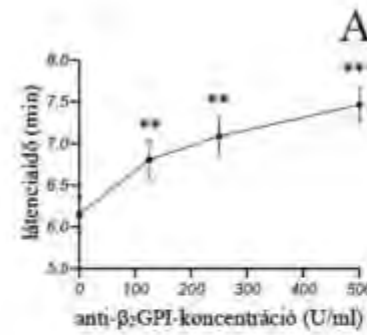
Role of age and PSGL-1 in MP formation

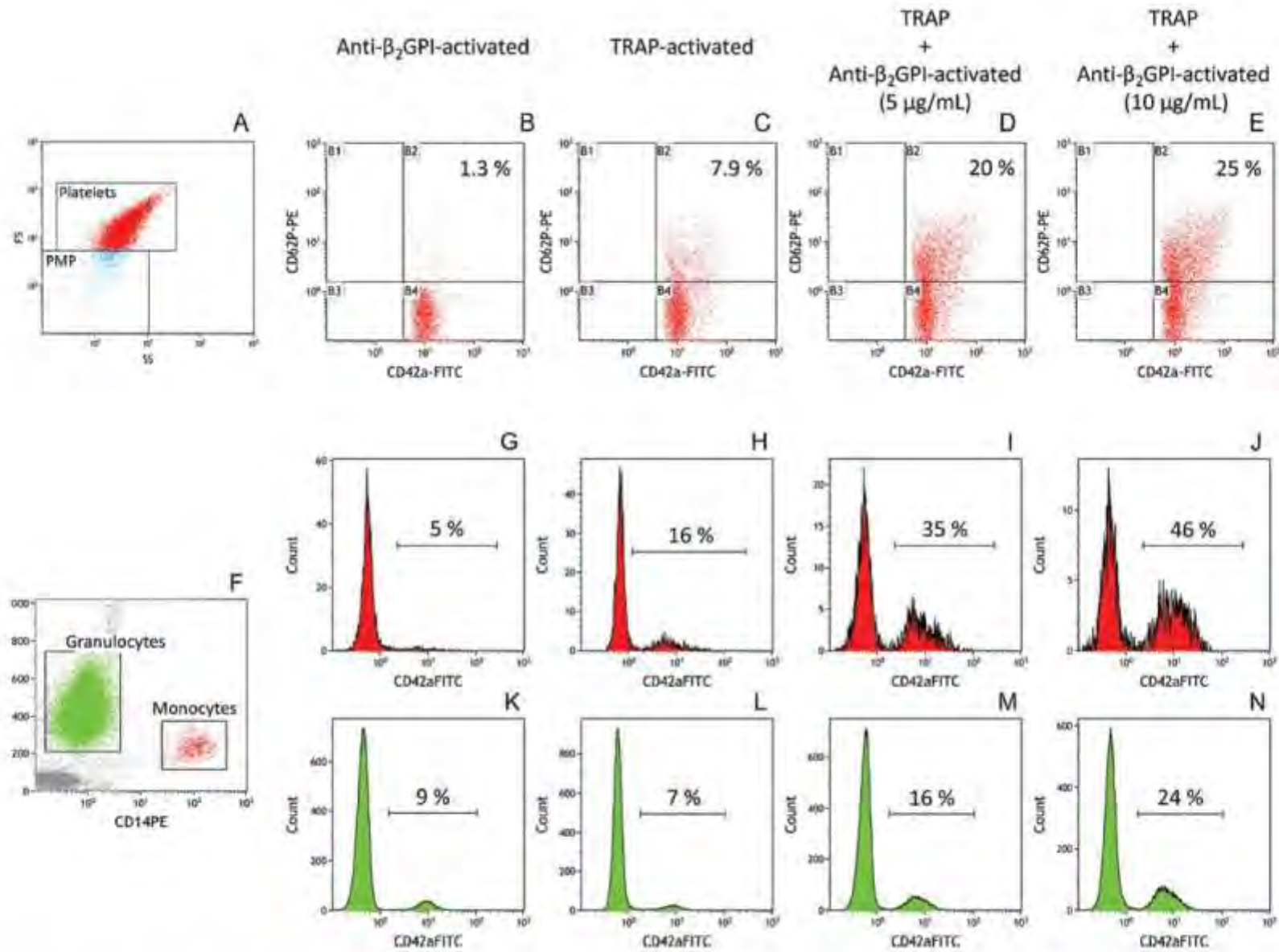
<u>MP number</u>	PSGL-1 +/+	PSGL-1 -/-	p value
9-12 weeks	12 173 ± 2243	14 399 ± 2746	0.54
17-20 weeks	29 404 ± 2941	18 183 ± 1 532	< 0.001
<u>After administration of Psel-Ig</u>			
MP number/ml	833 ± 137	382 ± 101	< 0.03
TF (%)	7.3 ± 1.5	2.9 ± 0.3	< 0.02



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

Gábor Szabó^{1,4}, Ildikó Beke Debreceni¹, Tünde Tarr², Pál Soltész¹, Bjarne Østerud³, János Kappelmaier^{1,2}

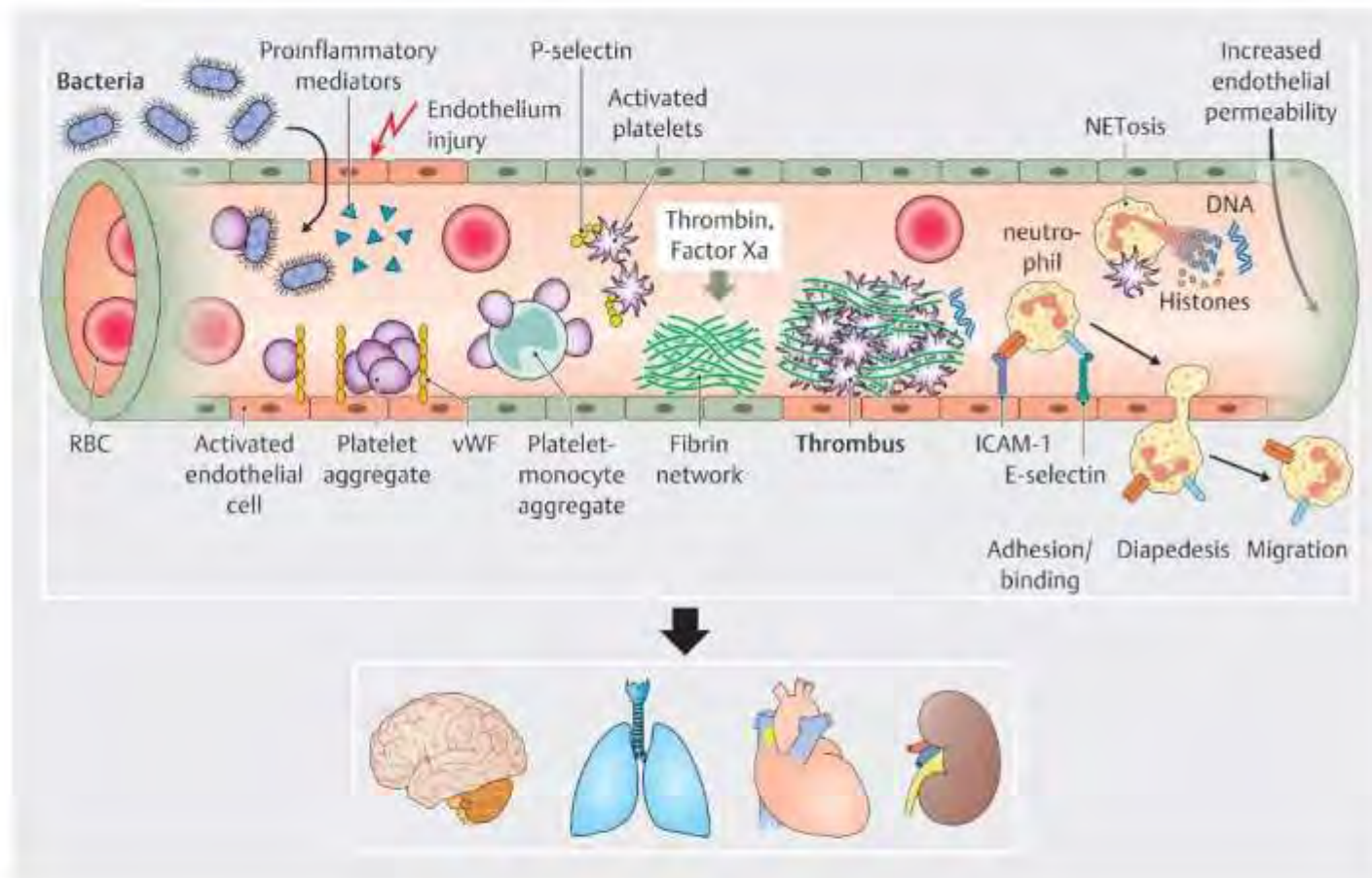




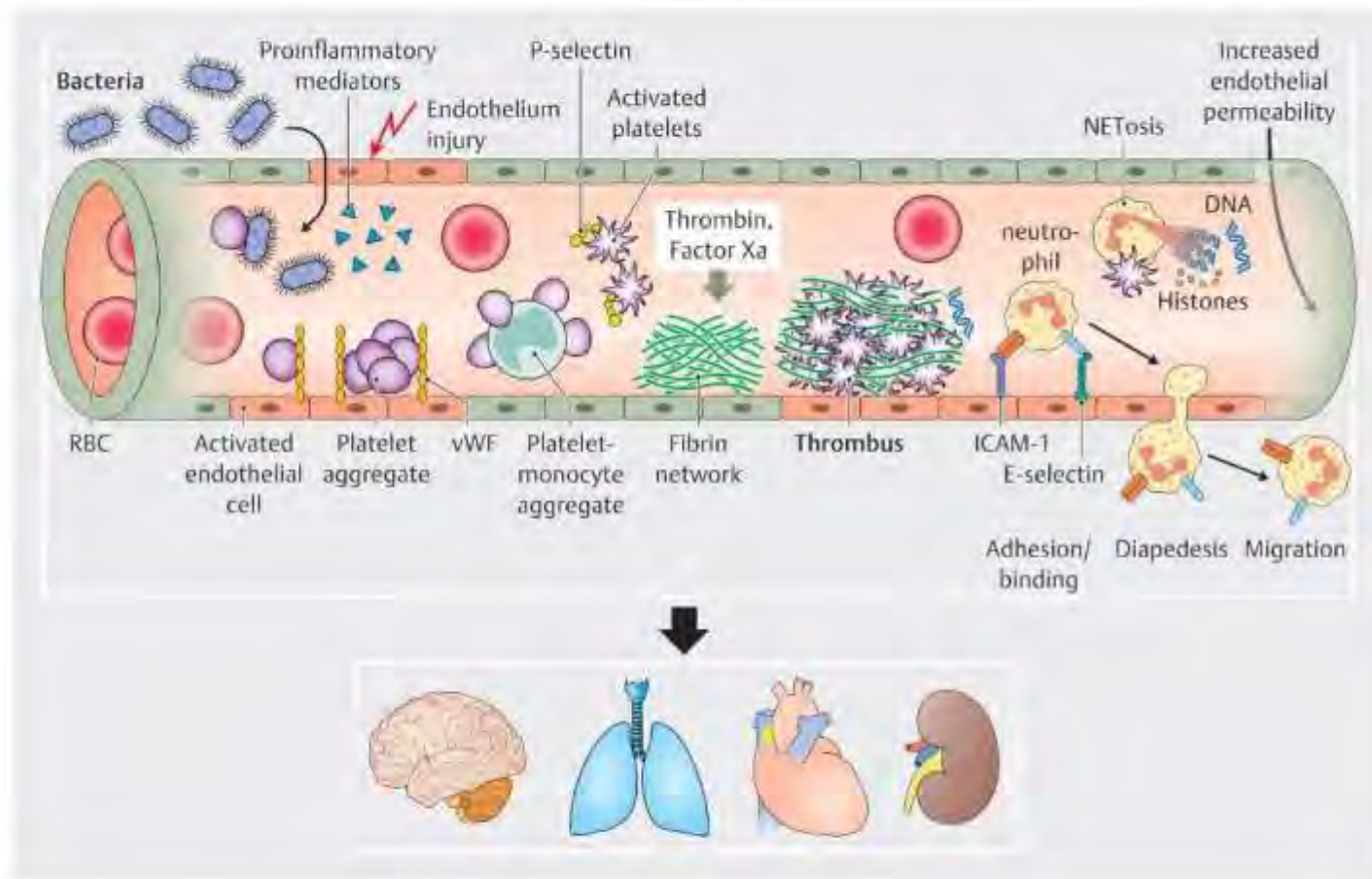
Laboratory Approaches to Test the Function of Antiphospholipid Antibodies.

Szabó G, Antal-Szalmás P, Kerényi A, Péntes K, Bécsi B, Kappelmayer J.

Semin Thromb Hemost. 2022 Mar;48(2):132-144.



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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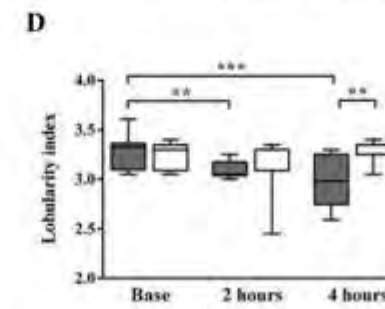
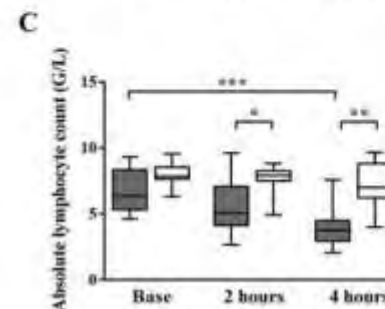
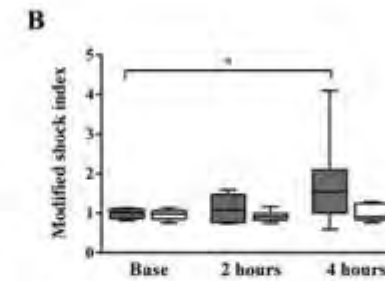
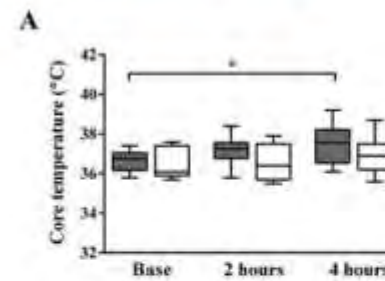
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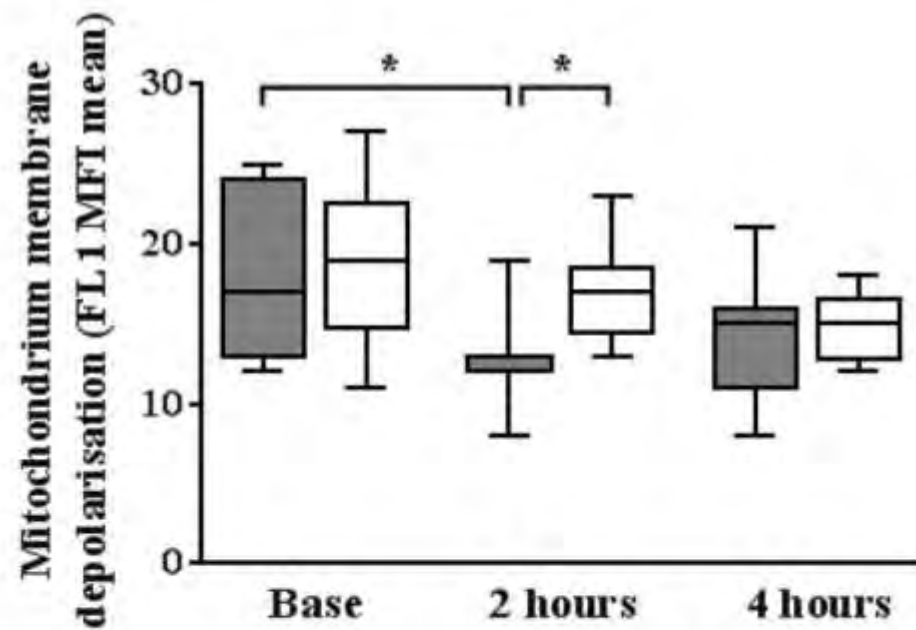
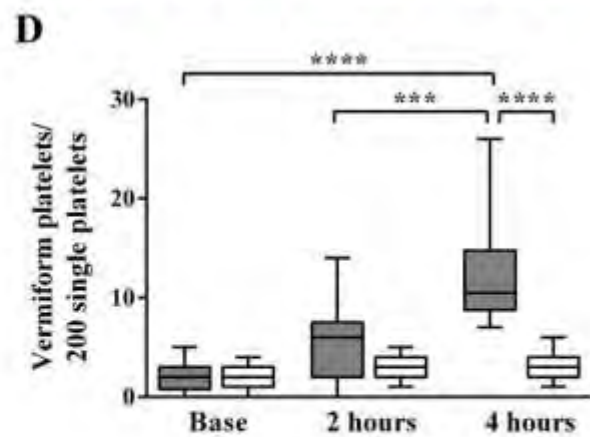
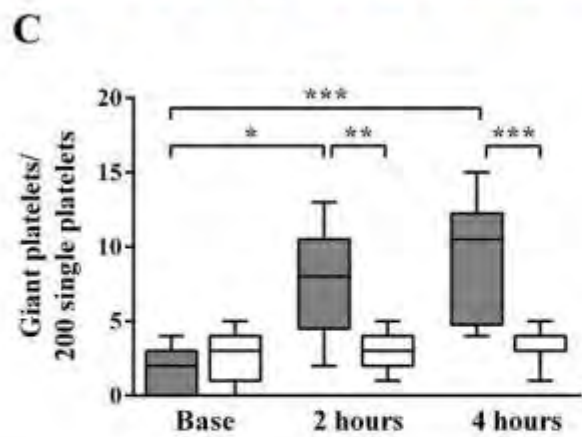
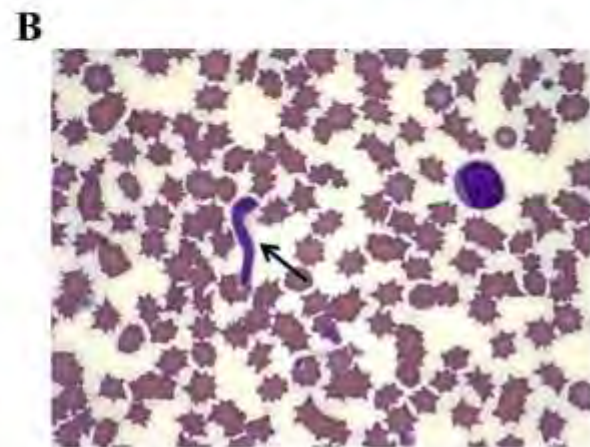
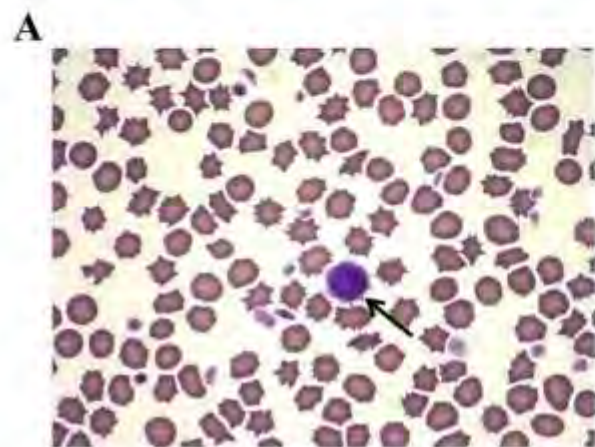
PPP:

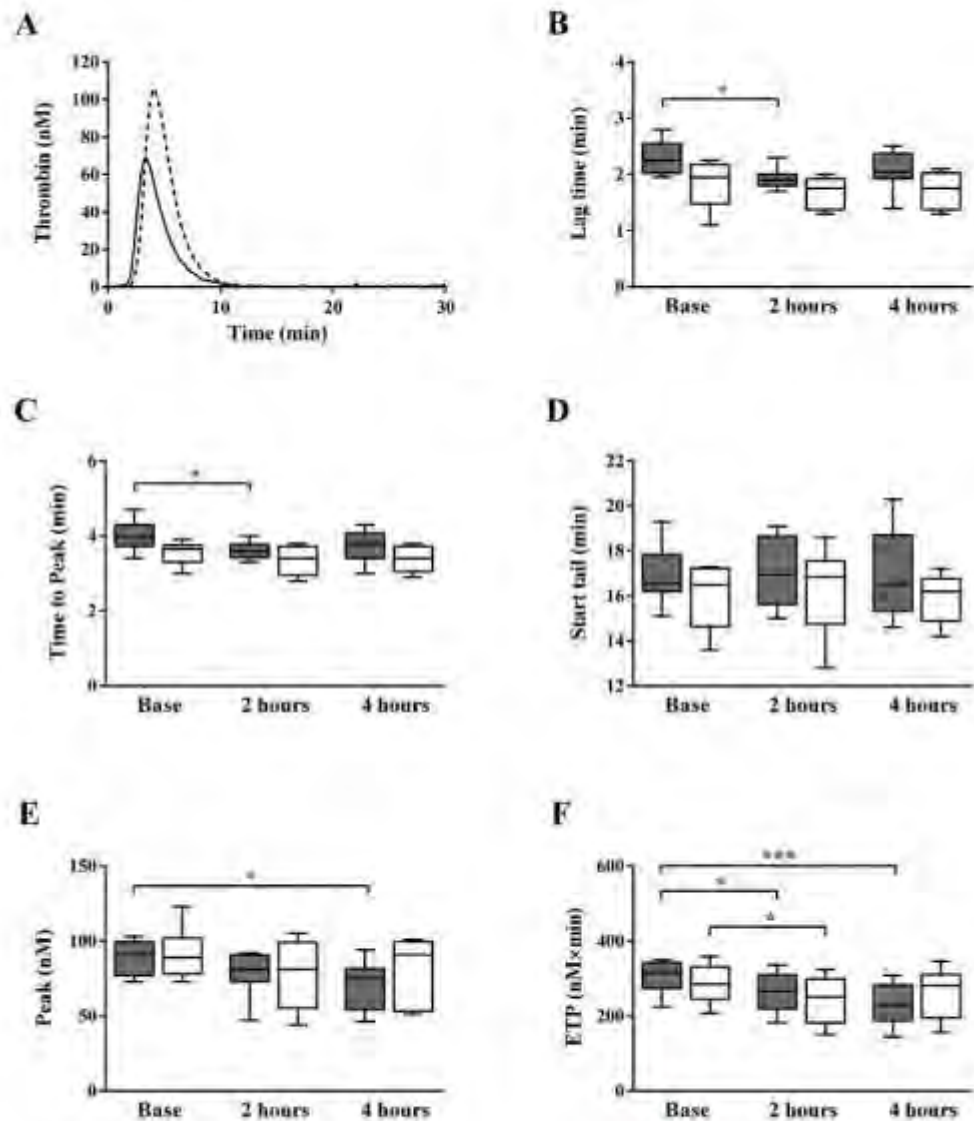
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In vitro experiments

Effect of the plasma samples on washed human RBCs



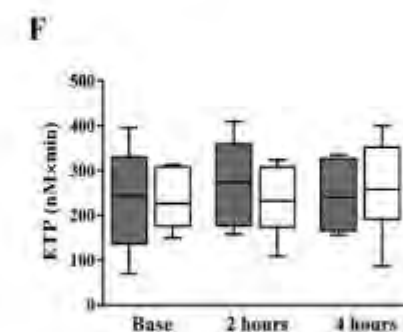
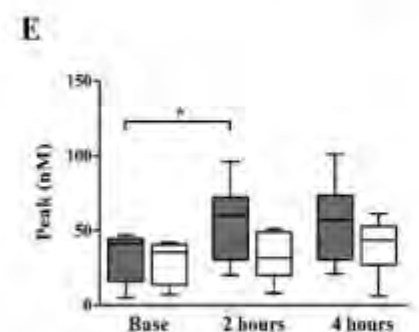
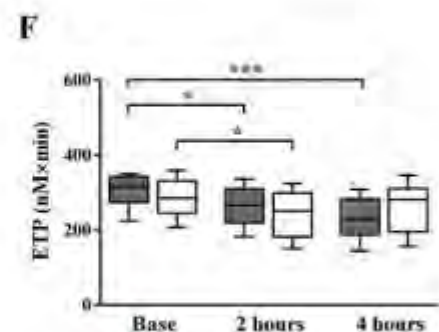
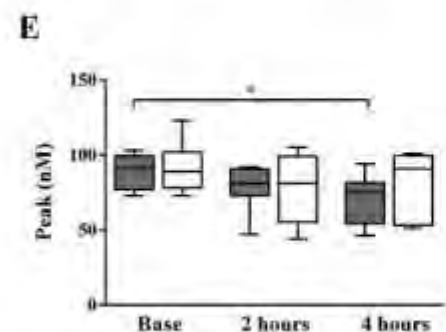
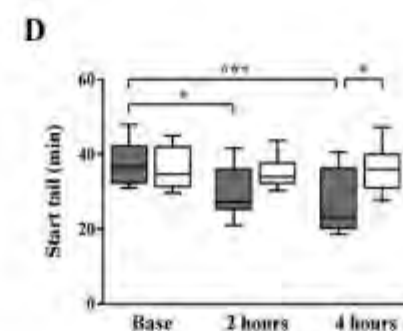
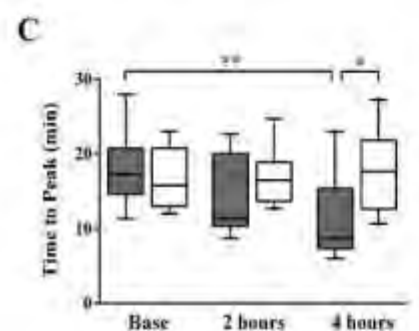
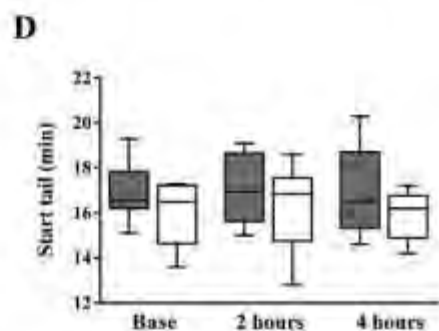
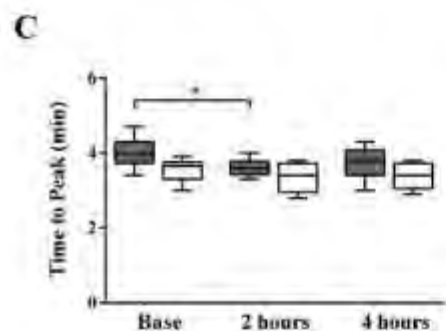
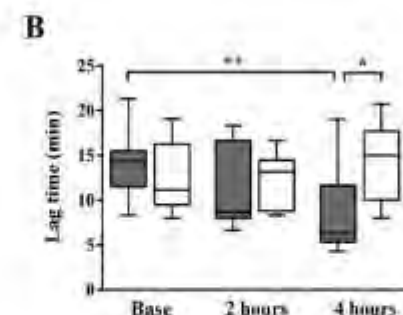
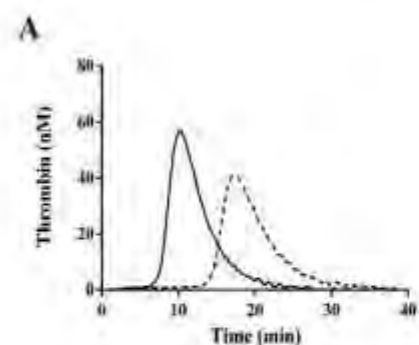
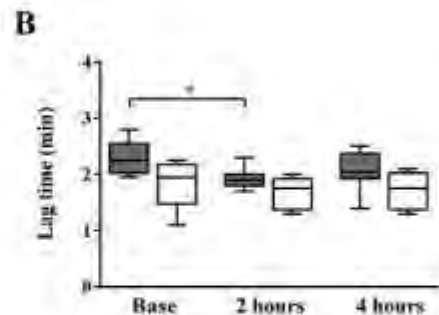
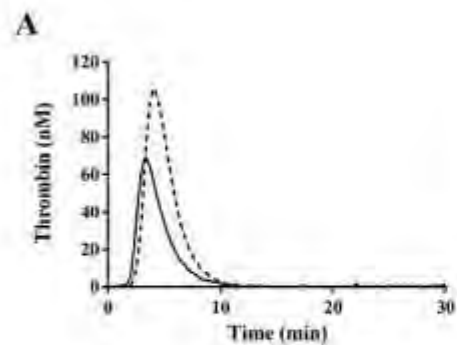




Characteristics of thrombin generation in a fulminant porcine sepsis model

Judit Tóth¹, József Beke Debreceeni², Ádám Desár³, Katalin Peró⁴, Mária Berné⁵, Endre Hajló⁶, Judit Szabó⁶, Norbert Márton⁶, Béla Püspöki⁷, János Koppelmayer^{8*}





Characteristics of thrombin generation in a fulminant porcine sepsis model

Judit Tóth¹, Ildikó Beke Debrecei², Ádám Desák³, Katalin Peró⁴, Marianna Berbécs⁵, Endre Hajló⁶, Judit Szabó⁶, Norbert Németó⁶, Béla Püspöki⁷, János Koppelmayer^{8*}



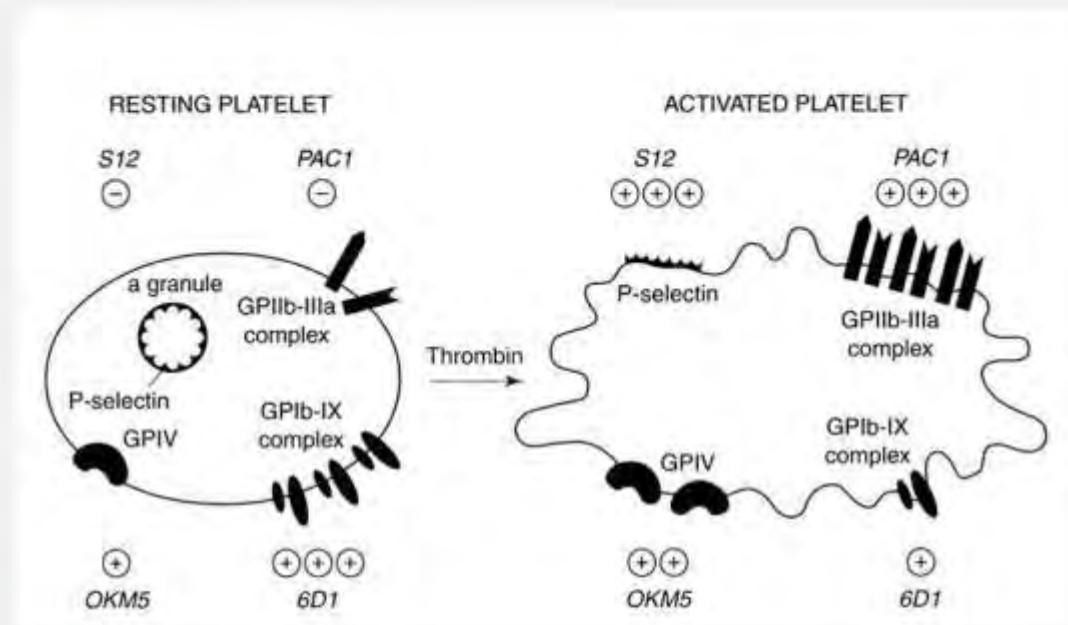
A thrombocyták aktiváltsági állapotának jellemzői (Platelet Activation Status=PAS)

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)

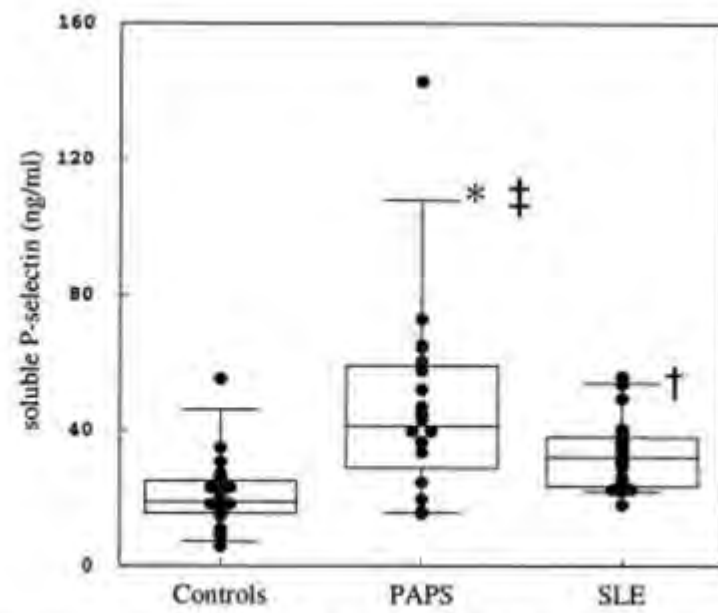
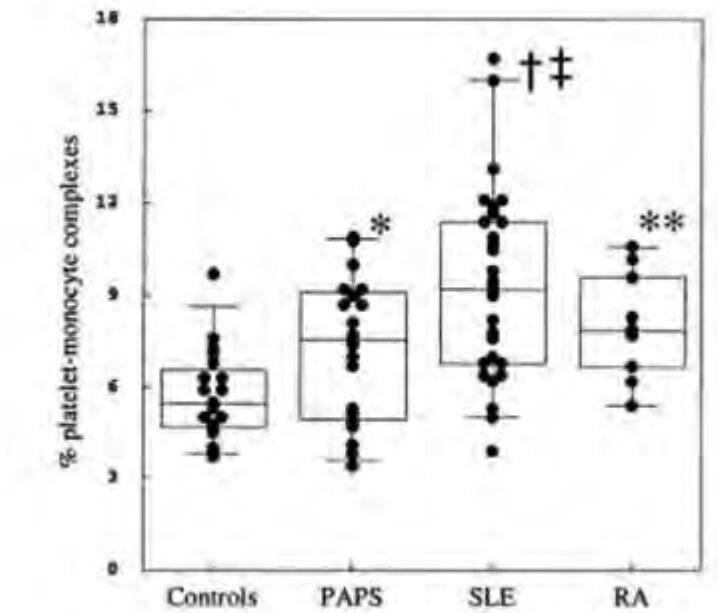
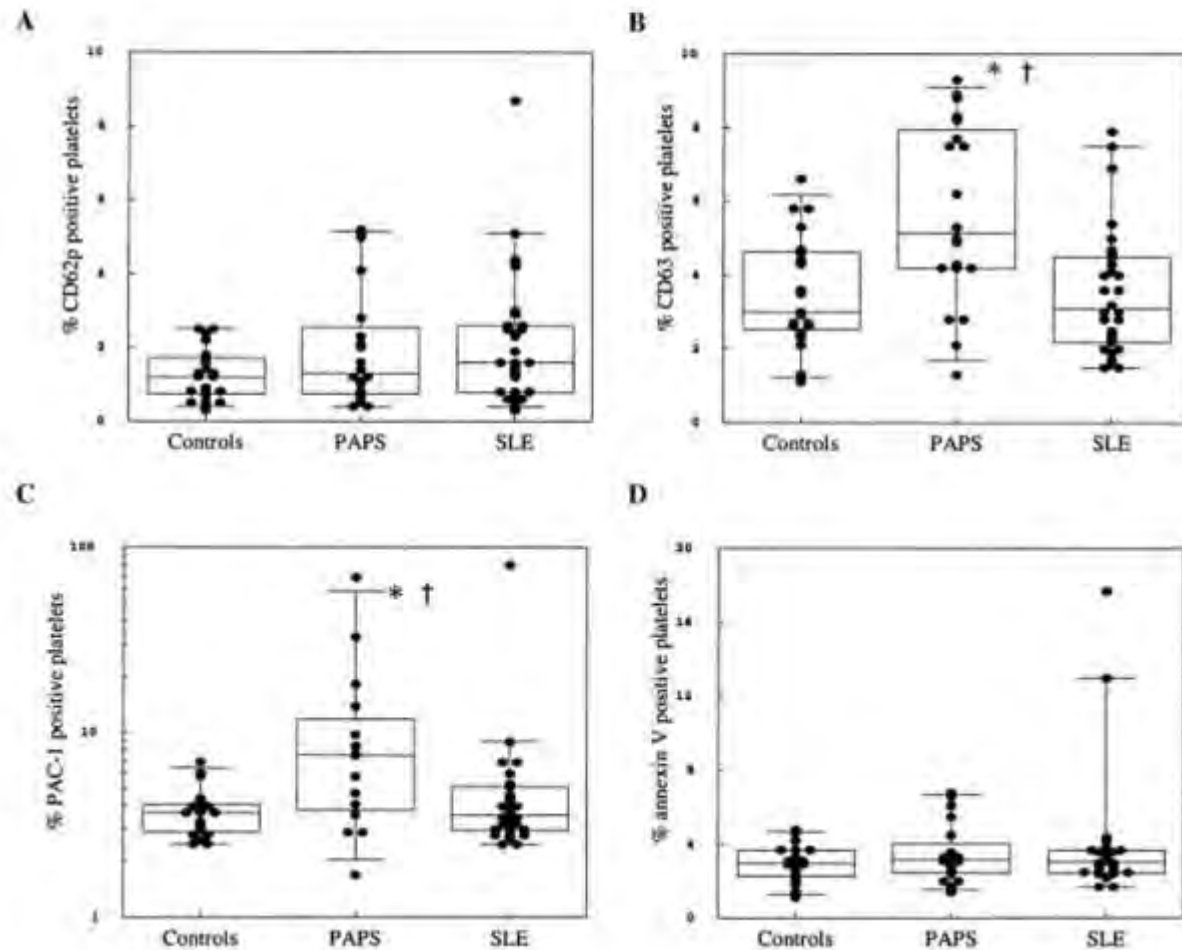
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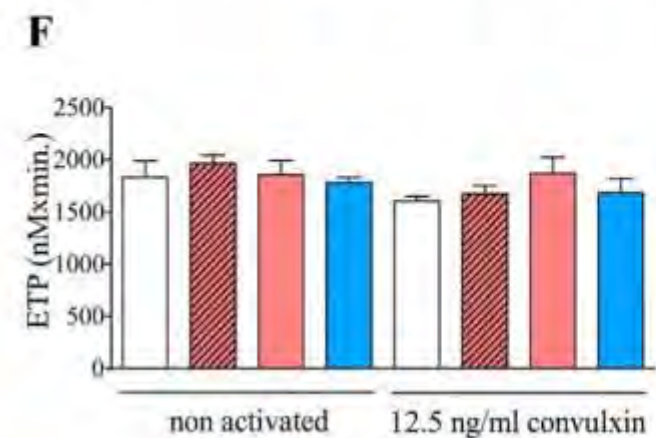
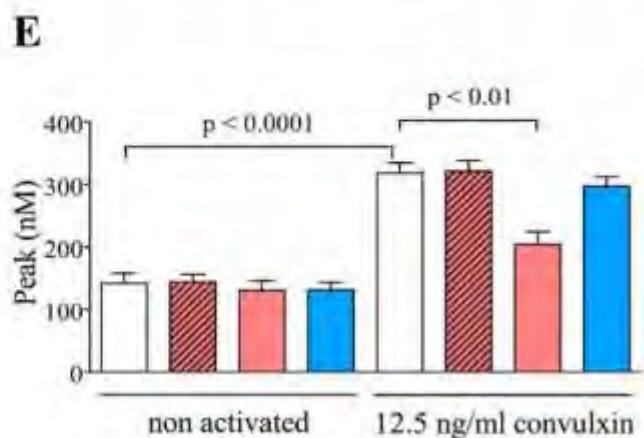
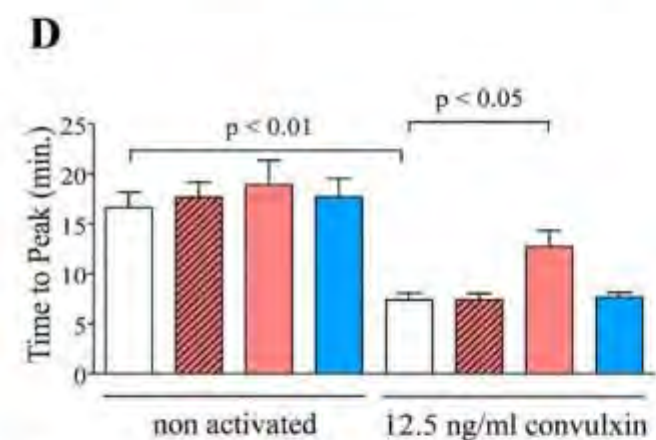
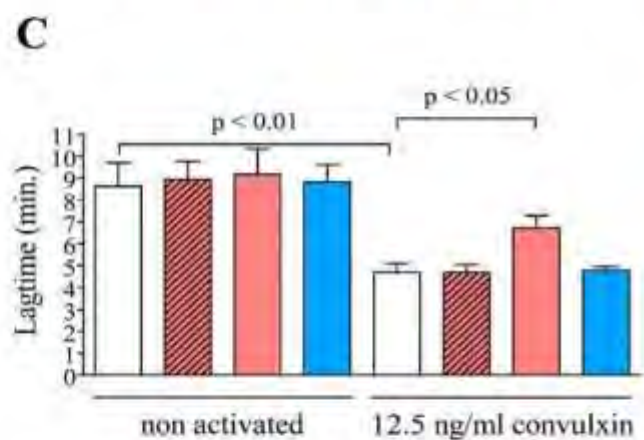
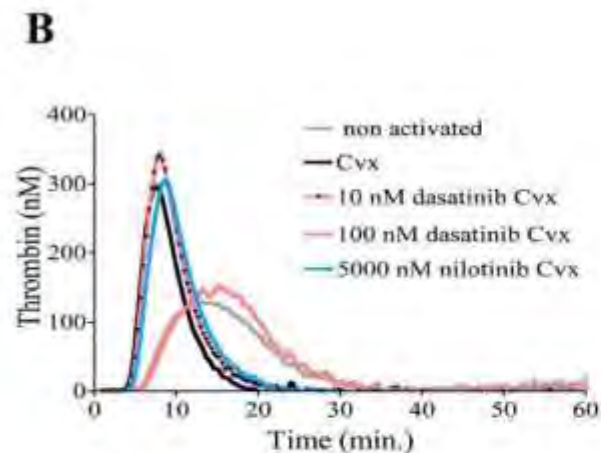
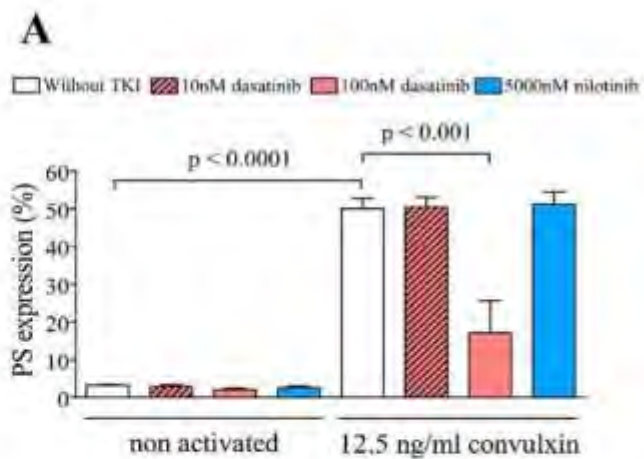
- a thrombocytá-leukocytá heterotipikus aggregátumok mennyiségének változása
- monocytá szöveti faktor (TF) expresszió vizsgálata

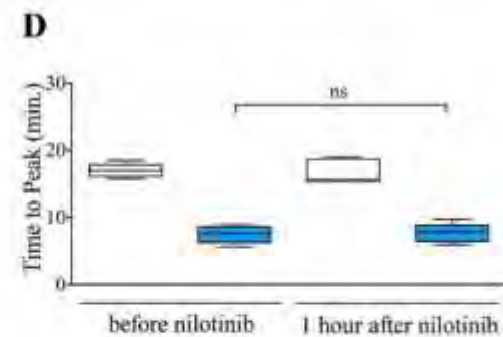
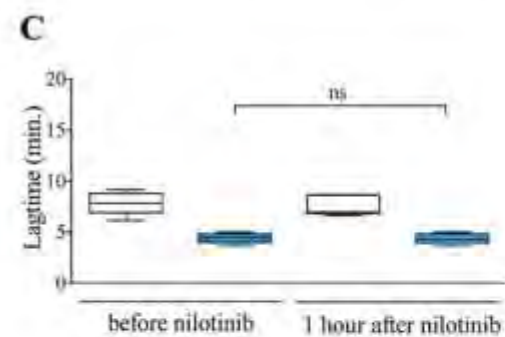
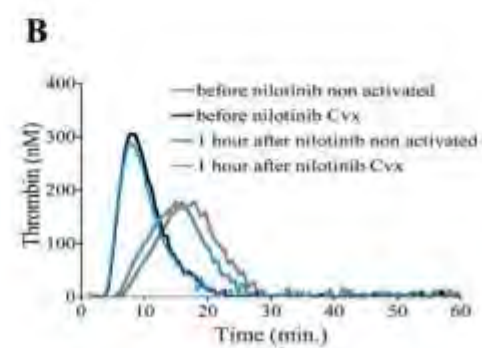
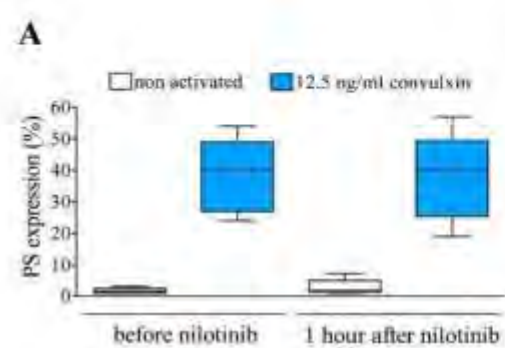
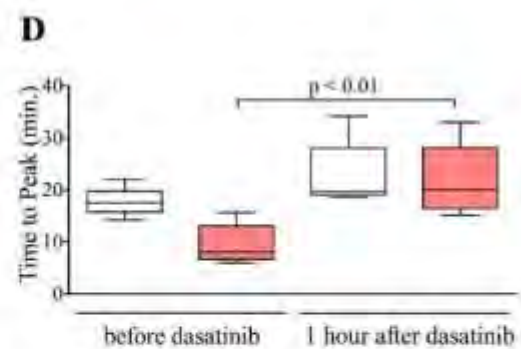
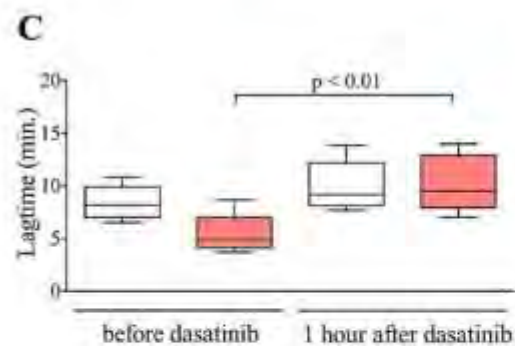
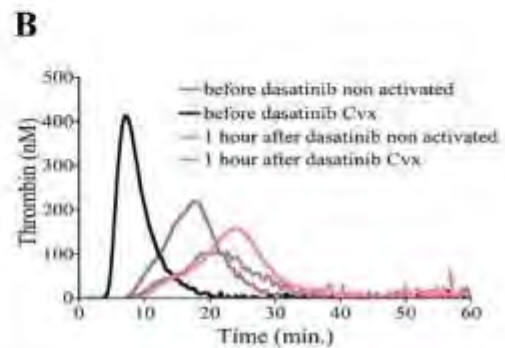
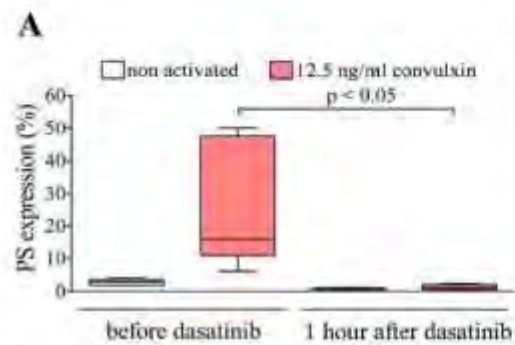


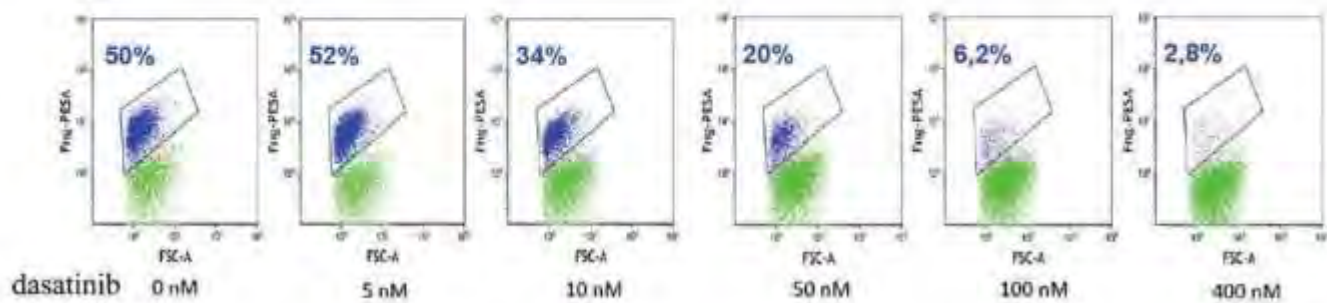
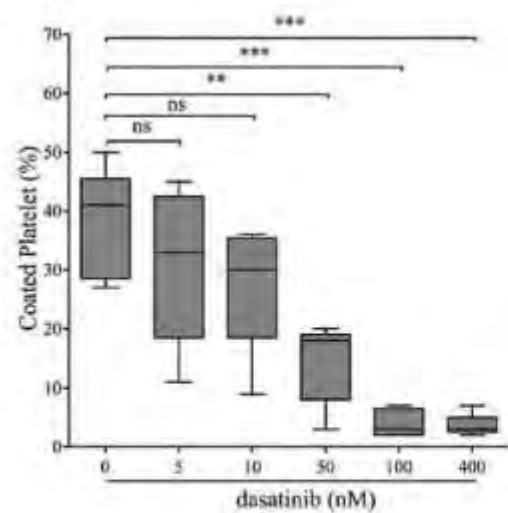
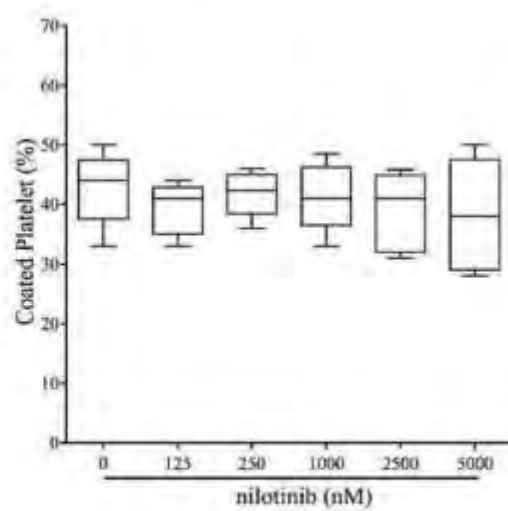
Increased circulating platelet–leucocyte complexes and platelet activation in patients with antiphospholipid syndrome, systemic lupus erythematosus and rheumatoid arthritis

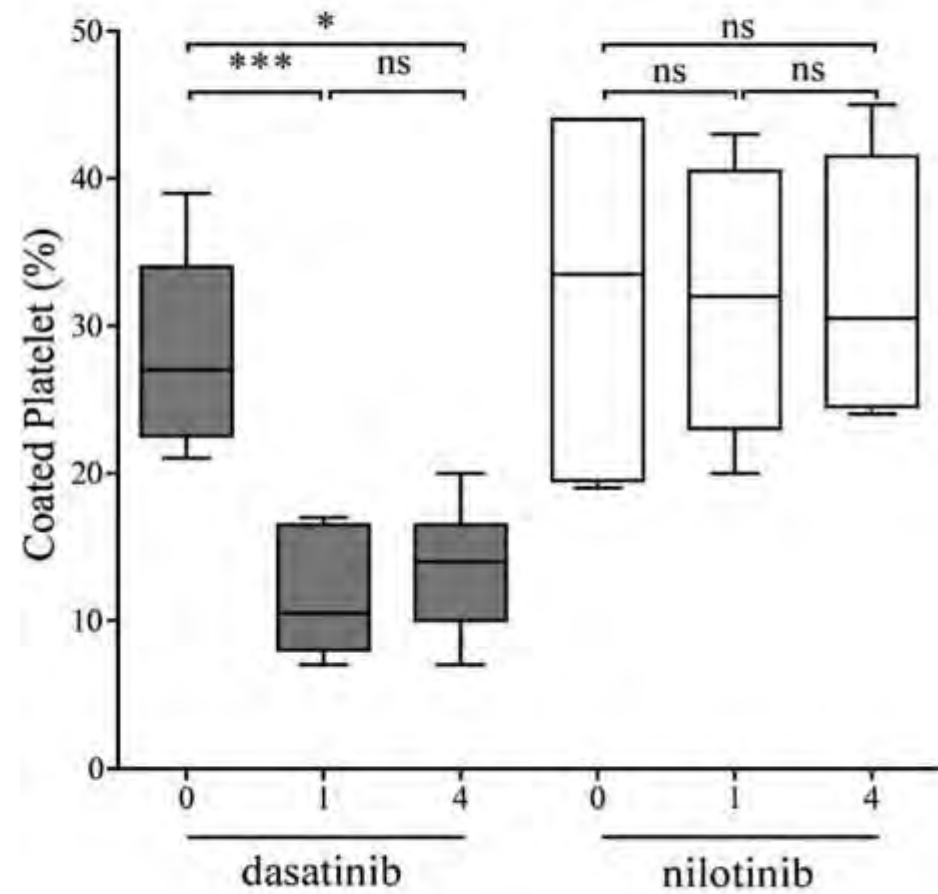
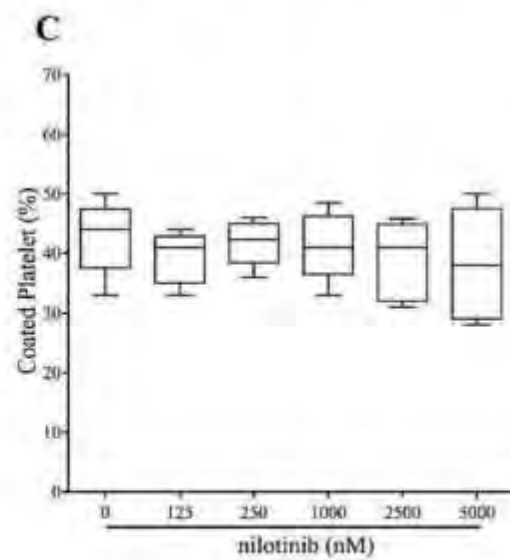
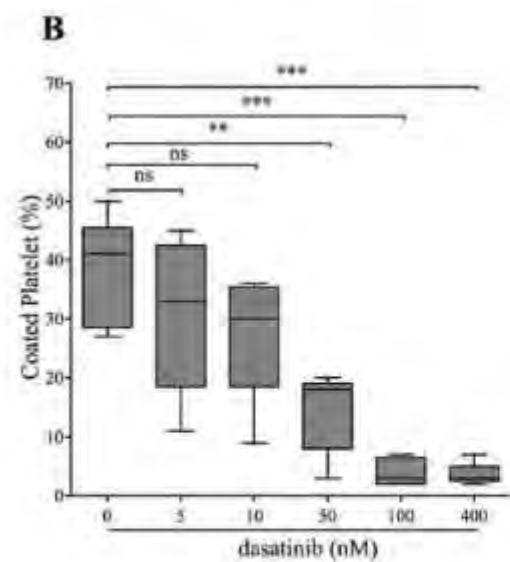
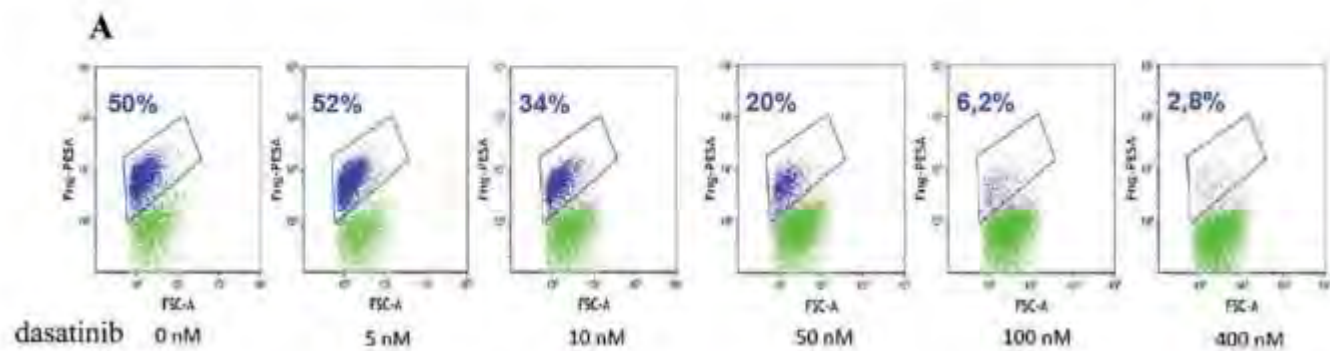
JOANNE E. JOSEPH,¹ PAUL HARRISON,¹ IAN J. MACKIE,¹ DAVID A. ISENBERG² AND SAMUEL J. MACHIN¹ ¹*Haemostasis Research Unit and* ²*Centre for Rheumatology, Department of Medicine, University College London, UK*



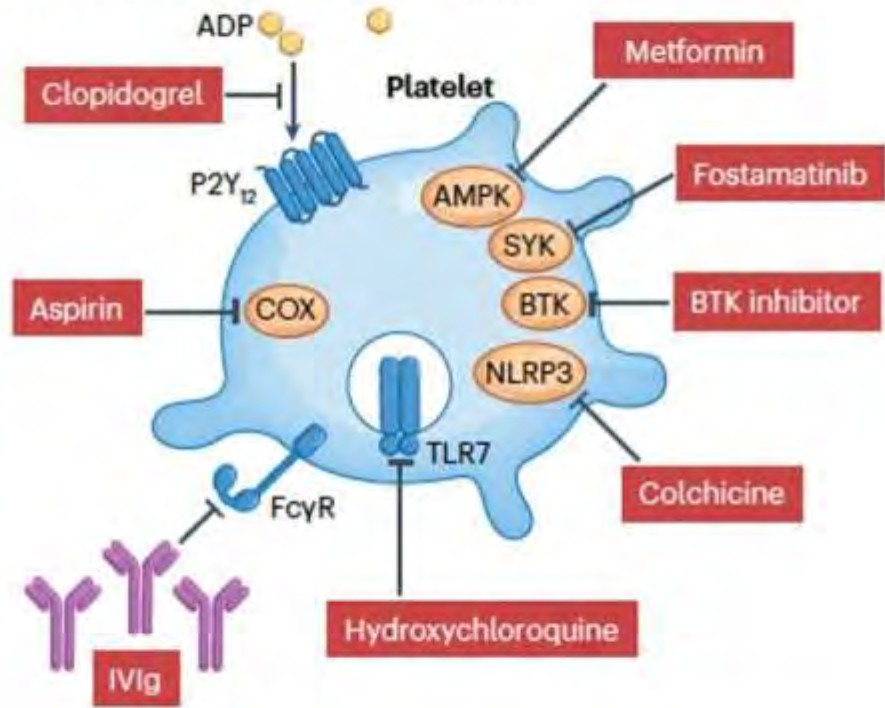




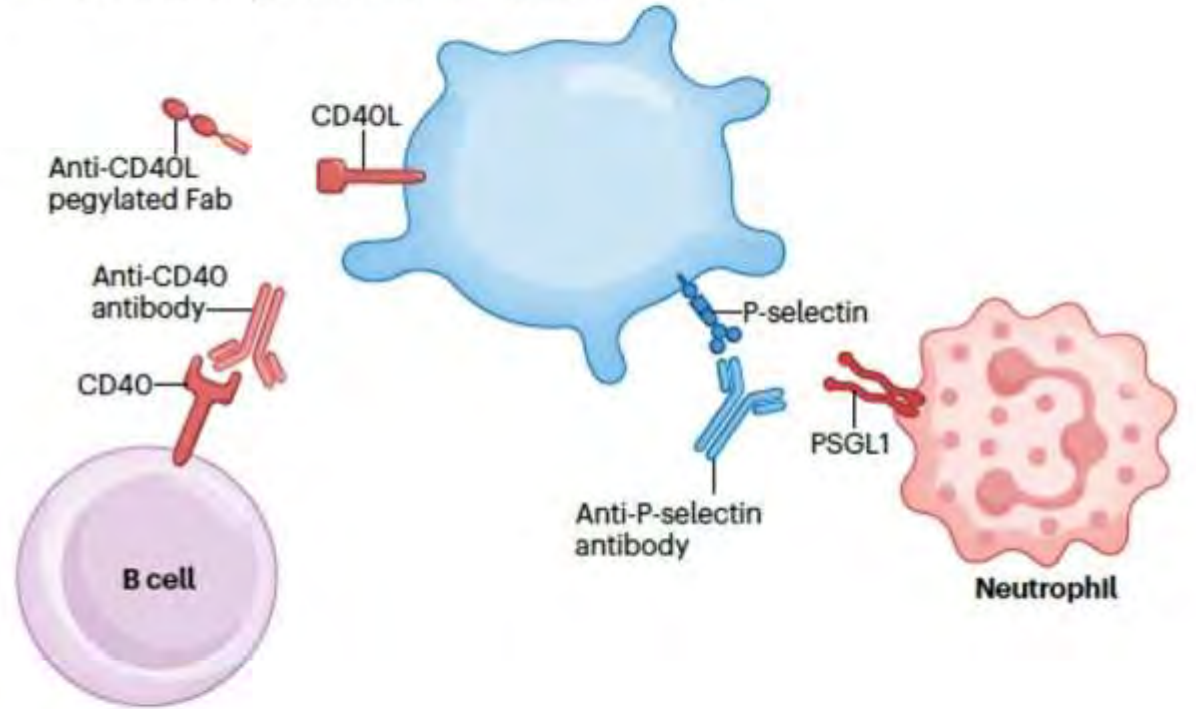
A**B****C**



a Inhibition of platelet activation



b Inhibition of platelet-immune cell interaction



The role of platelets in immune-mediated inflammatory diseases

Marc Scherlinger^{1,2,3}, Christophe Riches^{1,4}, George C. Tsokos⁵, Eric Boitard^{6,7} & Patrick Bianco⁸

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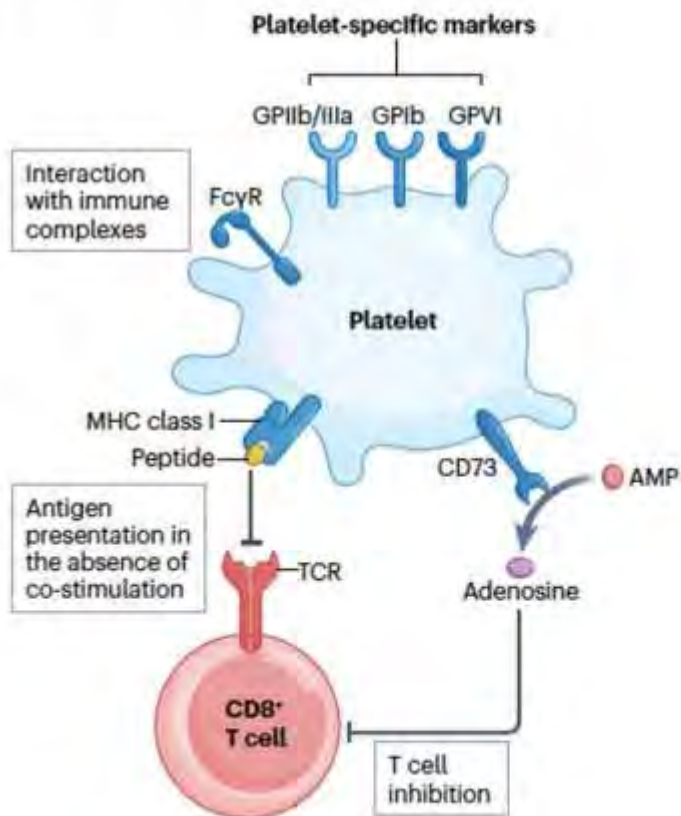
a Resting platelets



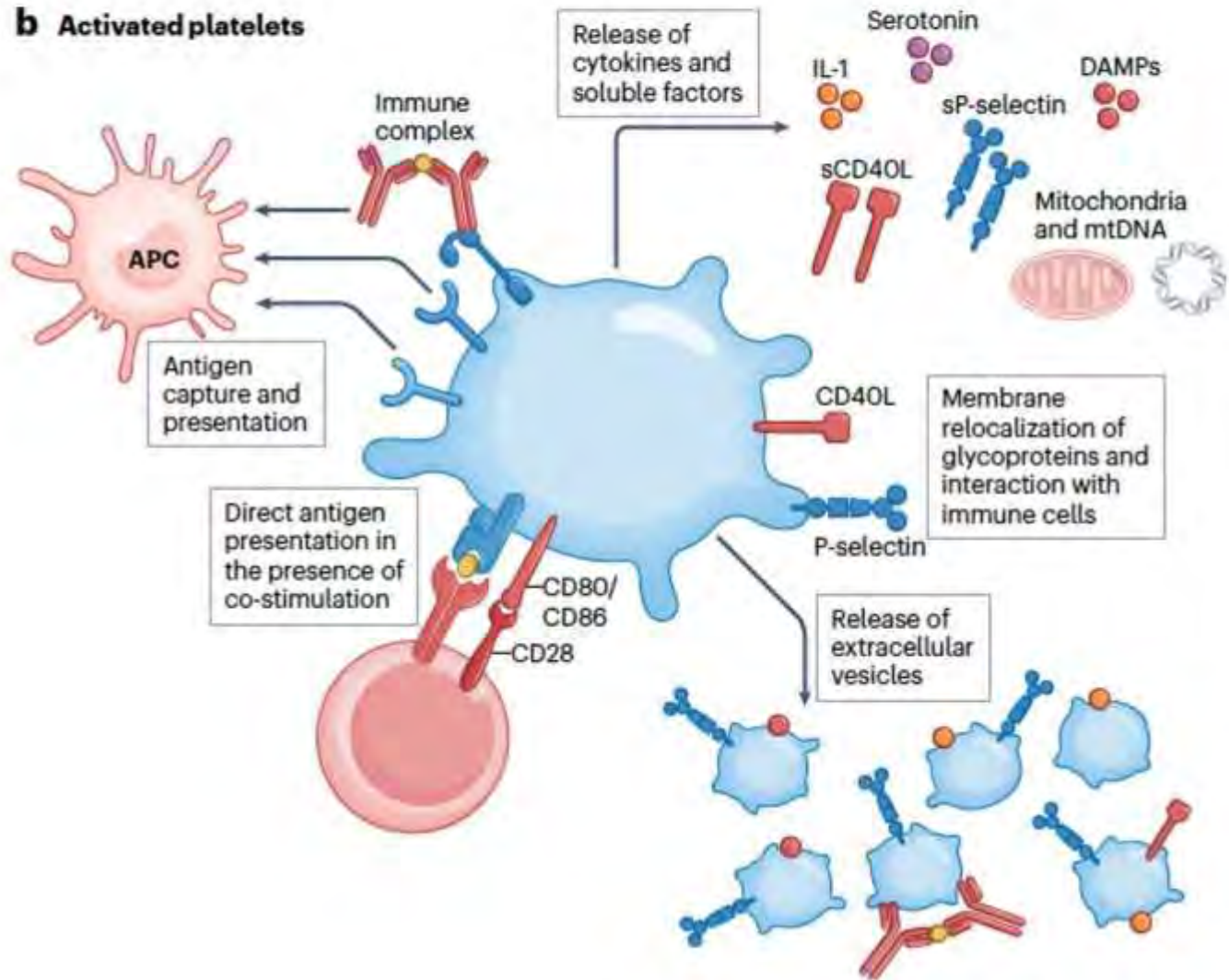
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a Resting platelets



b Activated platelets



Platelet-Rich Plasma for Rheumatoid Arthritis: A Case Series

Dana Shively¹, Neel Amin²

A Platelet's Guide to Synovitis

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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 Badsha¹, Ghita Harifi¹ and William D. Murrell^{2,3,4,5}

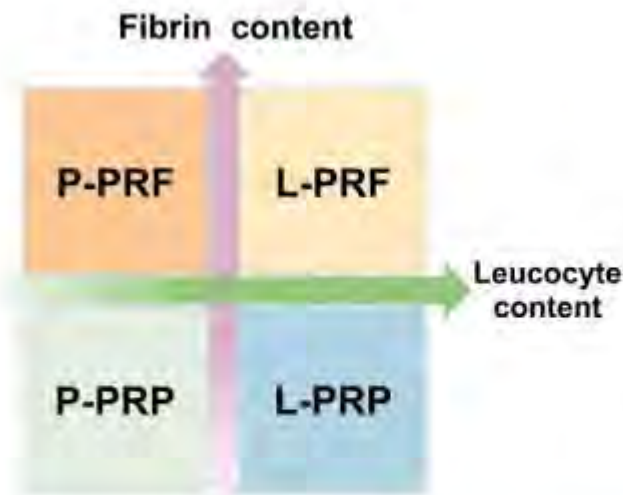


Table 1. Overview of active ingredients of PRP

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 ¹⁴
IGF-1	Hepatic stellate cells, osteoblasts, fibroblasts, macrophages ¹⁵	Promotes growth, cell differentiation and cell proliferation ¹⁵
bFGF	Endothelial cells, bone cells ^{17,16}	Induction of neovascularization and neurotrophs ^{16,17}
EGF	Endothelial cells, vascular smooth muscle cells, neutrophils, macrophages ¹⁷	Promoting wound healing and anti-inflammatory ¹⁷

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. ⁹⁰⁻⁹²
Pain medicine	Radiculopathy, lumbago, phantom limb pain, etc. ⁹³⁻⁹⁵
Plastic surgery	Skin healing, autologous fat transplantation, cartilage rebuilding, etc. ^{96,97}
Urology	Erectile dysfunction, urethral stricture, hypospadias, prostatic hyperplasia, bladder contracture, peyronie disease, etc. ⁹⁸⁻⁹⁹
Dermatology	Androgenetic alopecia, alopecia areata, alopecia cicatrisata, chronic vitiligo, chloasma, psoriasis, paronychia, acne scarring, skin aging, etc. ¹⁰¹⁻¹⁰⁴
Ophthalmology	Xerophthalmia, corneal ulcers, etc. ^{95,98}
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. ^{98,100}
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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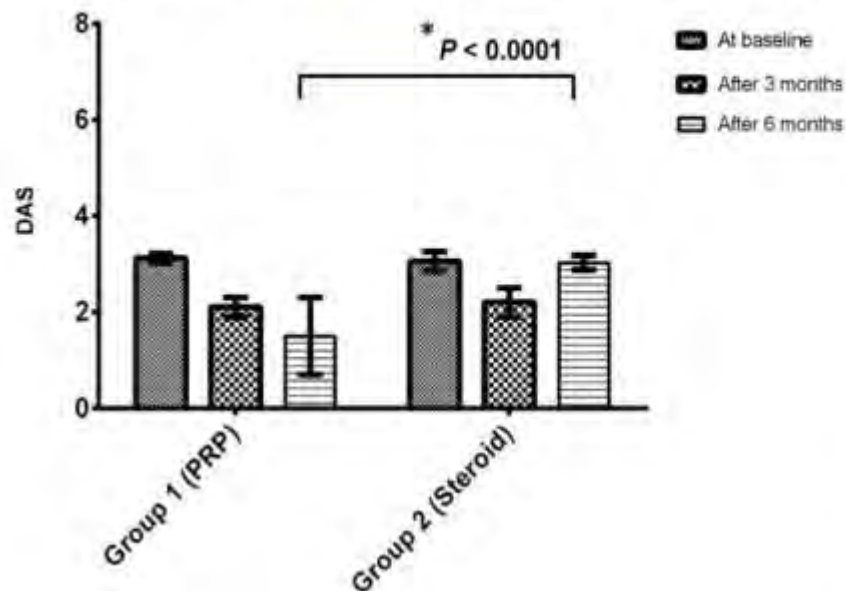
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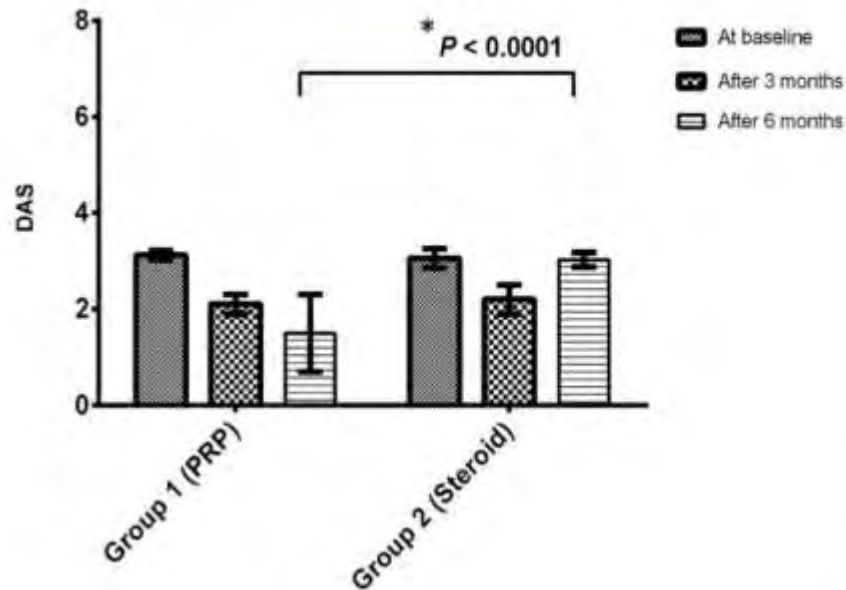
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A PRP egyfajta csodaszernek tűnhet
Amitől nekem rögtön gyanússá válik



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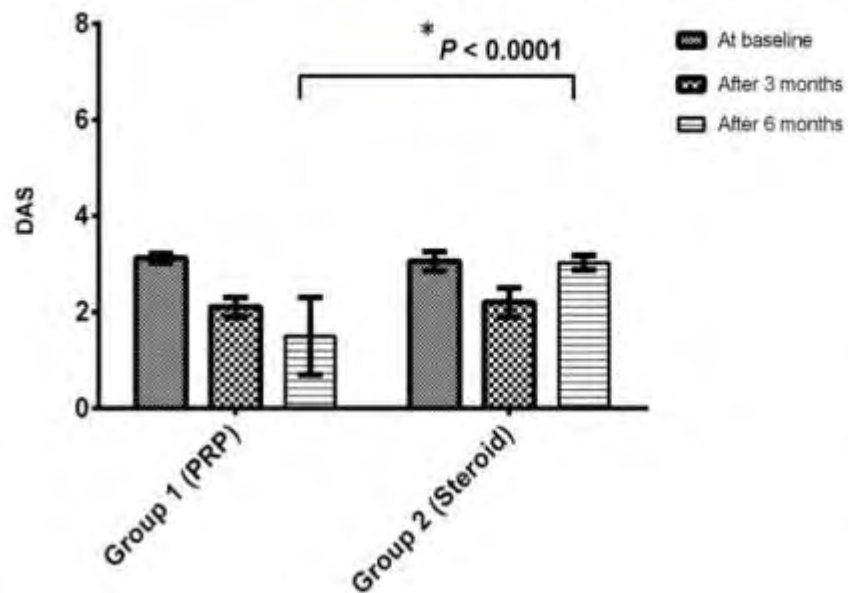
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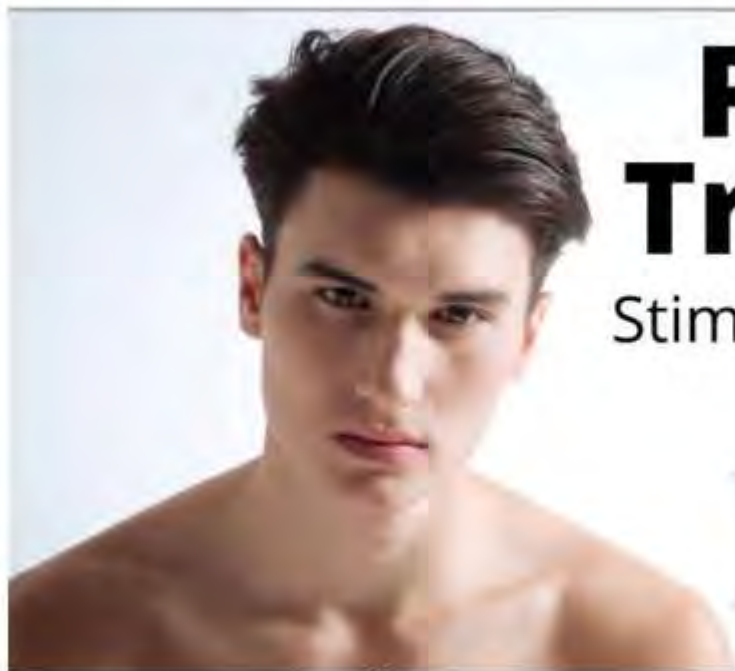
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PRP Hair Treatment

Stimulate and Accelerate Hair Growth

Maxim Hair Restoration
Manila, Philippines

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