# 2ND meeting of the European Research Consortium on ITP

## NEW INSIGHTS INTO IMMUNE THROMBOCYTOPENIA

**Paris** Crowne Plaza Paris République

**April 23-24, 2026**

# The role of platelets in innate and adaptive immunity

**John W. Semple**

Professor of Transfusion Medicine, Lund University, Lund Sweden
Professor of Pharmacology, University of Toronto, Toronto, Canada

# John W. Semple Disclosures

- **Amgen:** Honouraria, Ad boards
- **Argenx:** Honouraria, Ad boards
- **CellPhire Therapuetics:** Grants
- **Ionis:** Grants
- **Novartis:** Grants, Honouraria, Ad boards
- **Platelet BioGenesis:** Grants
- **Sobi:** Honouraria
- **Takeda:** Honouraria, Ad borads
- **UCB:** Honouraria, Ad boards

# Platelets

A thrombocyte said to his mate:
Come on, let's start to aggregate.
Clinicians always call us a clot.
But we know better: we are not!
Not to be understood is our fate ...

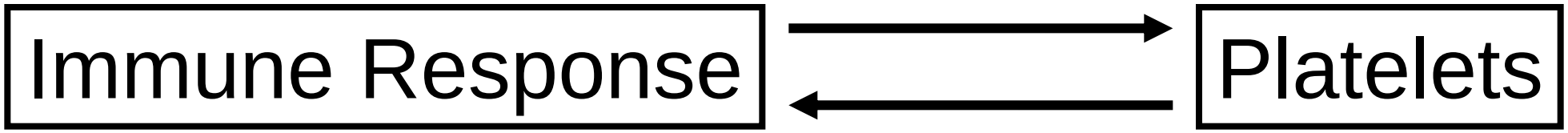
1. PLATELET AGGREGATION IN PHYSIOLOGICAL SYSTEMS

G.V.R. Born

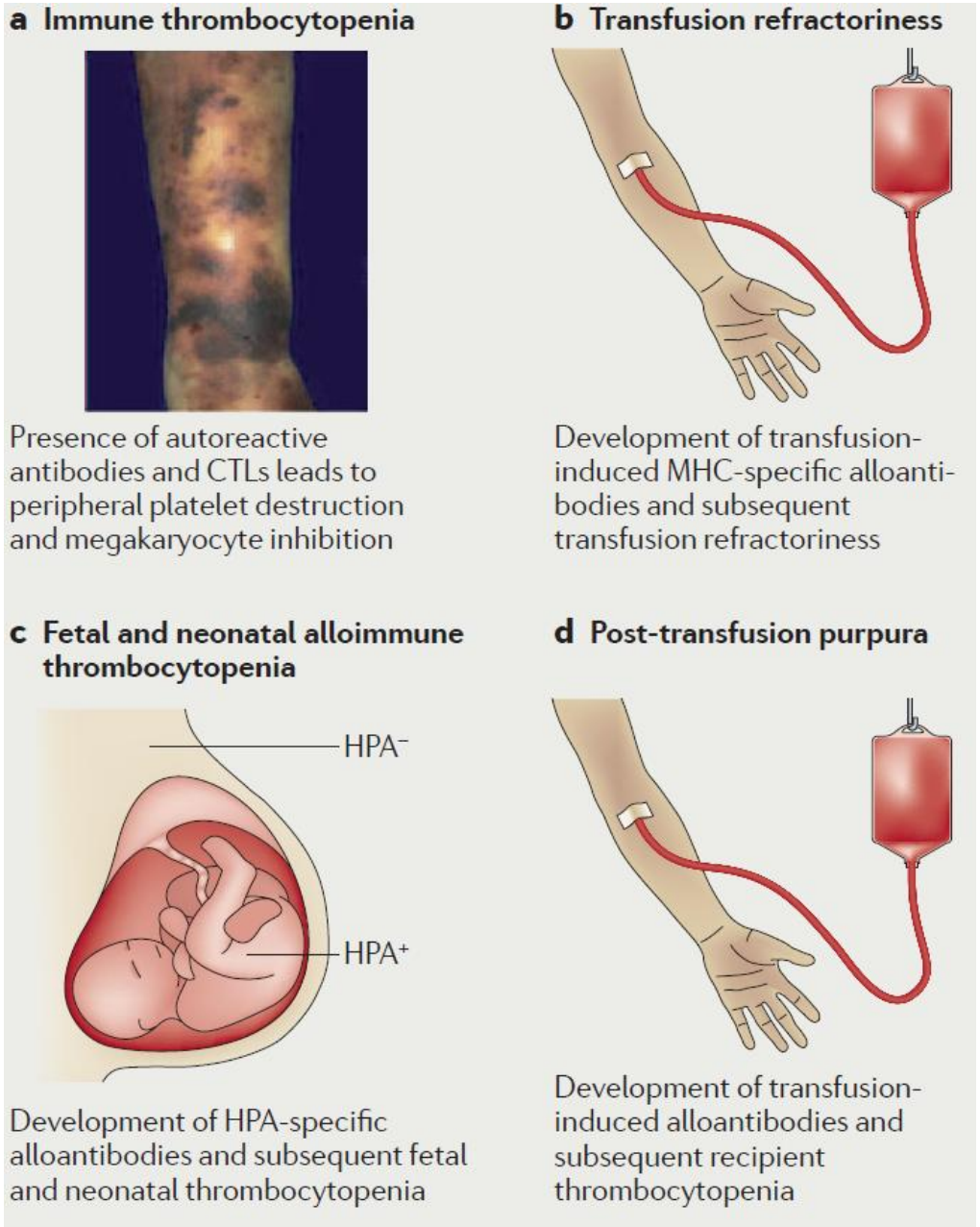
*Department of Pharmacology*
*Royal College of Surgeons of England*
*London, England*

*Acta Medica Sand, 1971*

# Platelets can be the prey, but also the predator when it comes to immunity

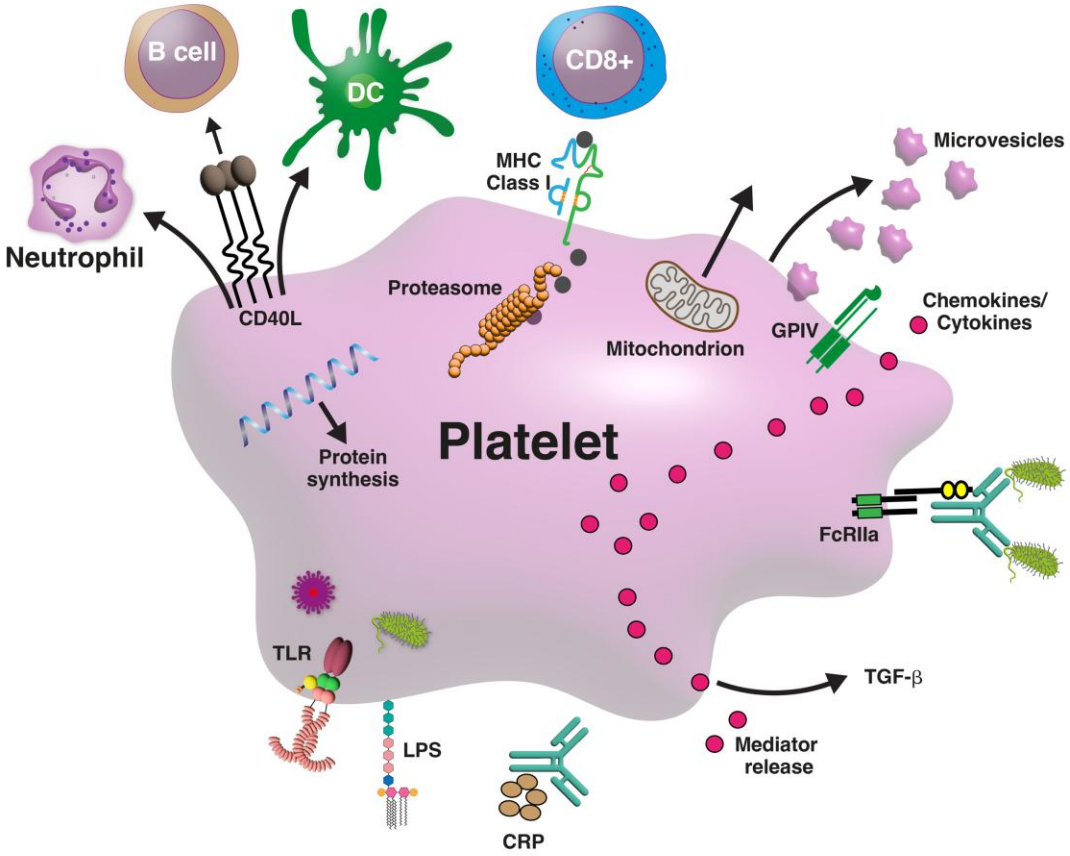


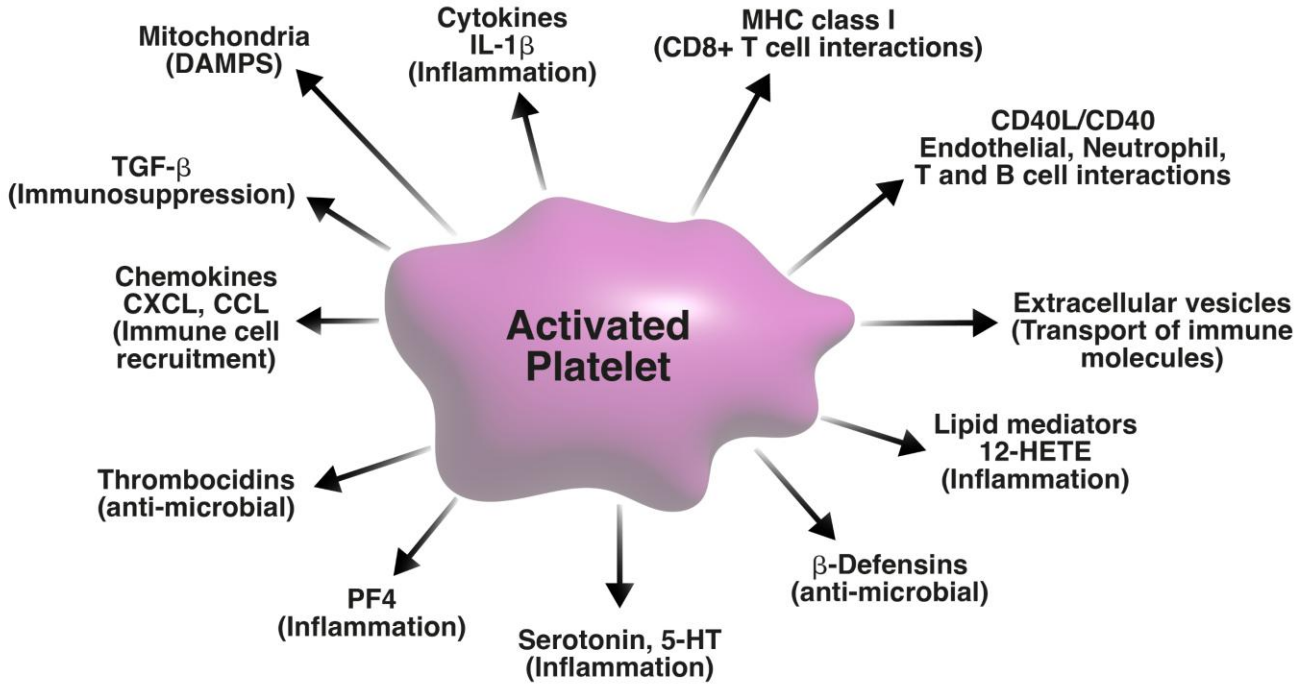
# Immunity against platelets (prey)




*Semple JW et al. Nat Rev Immunol, 2011*

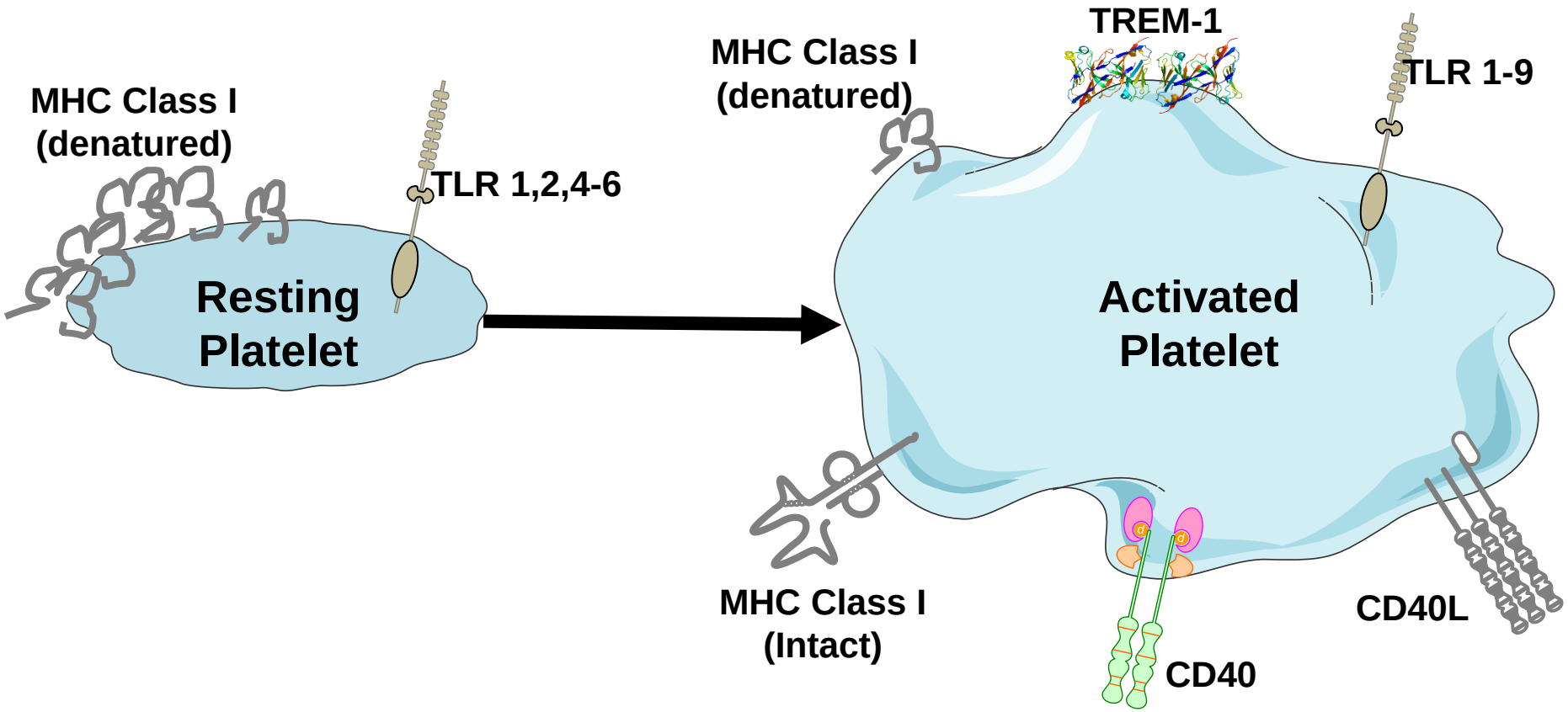
# Platelets are Immune Cells (predators)




*Marcoux G et al. Platelets and Immunity. In: Platelets in Thrombotic and Non-Thrombotic Disorders: Pathophysiology, Pharmacology and Therapeutics, 2nd edition, (Paolo Gresele, Dominick J. Angiolillo, Clive P. Page, eds). Springer Verlag. 2025, pp 287-305.*

# Activated platelets are more Immunoregulatory than resting platelets



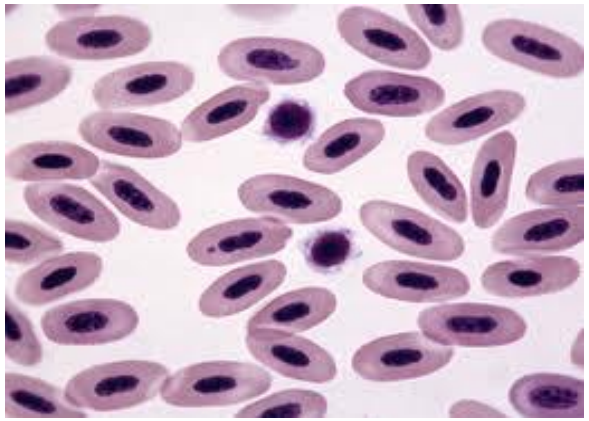

**Suppression**

**B cell, T cell, DC Activation (and sometimes Suppression)**

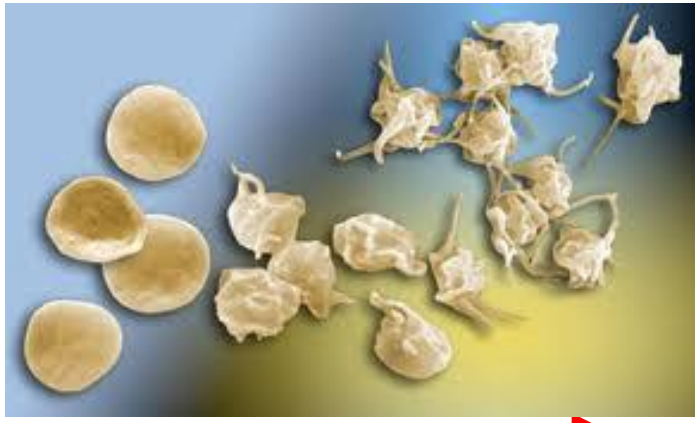
# Evolutionary links of platelet immunity

Hemocytes

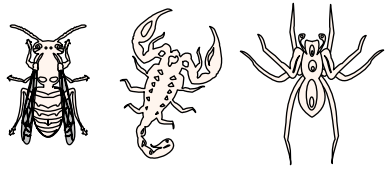
Thrombocytes



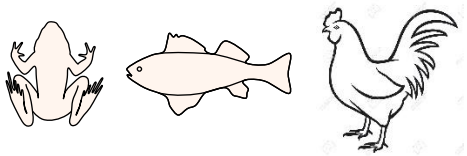
Platelets



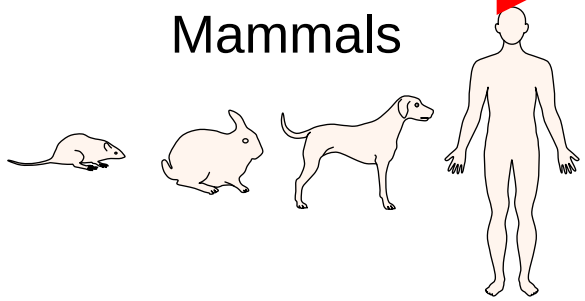
Invertebrates



Vertebrates



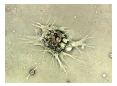
Mammals



*Levin J In: Platelets, 4th Ed., 2019*

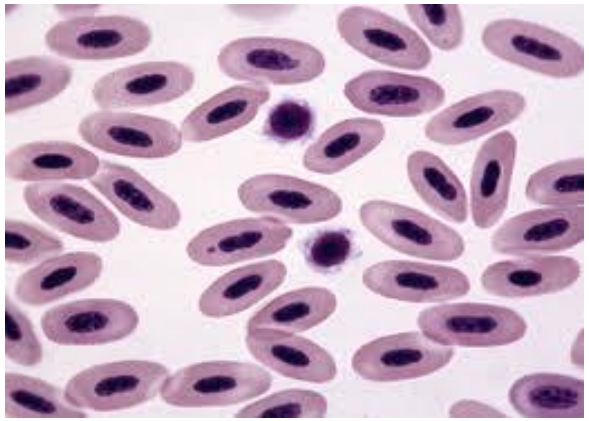
# Evolutionary links of platelet immunity

Hemocytes

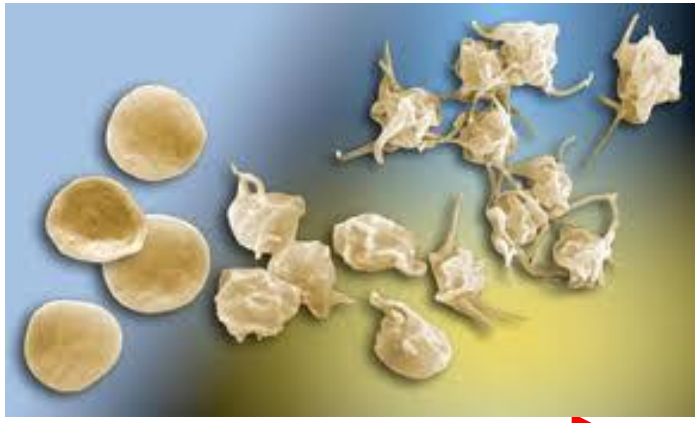


- **Phagocytes (Mac.-like).**
- **Anti-bacterial peptides.**
- **Express TLR/innate receptors.**
- **Can aggregate and clot hemolymph at sites of injury.**

Thrombocytes



Platelets



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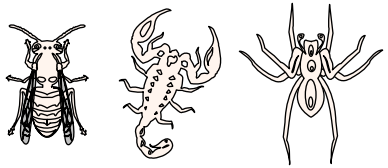

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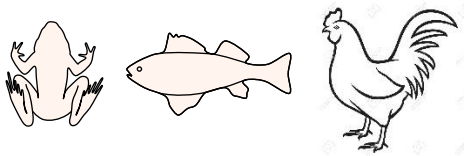

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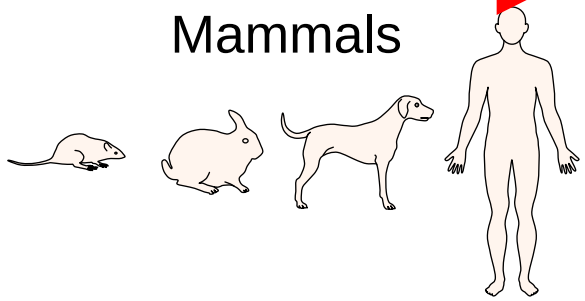

*Levin J In: Platelets, 4th Ed., 2019*

# Evolutionary links of platelet immunity

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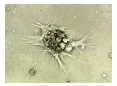

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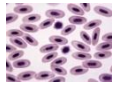

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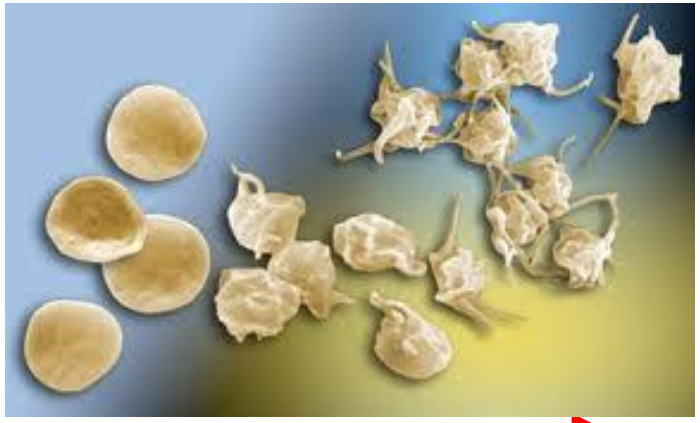
## Platelets



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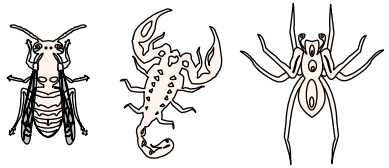

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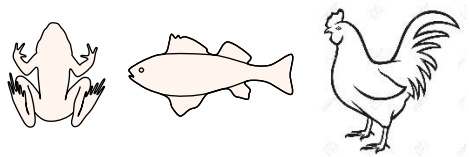

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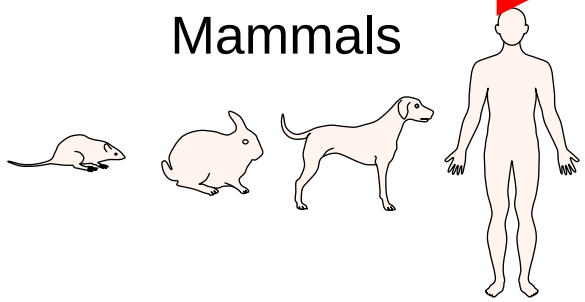

*Levin J In: Platelets, 4th Ed., 2019*

# Evolutionary links of platelet immunity

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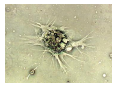

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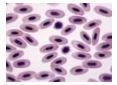

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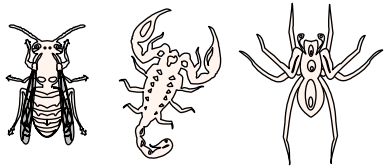

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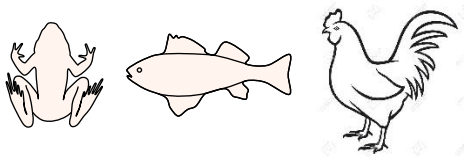

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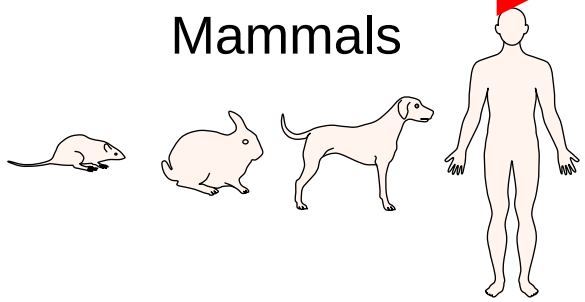

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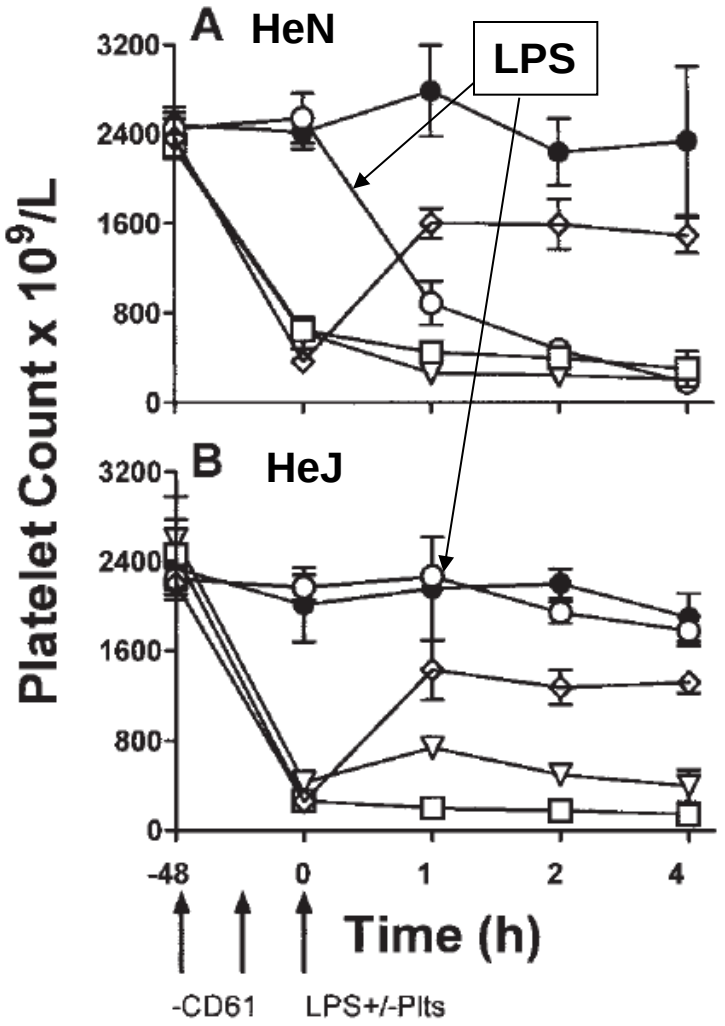
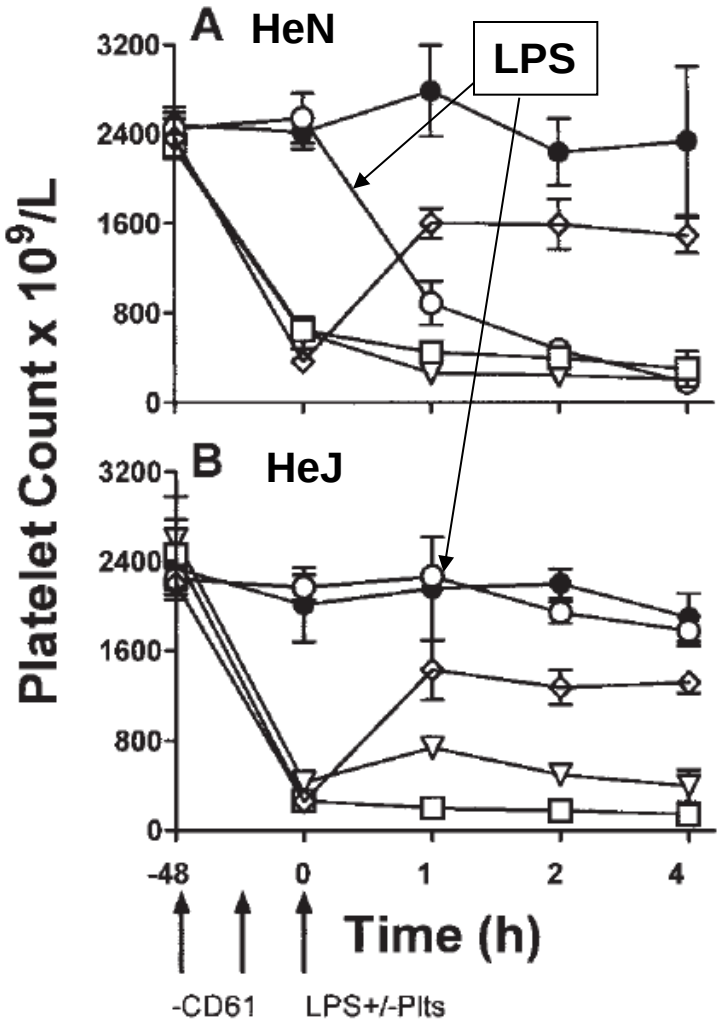
# Platelets Interact with Bacteria

# Platelet-TLR expression is responsible for sepsis-induced thrombocytopenia




*Aslam R et al. Blood, 2006;107:637-641)*

# Platelet-TLR expression is responsible for sepsis-induced thrombocytopenia

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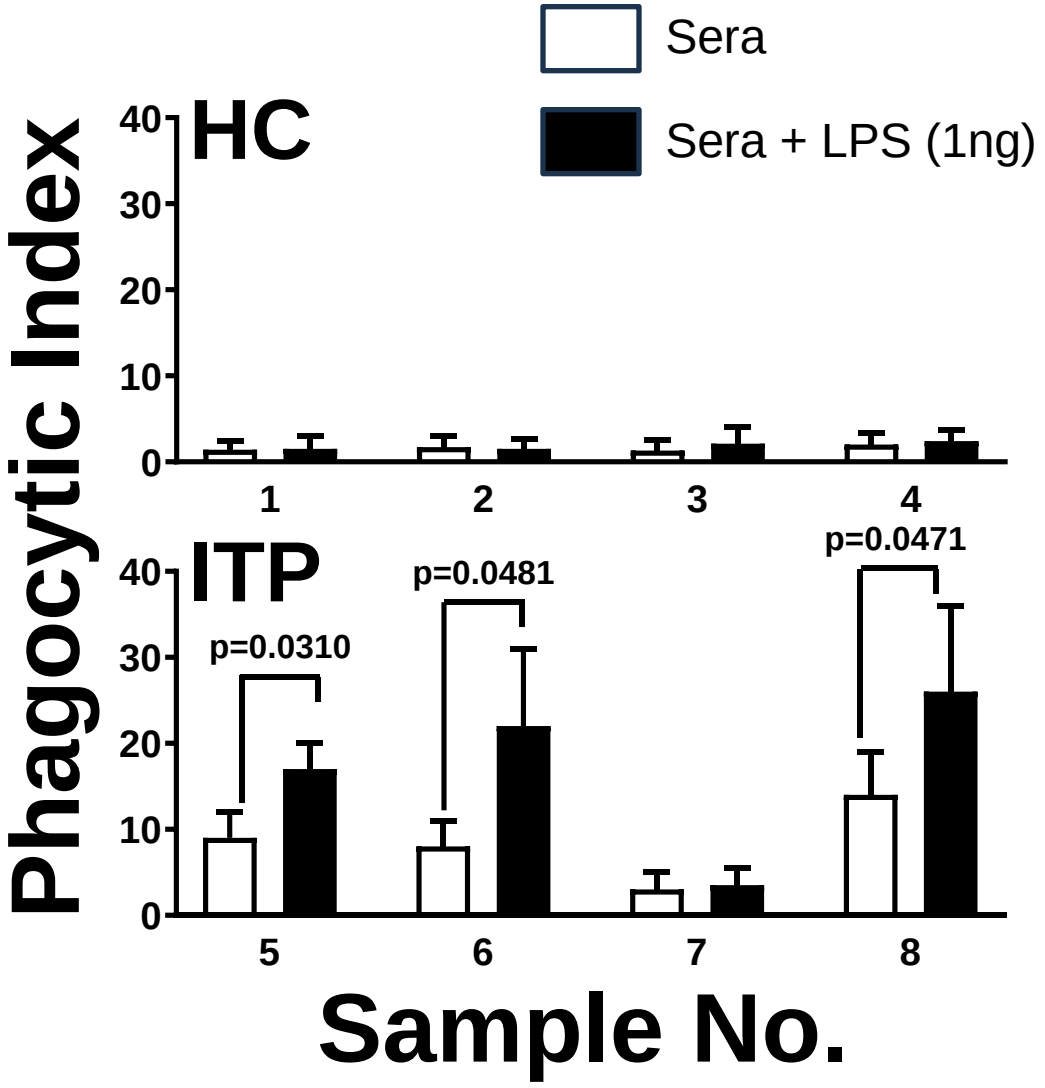



*Semple JW et al. Blood. 2007;109:4803-4805*

OPEN ACCESS Freely available online

PLoS PATHOGENS

# Novel Anti-bacterial Activities of β-defensin 1 in Human Platelets: Suppression of Pathogen Growth and Signaling of Neutrophil Extracellular Trap Formation

Bjoern F. Kraemer[1,2☯], Robert A. Campbell[1☯], Hansjörg Schwertz[1,3], Mark J. Cody[1], Zechariah Franks[1], Neal D. Tolley[1], Walter H. A. Kahr[4], Stephan Lindemann[5], Peter Seizer[2], Christian C. Yost[1,6], Guy A. Zimmerman[7], Andrew S. Weyrich[7*☯]

*November 2011 | Volume 7 | Issue 11 | e1002355*

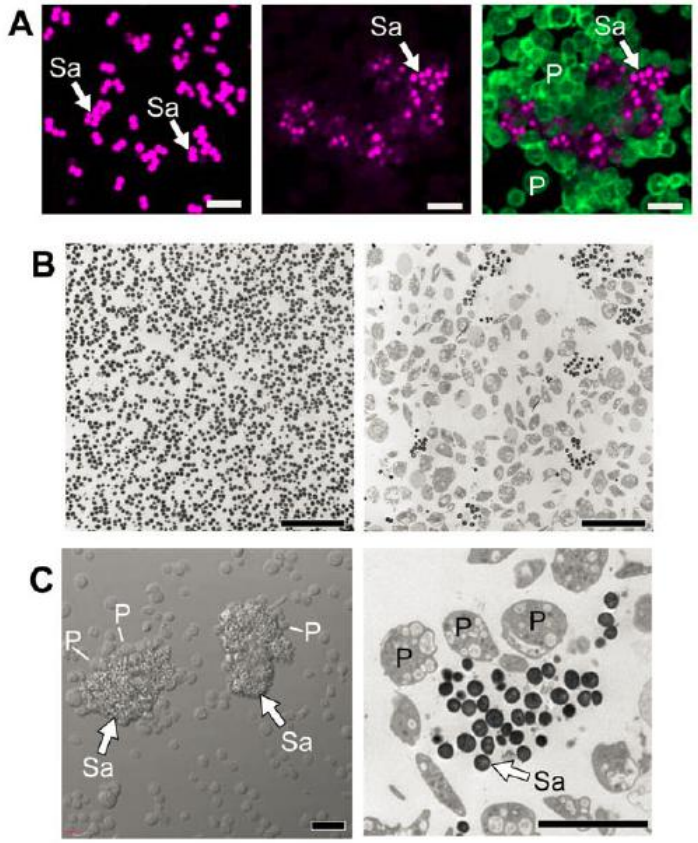



**Figure 1. Platelets sequester *S. aureus*.** Cultured *S. aureus* were

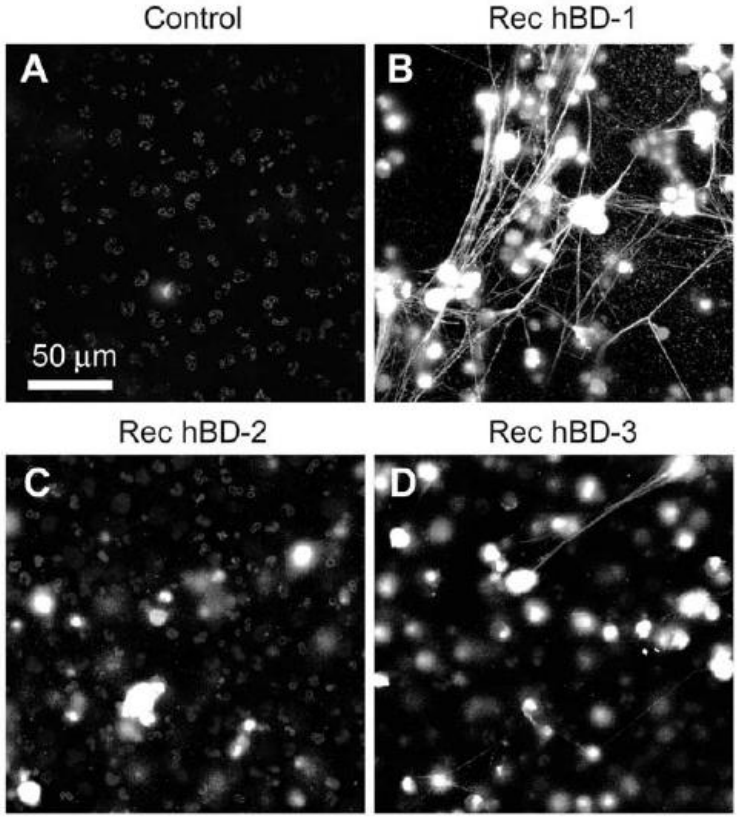
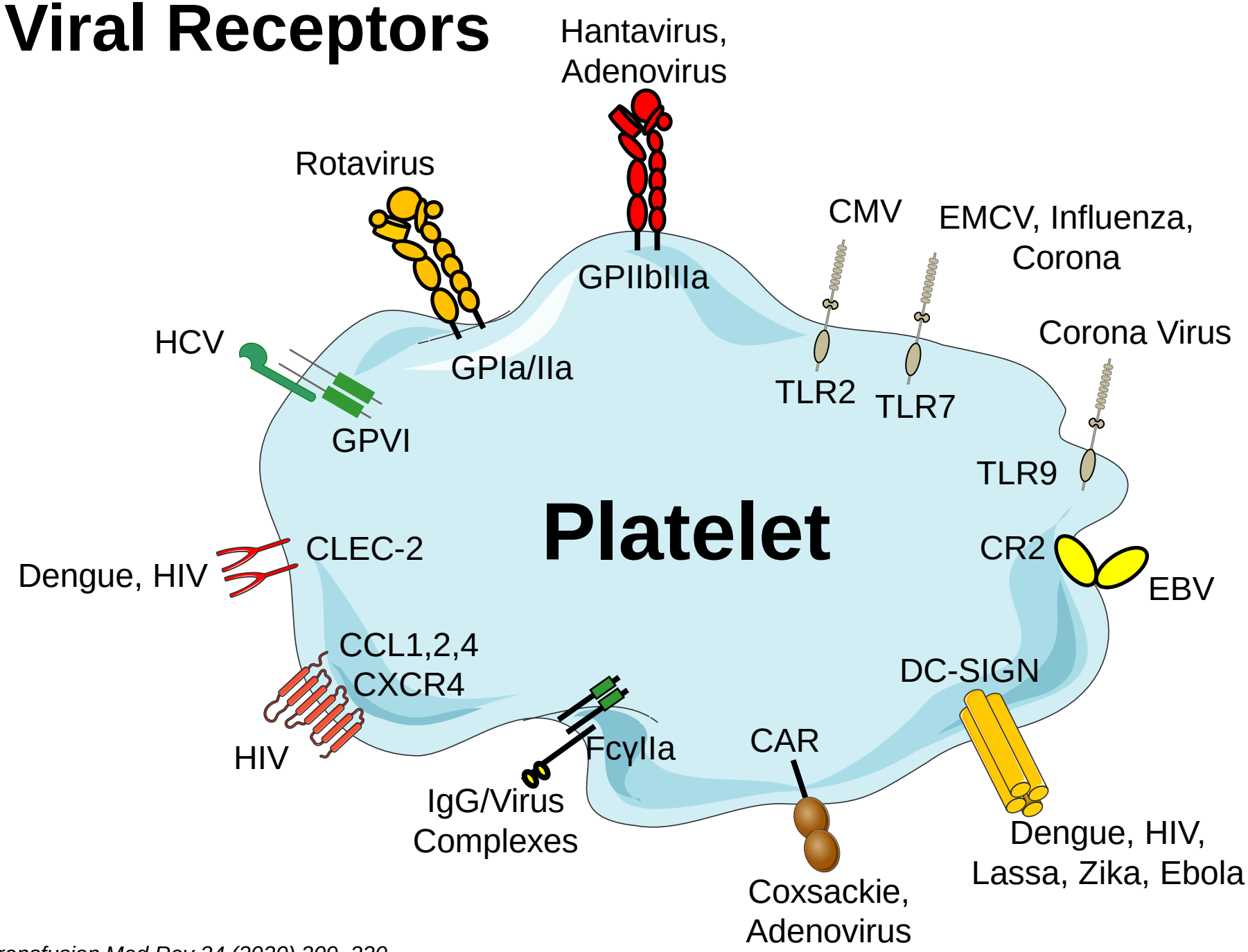



**Figure 6. β-defensin 1, but not other β-defensin family members, induce PMNs to form NETs.** PMNs were left untreated

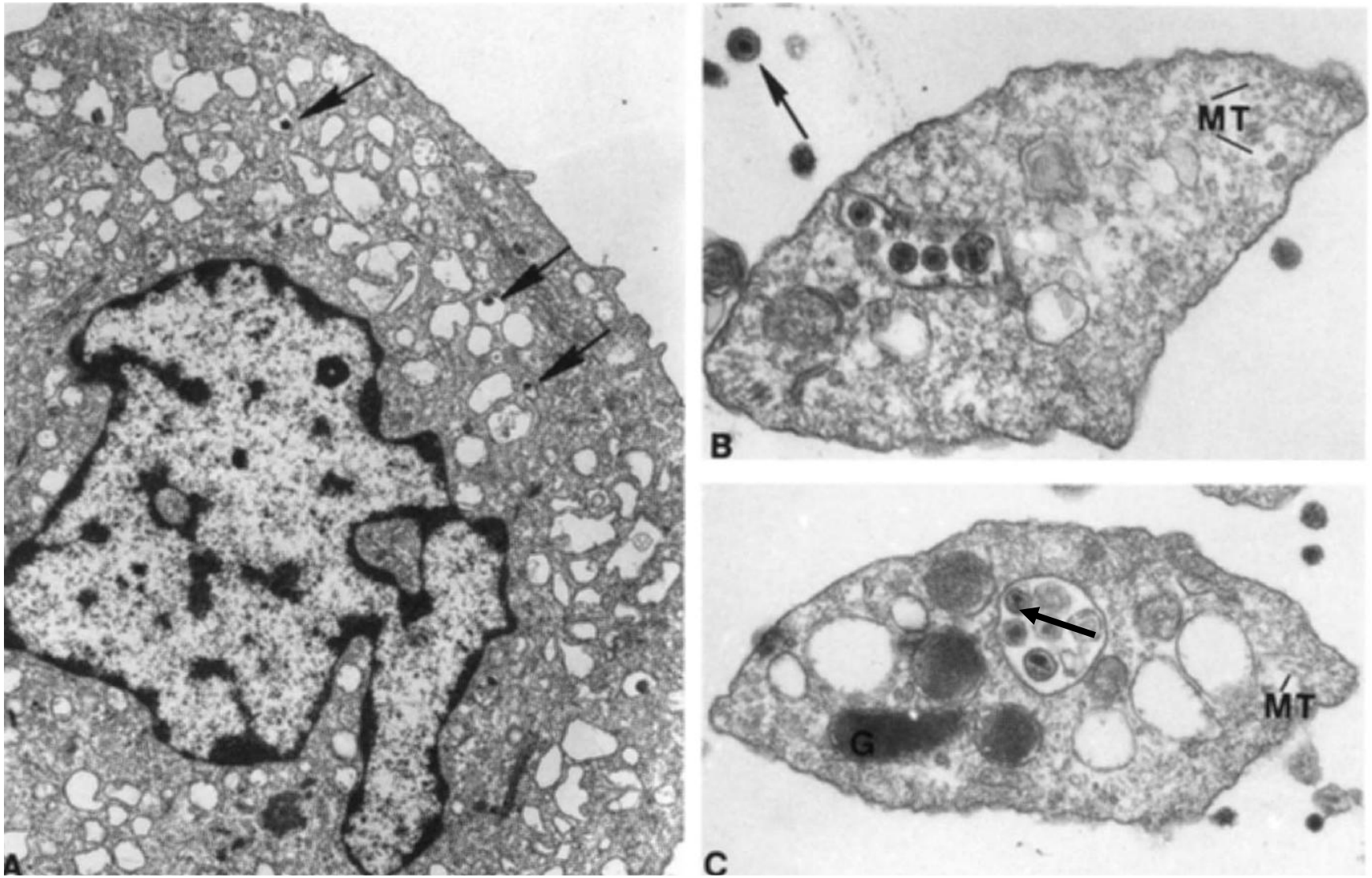
# Platelets Readily Take up Viruses

# Platelet Viral Receptors




*Adapted from Maouia A Transfusion Med Rev 34 (2020) 209–220*

# Platelets readily Uptake HIV Particles




*Zucker-Franklin D et al. Blood. 1990;75:1920–1923.*

# In their first year after diagnosis, patients with ITP are 3-5 times more susceptible to infections

## It’s not just bleeding.

Figure 1 - Cumulative incidence (95% CI) for all infections

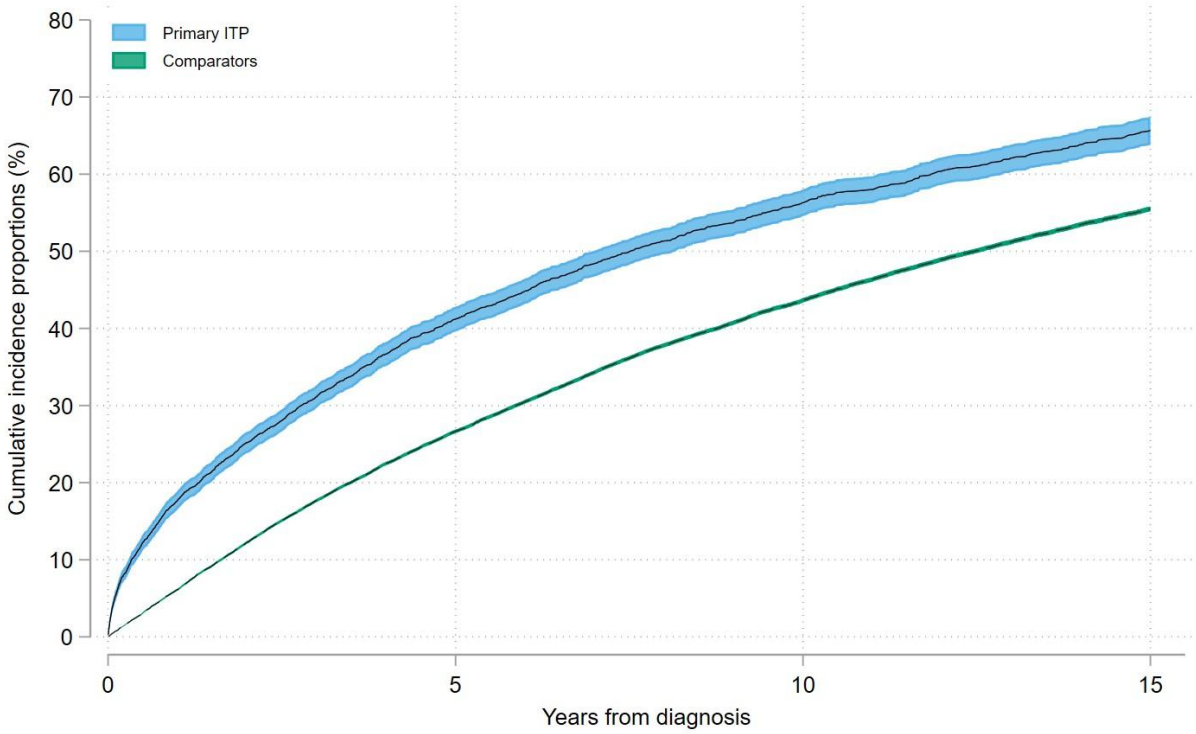
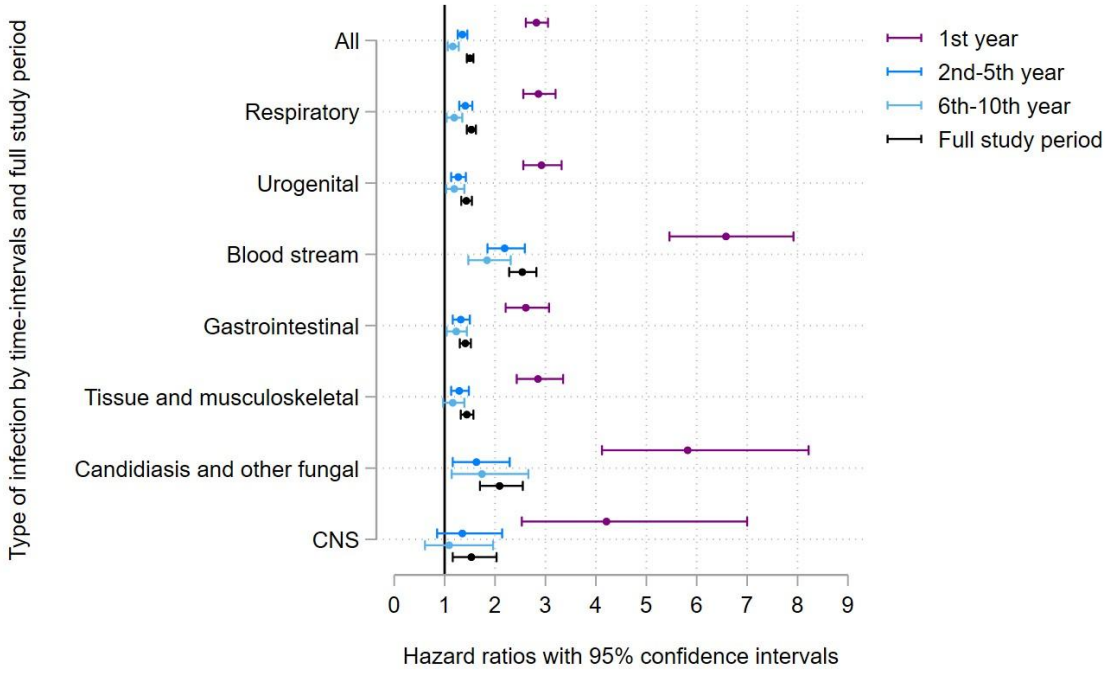
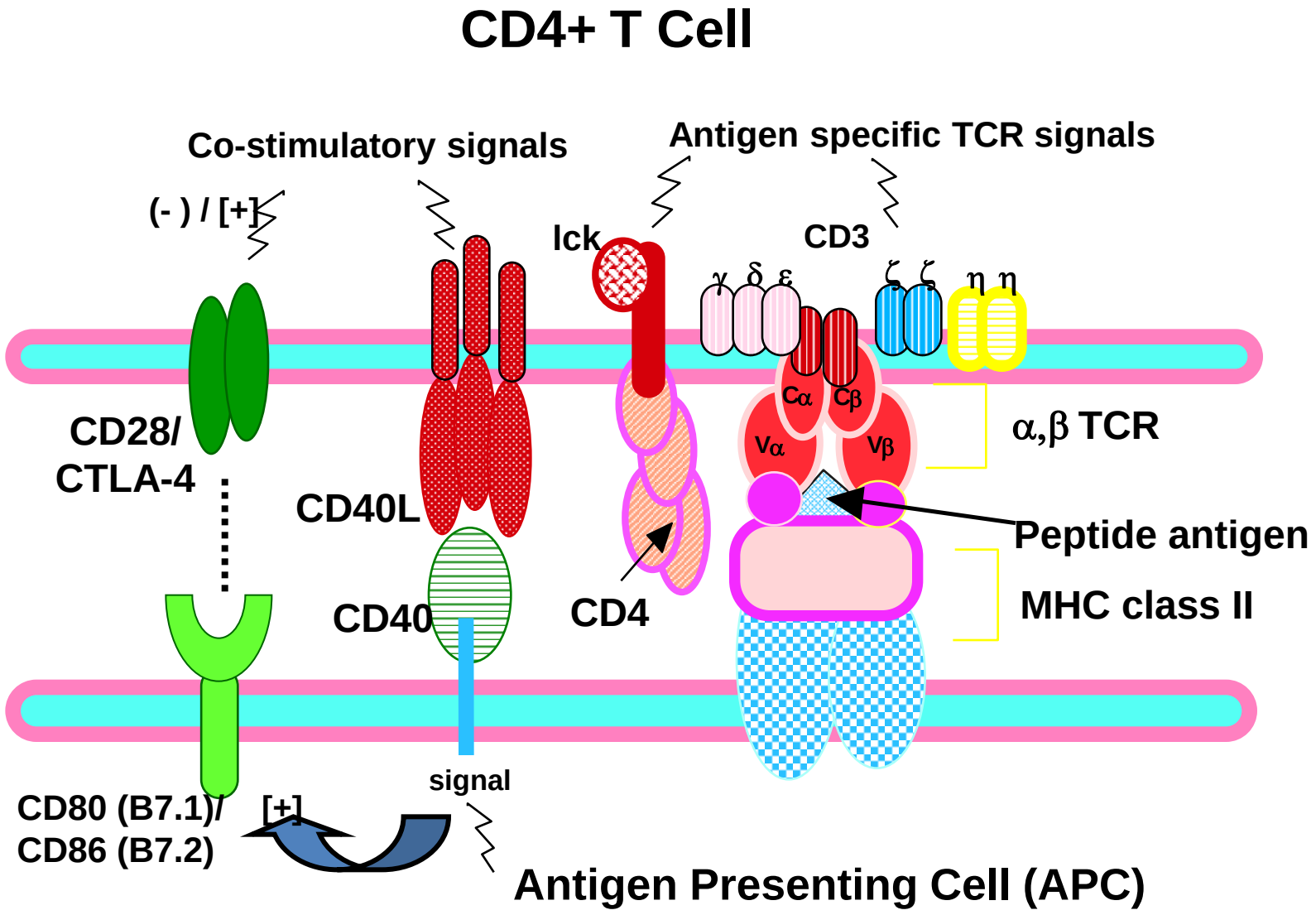



Figure 2 - Adjusted hazard ratios for infection subtypes

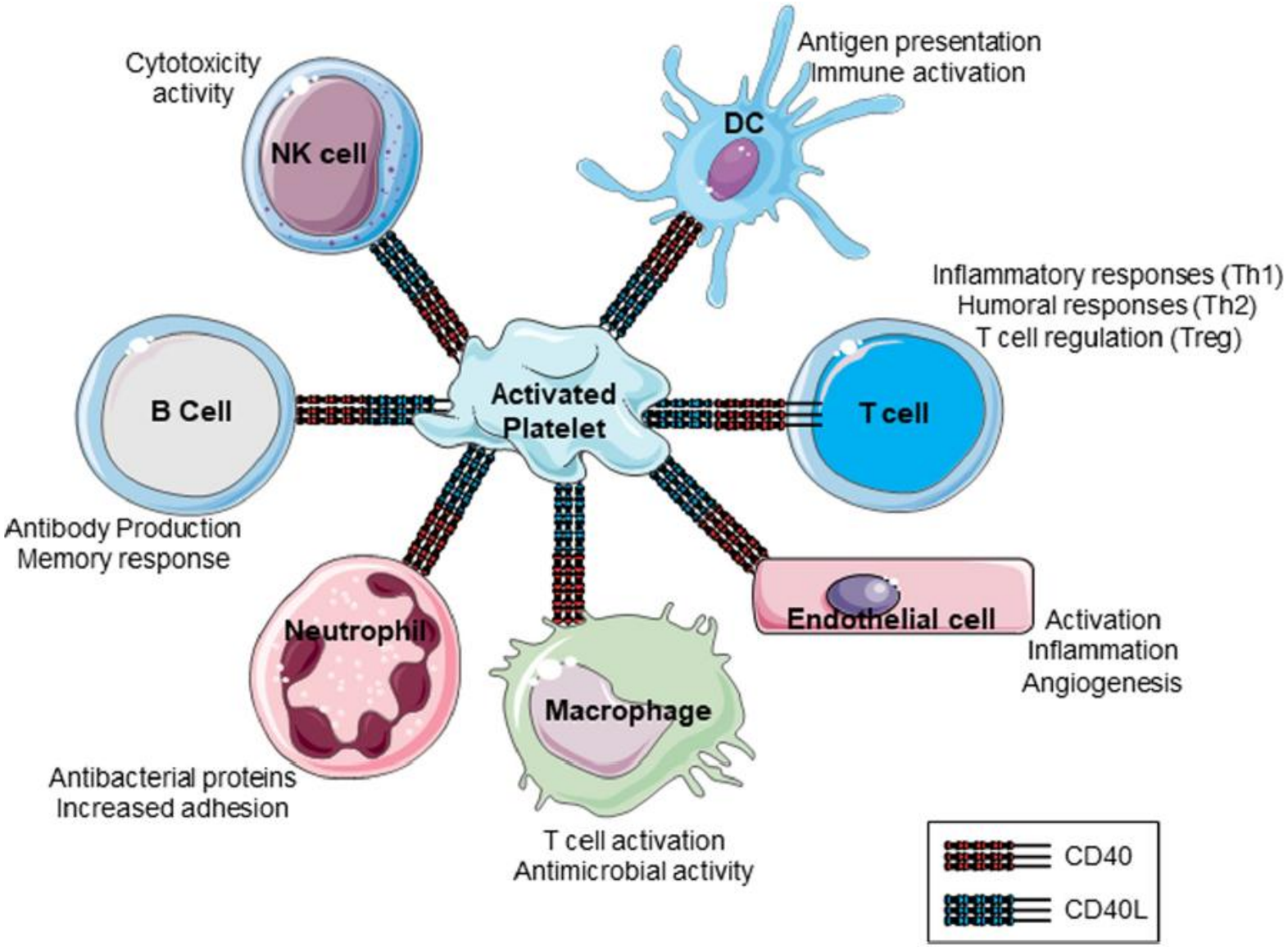



*Frandsen A et al. Blood 142 (Suppl 1); 394, 2023*

# CD154 (CD40L)

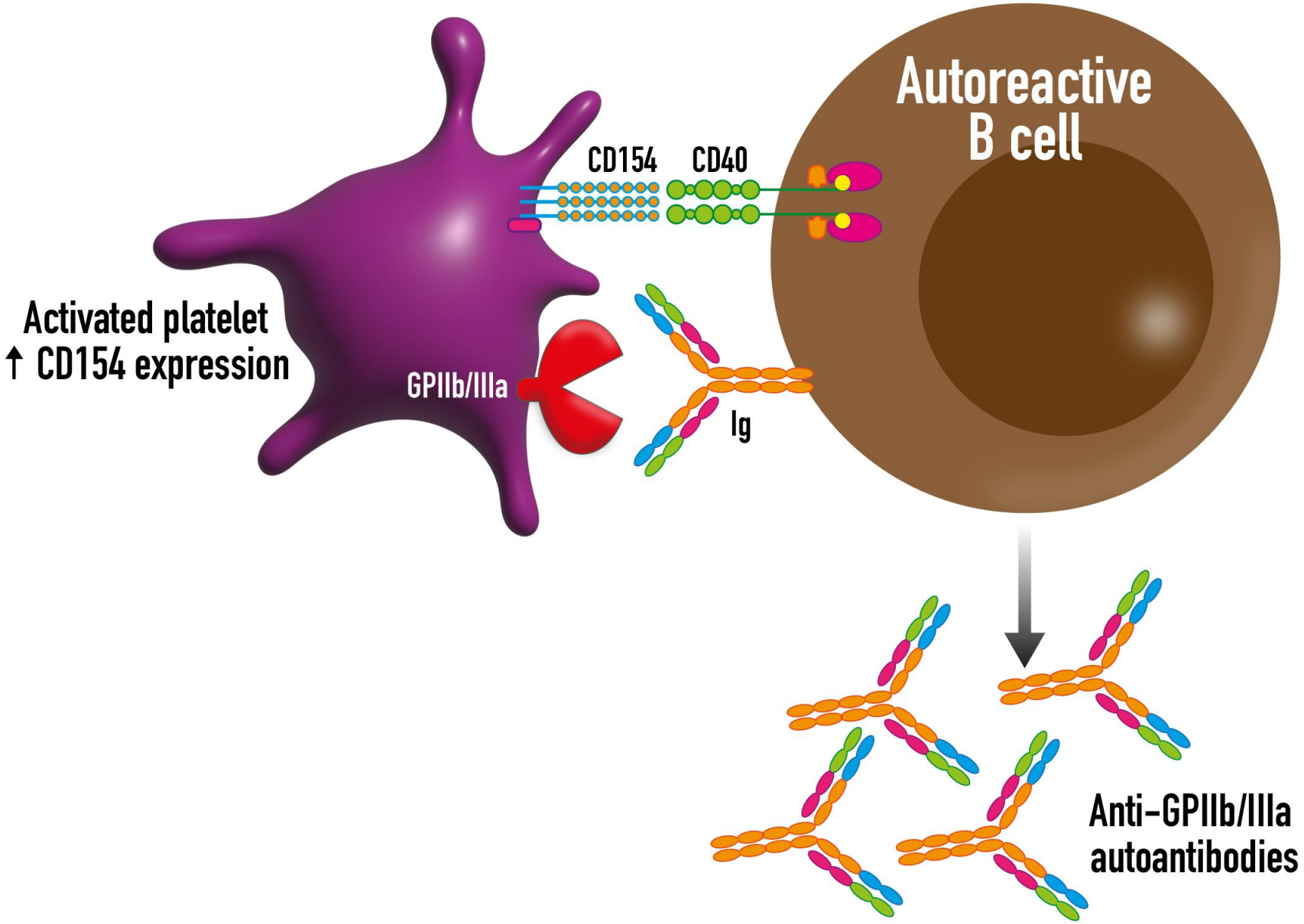

CD4+ T Cell
Co-stimulatory signals
Antigen specific TCR signals
(- ) / [+]
lck
CD3
γ δ ε
ζ ζ η η
Cα Cβ
Vα Vβ
α,β TCR
CD28/
CTLA-4
CD40L
Peptide antigen
MHC class II
CD40
CD4
signal
CD80 (B7.1)/
CD86 (B7.2)
[+]
Antigen Presenting Cell (APC)

# Platelet CD154 (CD40L) has a wide array of immune effects




*Maouia A et al, Transfusion Med Rev 34 (2020) 209–220*

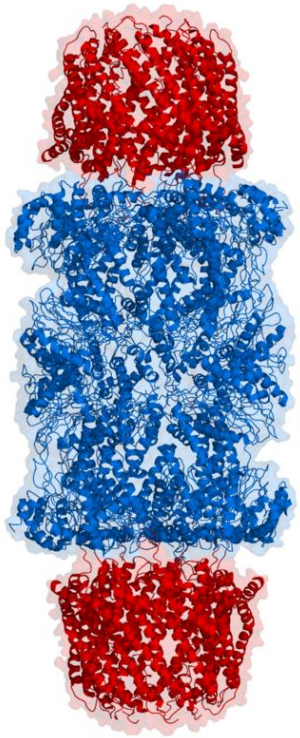
# Platelet CD40L (CD154) expression and function in ITP

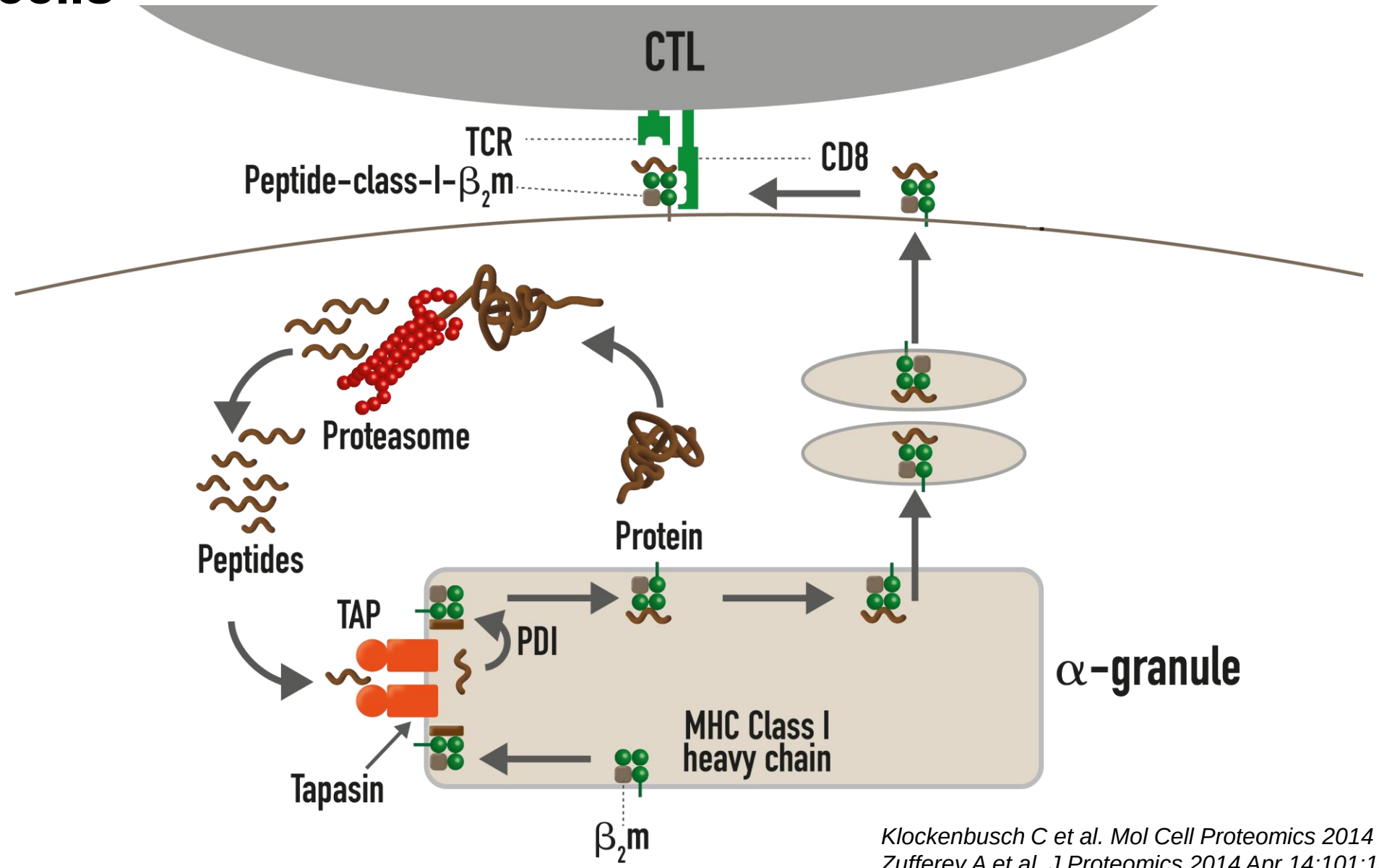



*Solanilla A et al.Blood. 2005;105:215-218*

# Platelets and Antigen Presentation

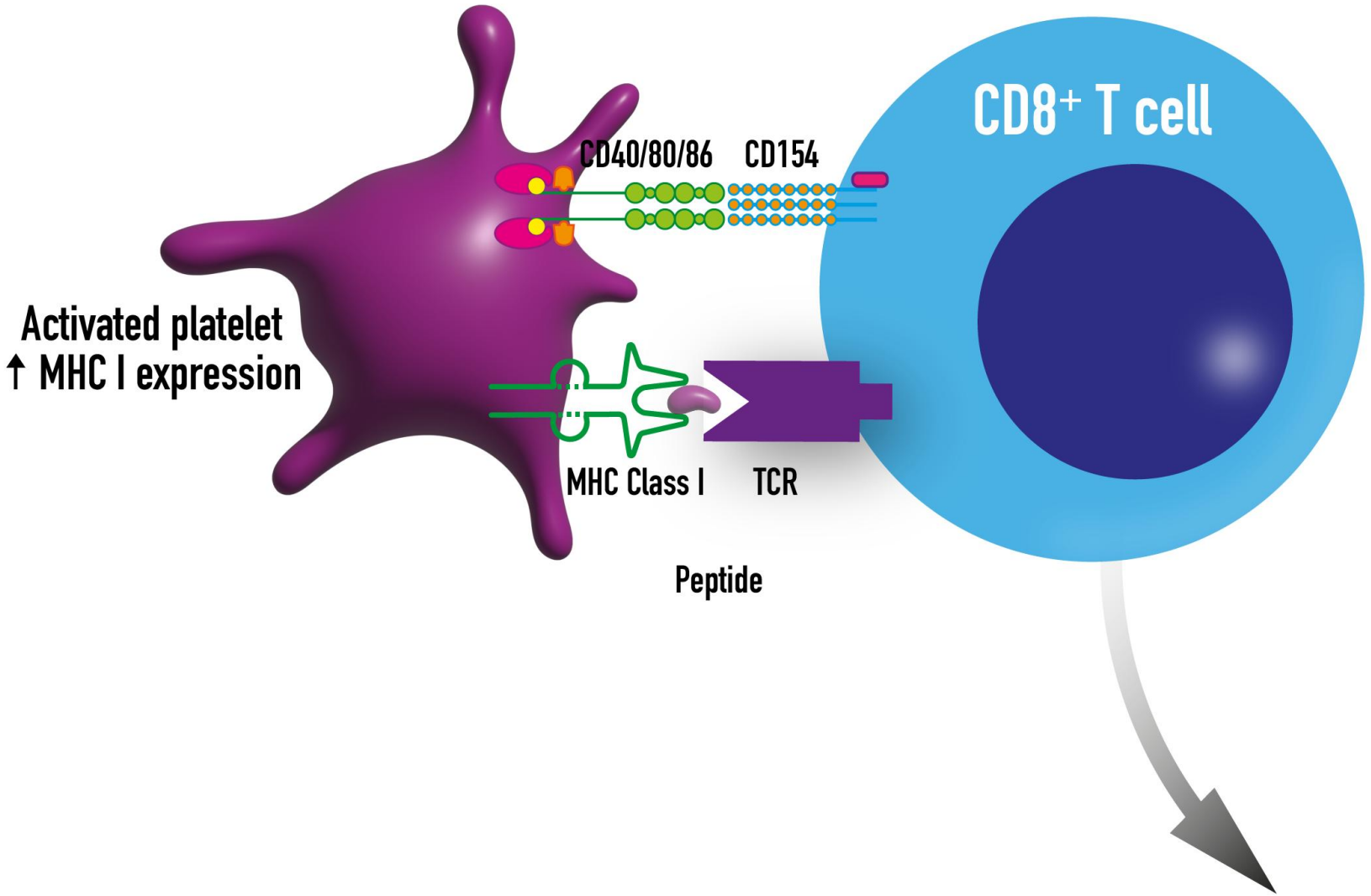
# Platelets contain a functional proteasome for cross presentation to CD8+ T cells





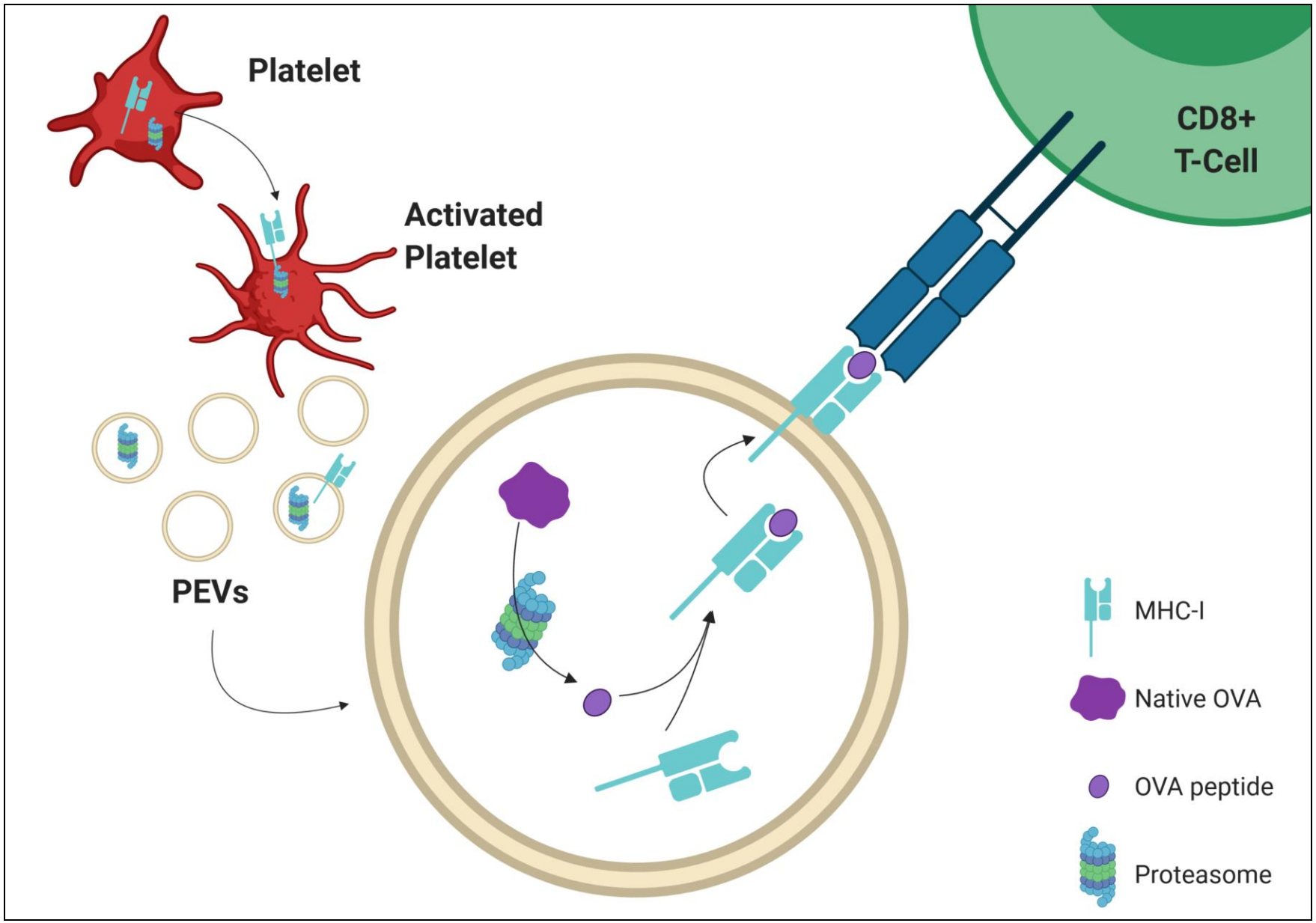

*Klockenbusch C et al. Mol Cell Proteomics 2014 Dec;13(12):3308-19.*
*Zufferey A et al. J Proteomics 2014 Apr 14;101:130-40.*
*Shi D et al. JCI 2014 Sep;124(9):3757-66.*

# Platelets cross-present Antigen to CD8+ T cells



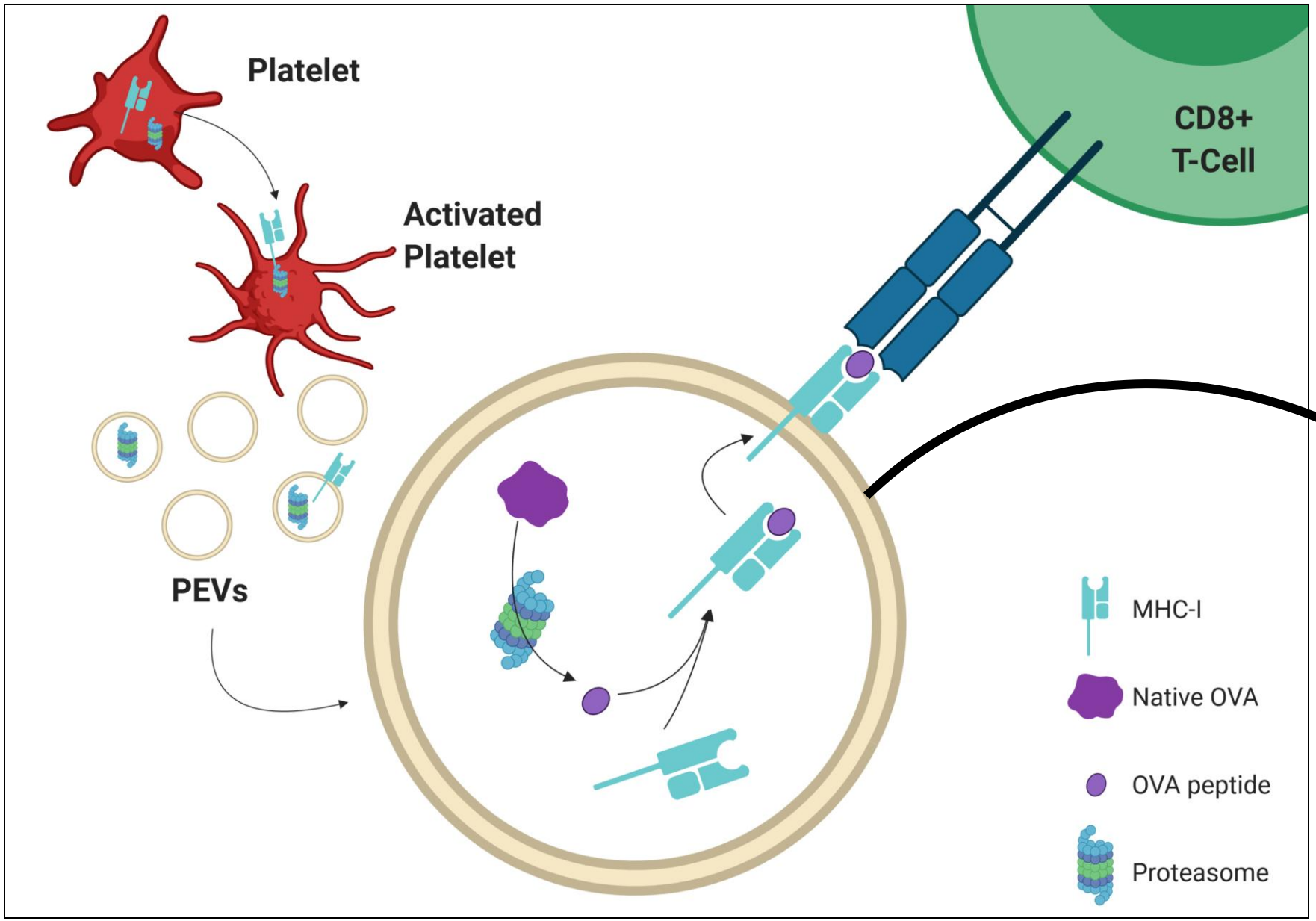

*Chapman LM et al. J Immunol 2012;189,916-923*

# Platelet EV cross-present antigen to T cells.




*Marcoux et al. Blood (2021)*

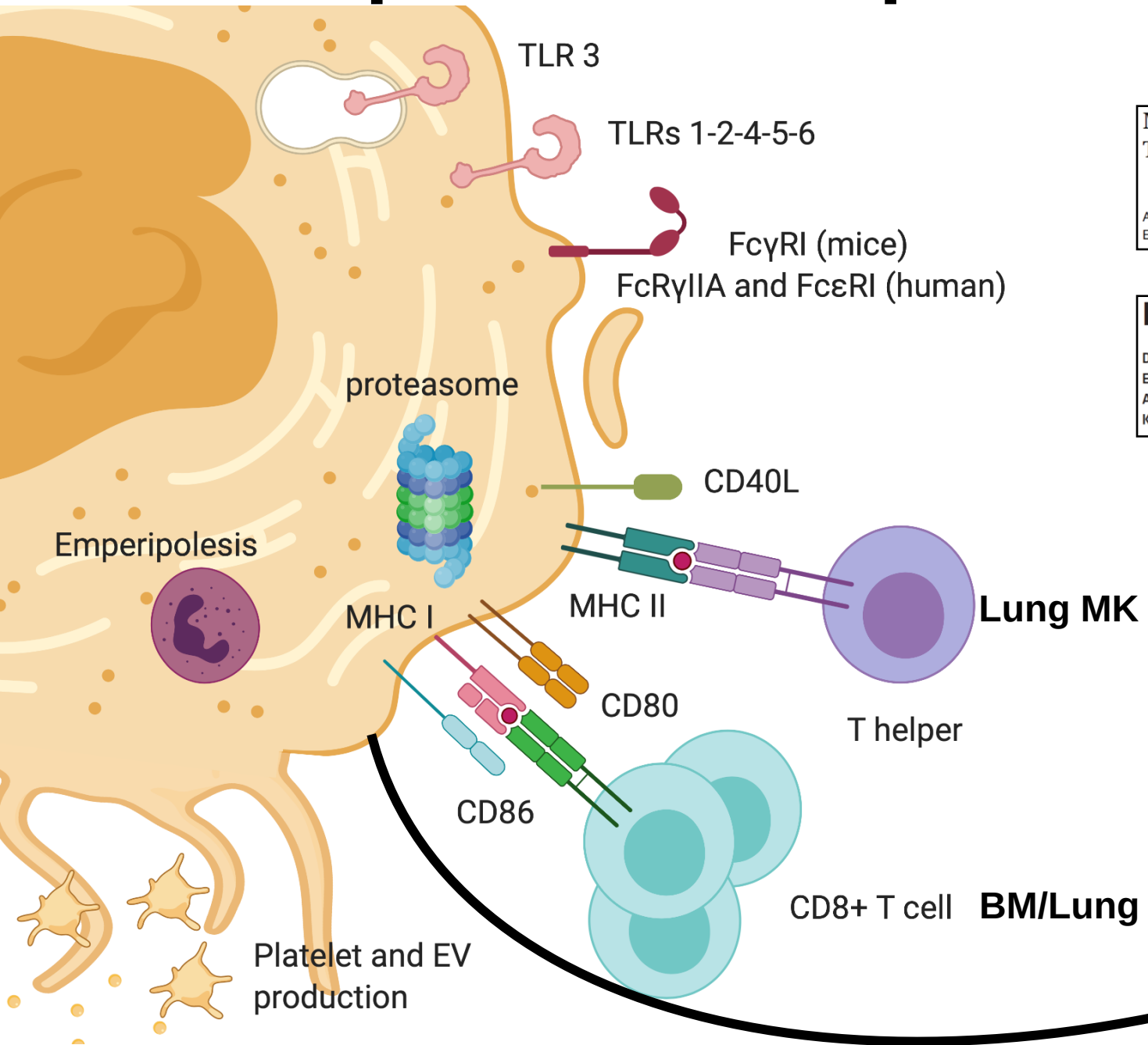
# Platelet EV cross-present antigen to T cells.




**Can migrate to lymph nodes**

*Marcoux et al. Blood (2021)*

# MK also process and present antigens.




Mature murine megakaryocytes present antigen-MHC class I molecules to T cells and transfer them to platelets

*Blood Adv. 1(20):1773-1785, 2017.*

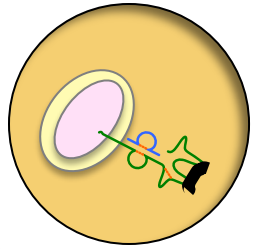
Anne Zufferey,[1] Edwin R. Speck,[1] Kellie R. Machlus,[2,3] Rukhsana Aslam,[1] Li Guo,[1] Mark J. McVey,[1,4] Michael Kim,[1] Rick Kapur,[1,5] Eric Boilard,[6] Joseph E. Italiano Jr,[2,3,7] and John W. Semple[1,5,8,9]

**Lung megakaryocytes are immune modulatory cells**

Daphne N. Pariser,[1,2] Zachary T. Hilt,[1] Sara K. Ture,[1] Sara K. Blick-Nitko,[1] Mark R. Looney,[3] Simon J. Cleary,[3] Estheany Roman-Pagan,[1] Jerry Saunders II,[4] Steve N. Georas,[2,5] Janelle Veazey,[2] Ferralita Madere,[2] Laura Tesoro Santos,[6] Allison Arne,[1] Nguyen P.T. Huynh,[7,8] Alison C. Livada,[1,9] Selena M. Guerrero-Martin,[10] Claire Lyons,[10] Kelly A. Metcalf-Pate,[10] Kathleen E. McGrath,[4] James Palis,[4] and Craig N. Morrell[1,2,5,9]

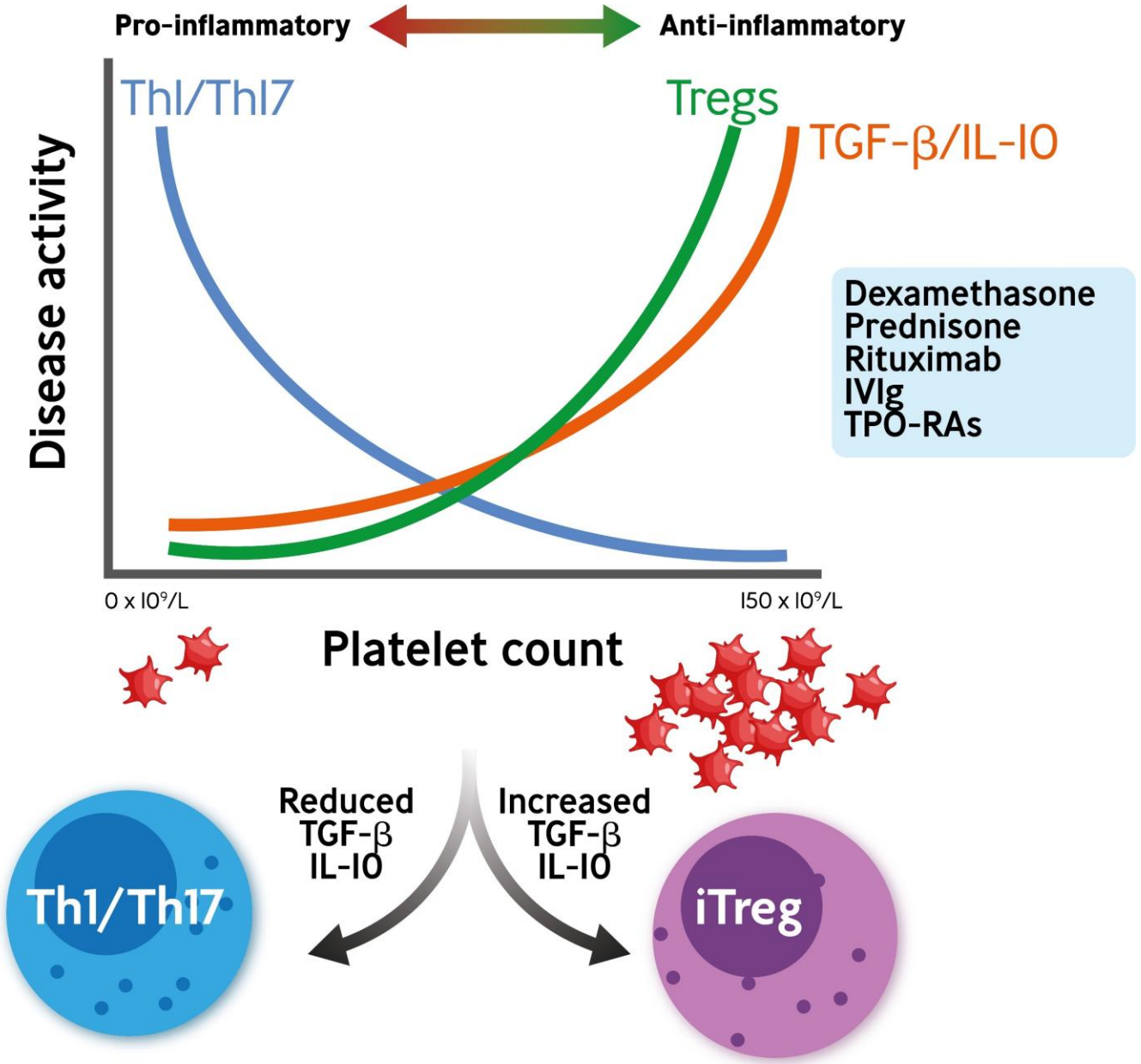
*J Clin Invest. 2021;131:137377.*

**Shed Platelets (with MHC/peptide)**



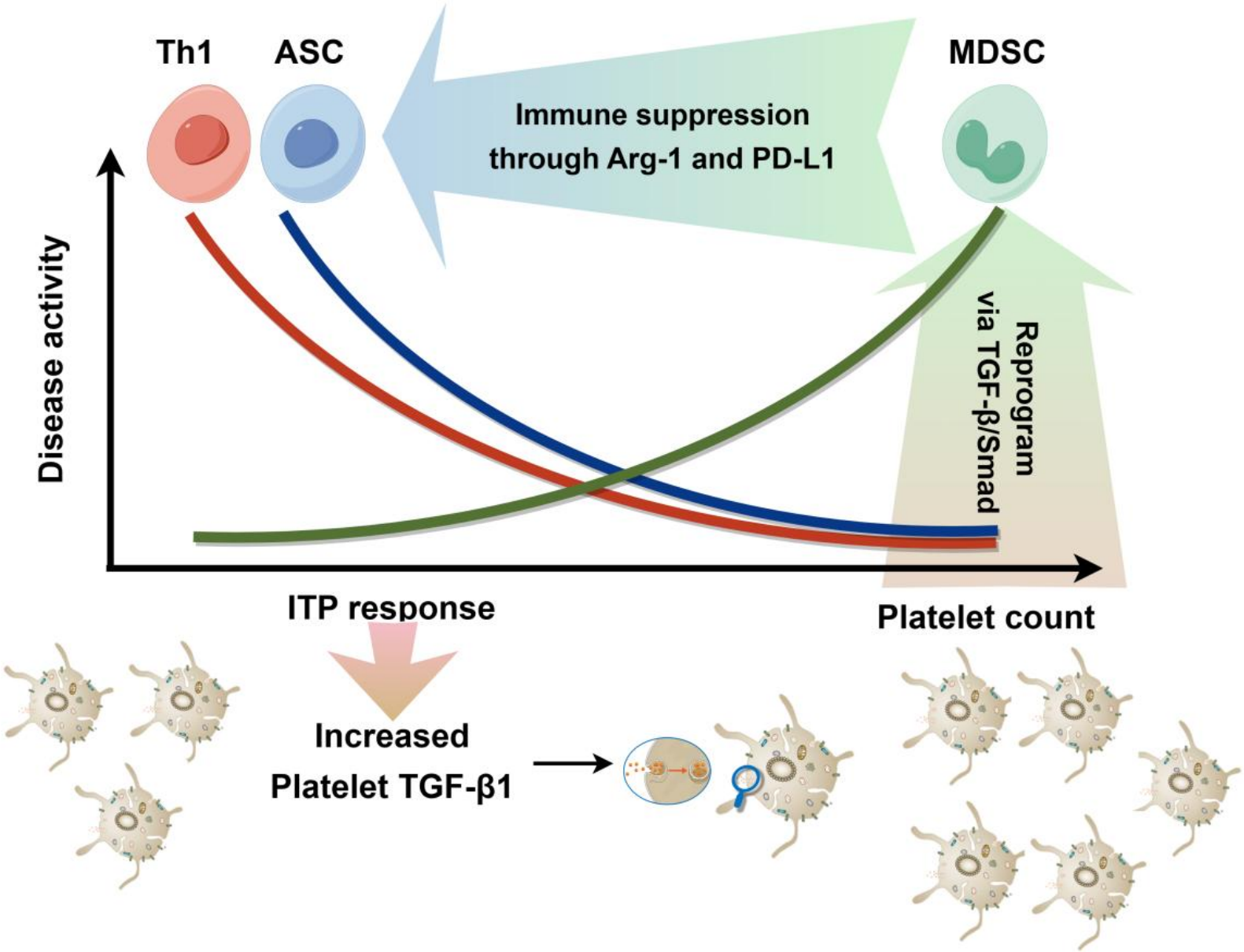
*Adapted from Marcoux et al. Platelets (2020)*

# Platelet – Treg Relationships in ITP:



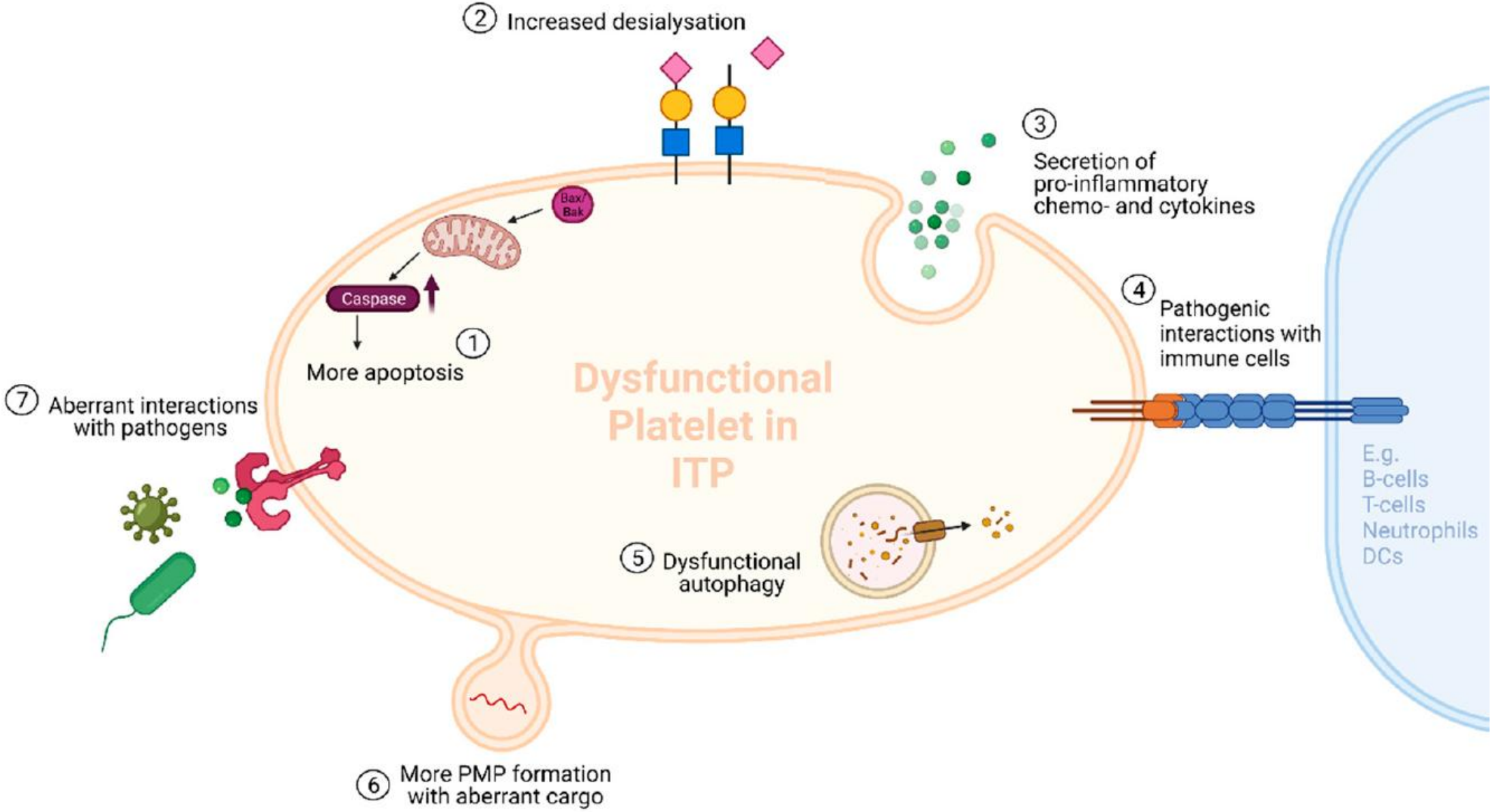

*Semple JW et al. ISBT Science Series (2020) 15, 315–319*

# Now, MDSCs have a similar relationship as Tregs




*Wang L et al. Blood 144;* 99-112, 2024

# Platelets in ITP: Victims in charge of their own fate?




*Courtesy of Rick Kapur*

*Nelson et al, Cells 2021*

# Conclusions

**Platelets are immunogenic and can be the target of potent humoral and cellular immune responses.**

**Platelets have a multitude of immune receptors and molecules that rightfully places them in the innate immune system. They can readily bind and internalize bacteria and virues.**

**Resting platelets tend to be immunosuppressive for immunity whereas activated platelets have the ability to turn on innate and adaptive immune responses.**

**Megakaryocytes, Platelets and their EVs can present antigens to T cells and the EVs can mediate immune effector reactions outside of the circulation.**

**These above properties perhaps link platelets to their immunological fate in ITP.**

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# Thank You

Questions?