Παθολογική αιμοποίηση και φλεγμονή

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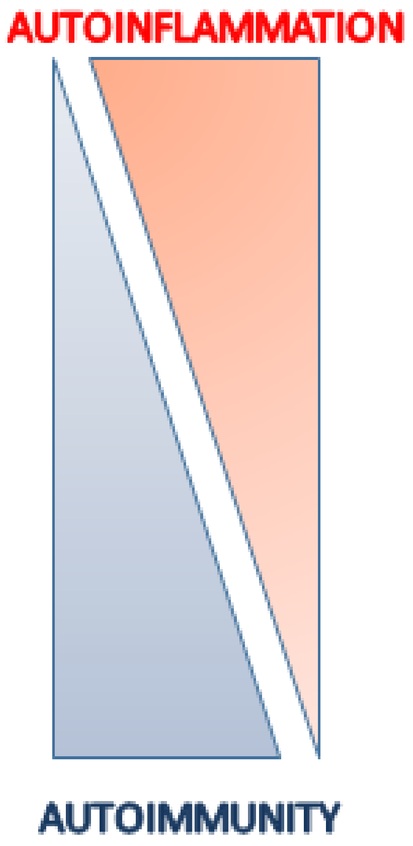
Αναπληρωτής Καθ Παθολογίας

50 ΧΡΟΝΙΑ 1973-2023

ΔΗΜΟΚΡΙΤΕΙΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΘΡΑΚΗΣ

Αυτό- φλεγμονή και ανοσία



TRAPS

FCAS

HIDS

CROHN'S DISEASE

GOUT

BEHCET'S SYNDROME

UVEITIS

RHEUMATOID ARTHRITIS

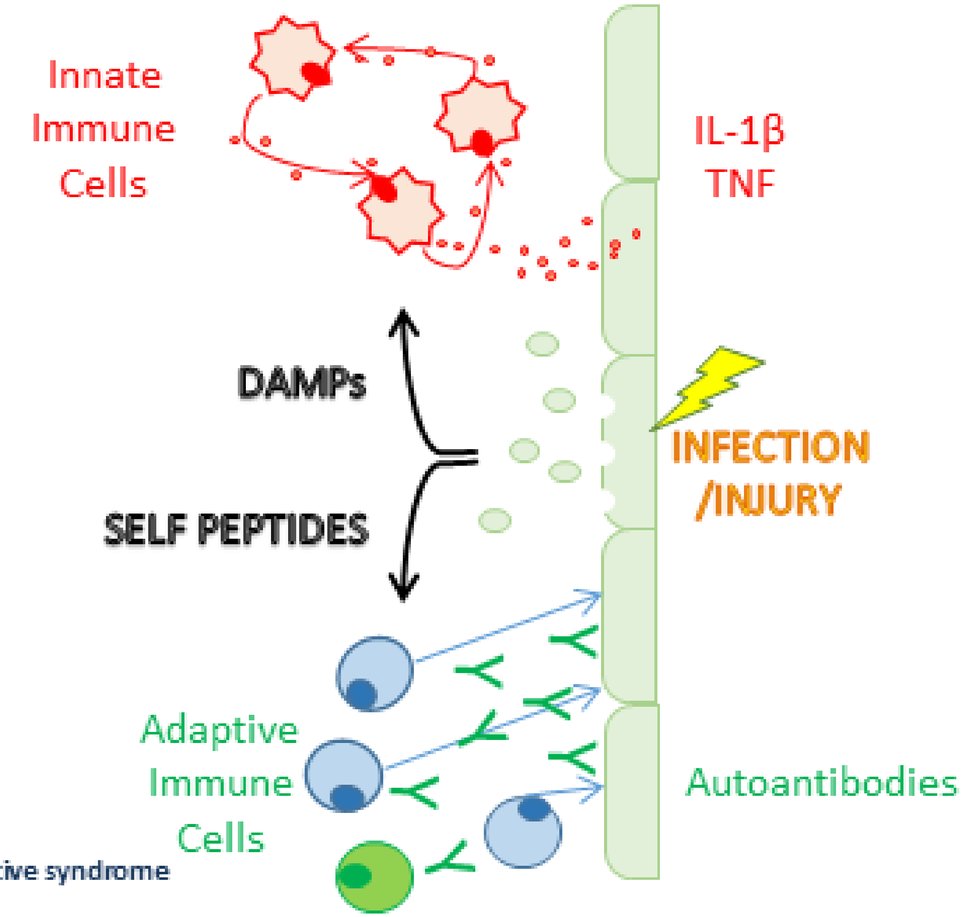
TYPE-1 DIABETES

SJORGREN SYNDROME

SYSTEMIC LUPUS ERYTHEMATOSUS

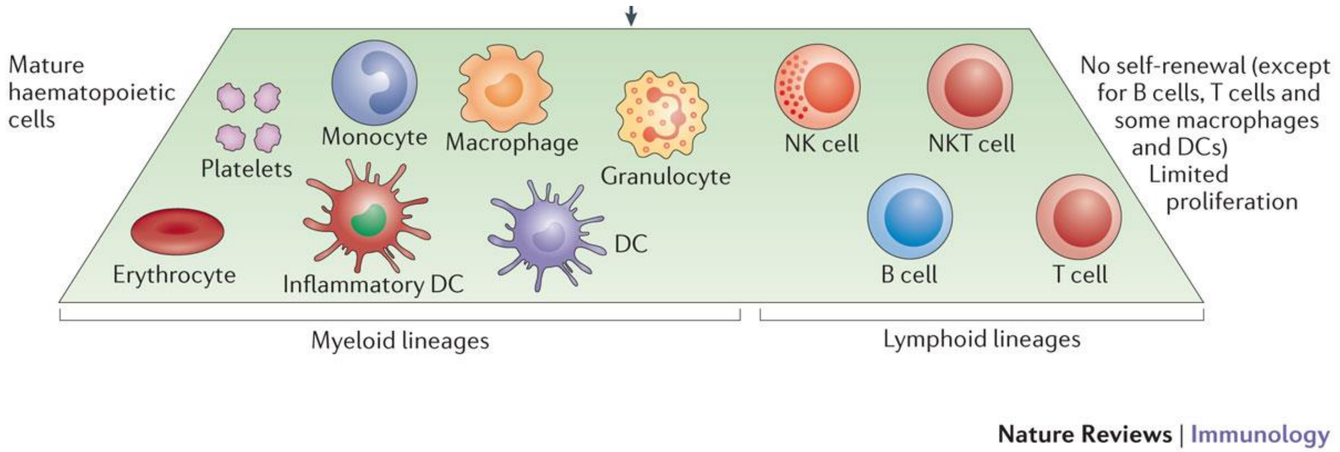
Autoimmune lymphoproliferative syndrome

IPEX



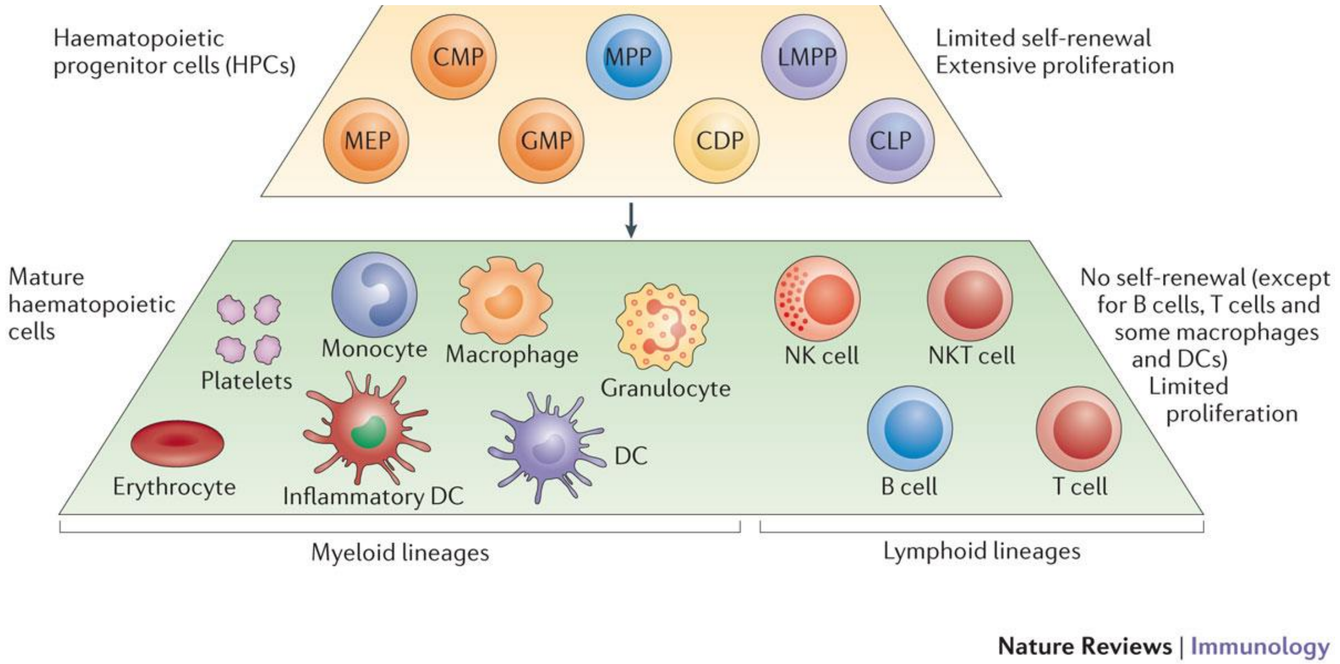
Scrambler, British s\Society of Immunology

Αιμοποιητικό-ανοσολογικό σύστημα



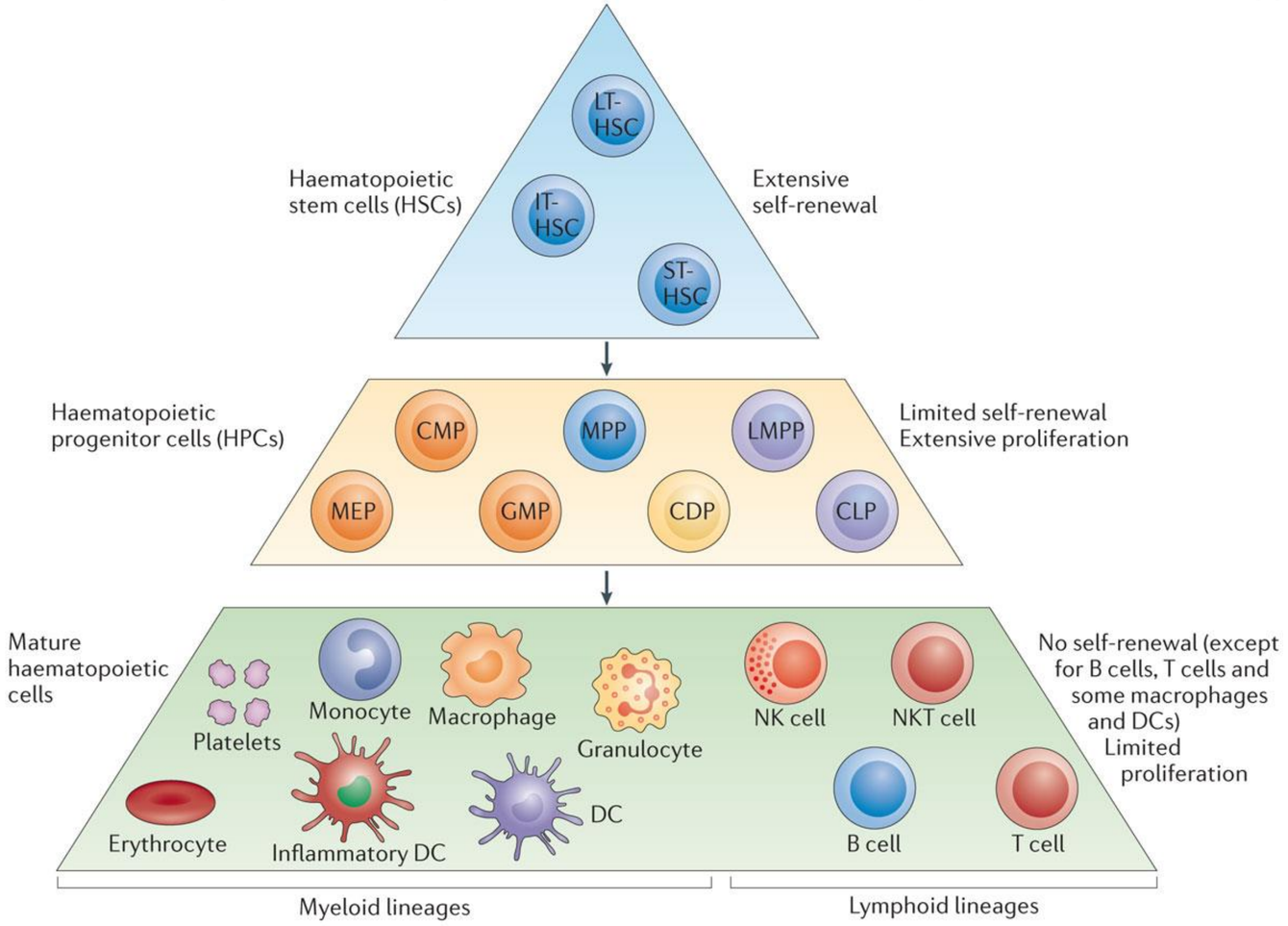
Manz and Boettcher, Nat Rev Immunol 2014

Αιμοποιητικό-ανοσολογικό σύστημα



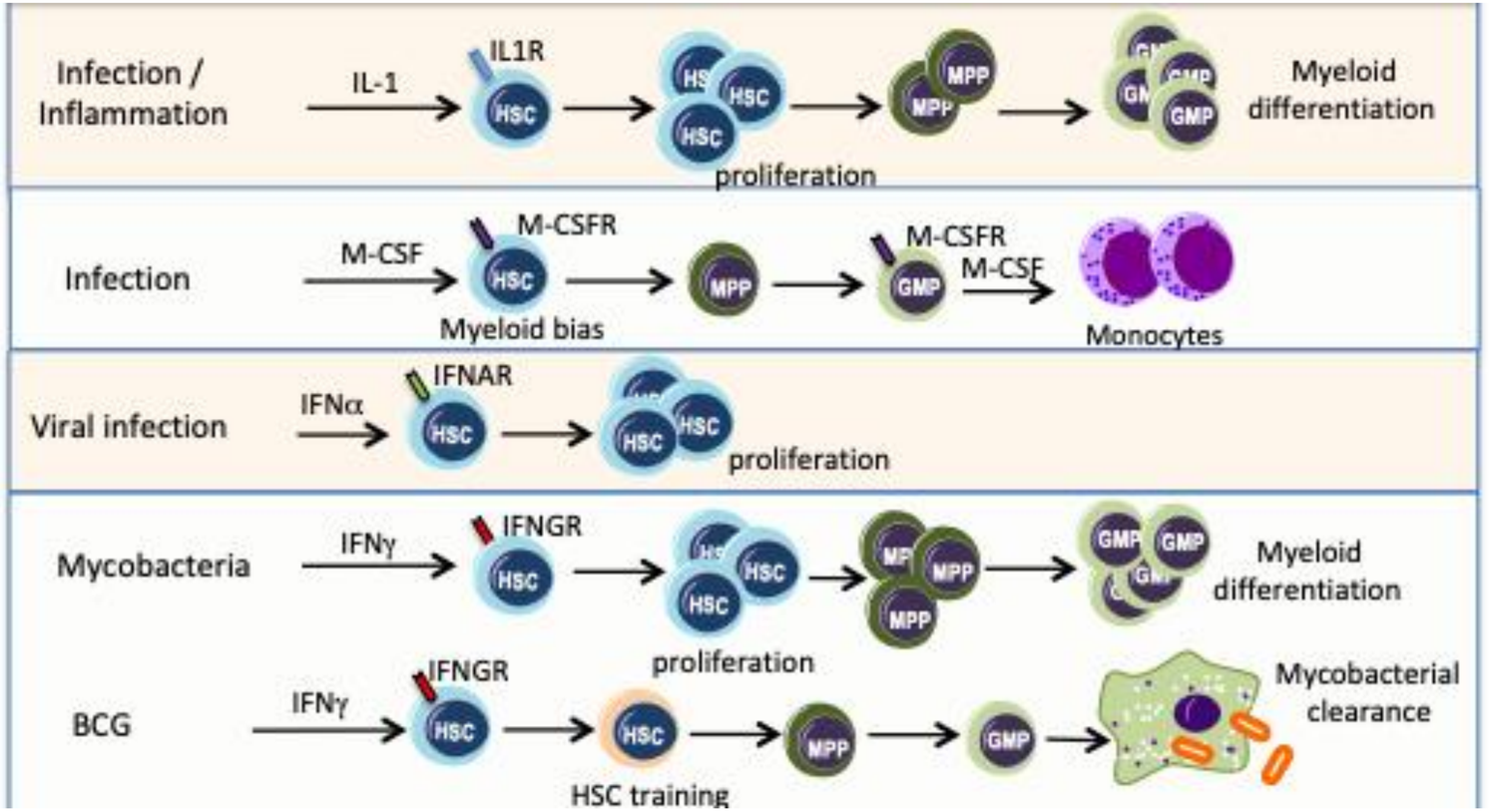
Manz and Boettcher, Nat Rev Immunol 2014

Αιμοποιητικό-ανοσολογικό σύστημα

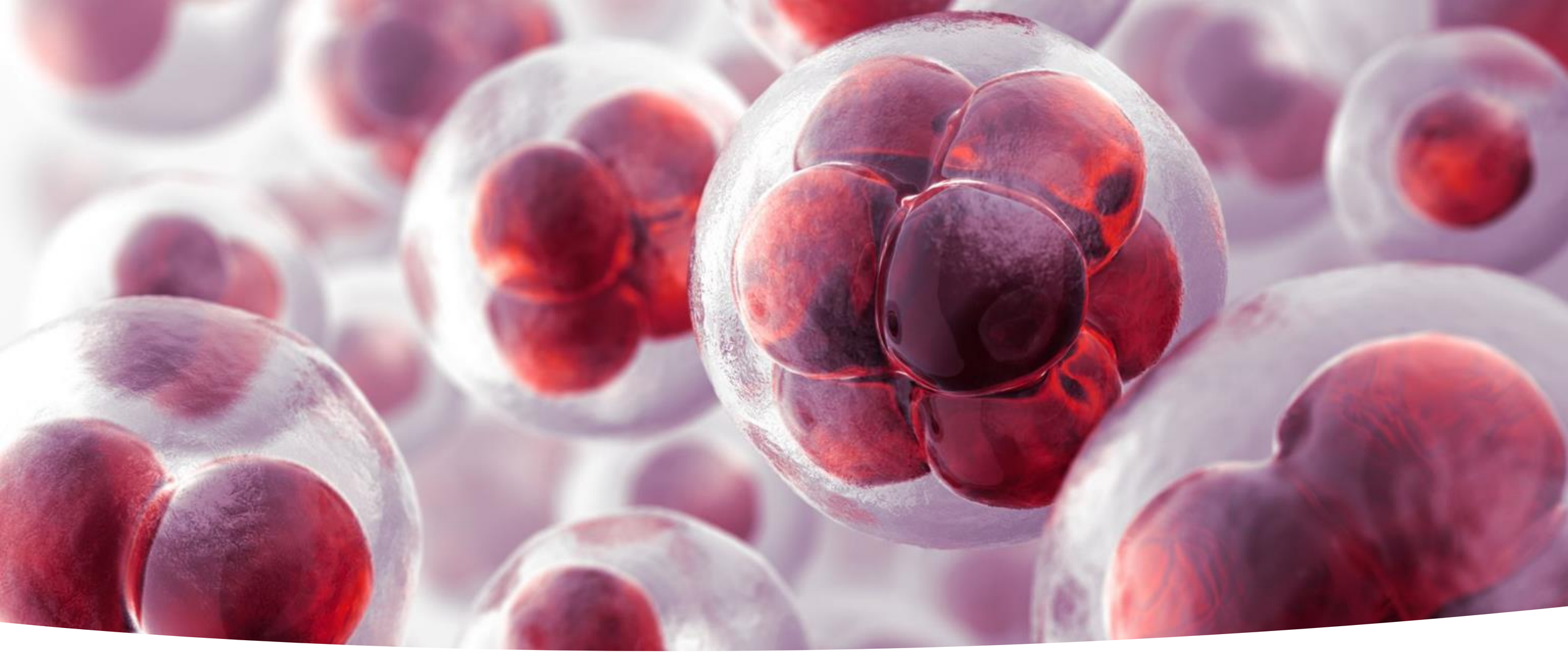


Manz and Boettcher, Nat Rev Immunol 2014

Η φλεγμονή ρυθμίζει την αιμοποίηση

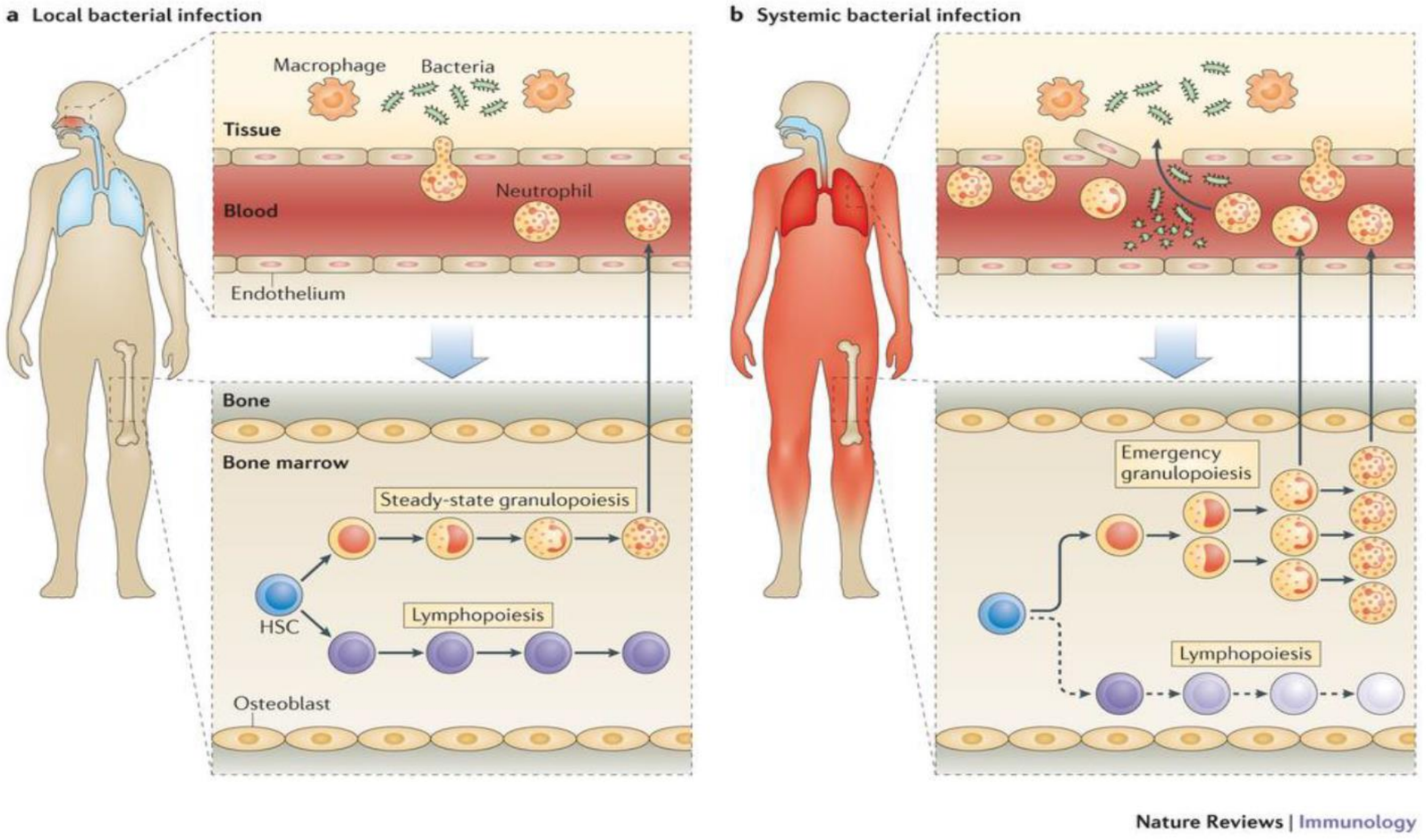


Chavakis, Mitroulis, Hajishengallis, Nat Immunol, 2019

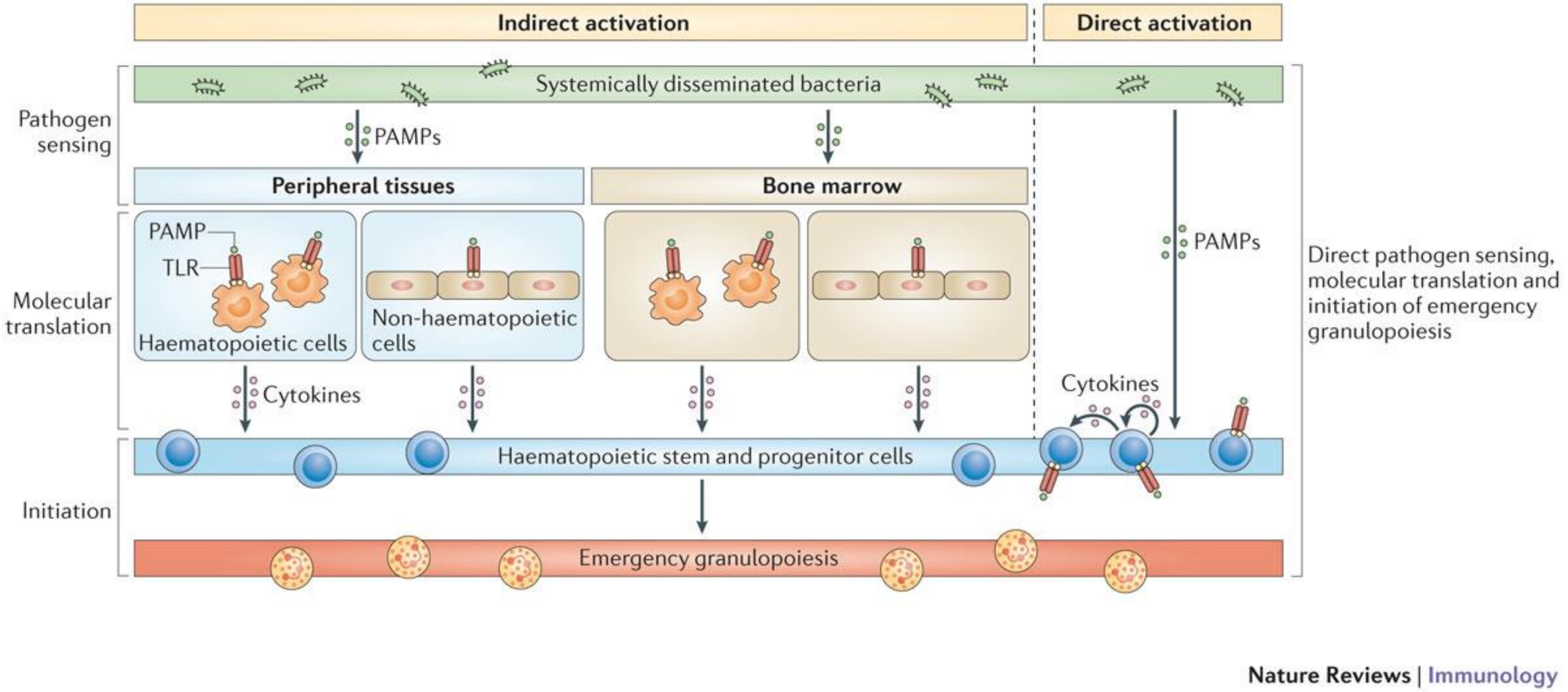


Οξεία φλεγμονή

Ενεργοποίηση της μυελοποίησης στην οξεία φλεγμονή



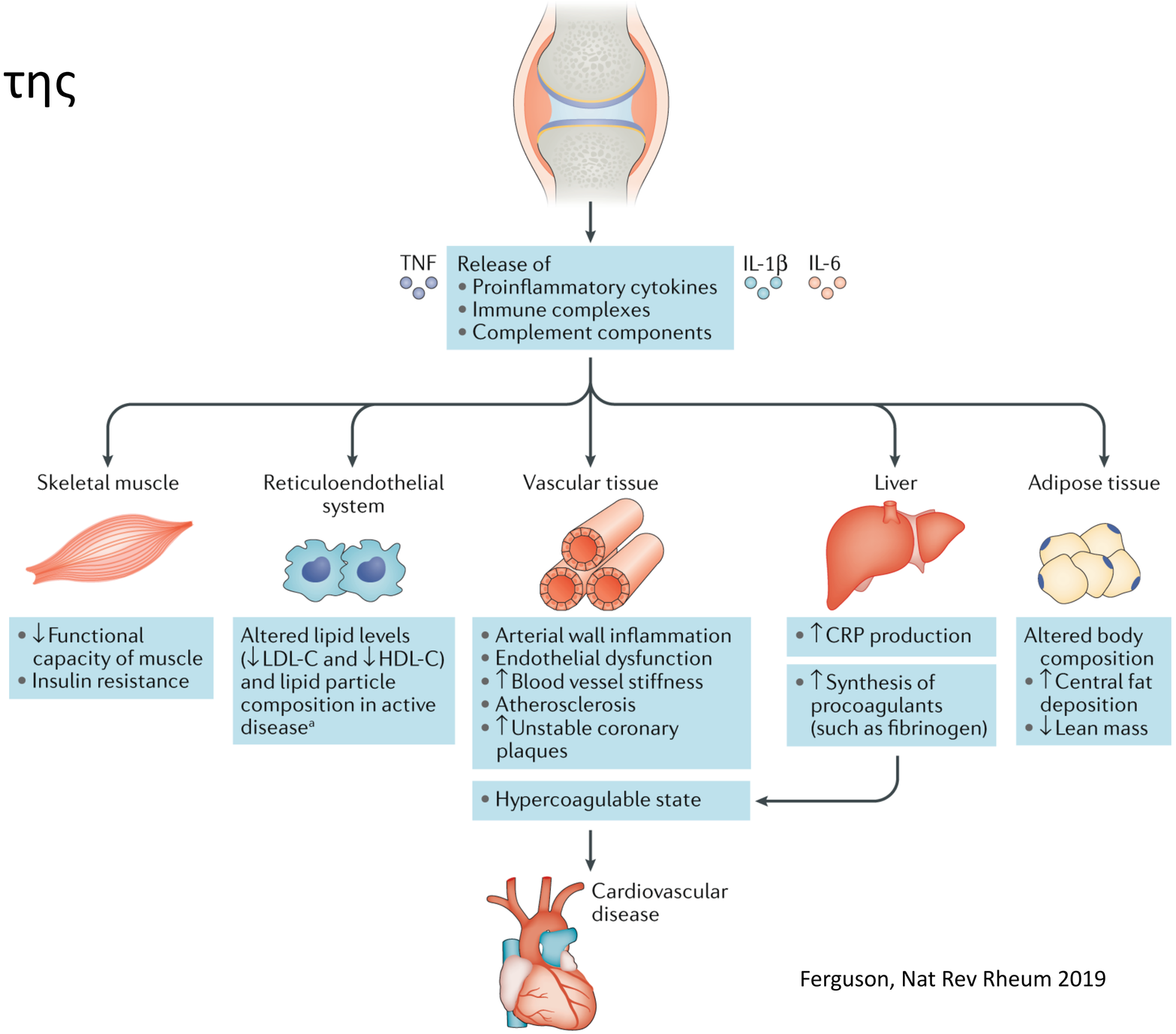
Αρχέγονα αιμοποιητικά κύτταρα και φλεγμονή



King KY and Goodell MA, Nature Reviews Immunology, 2014

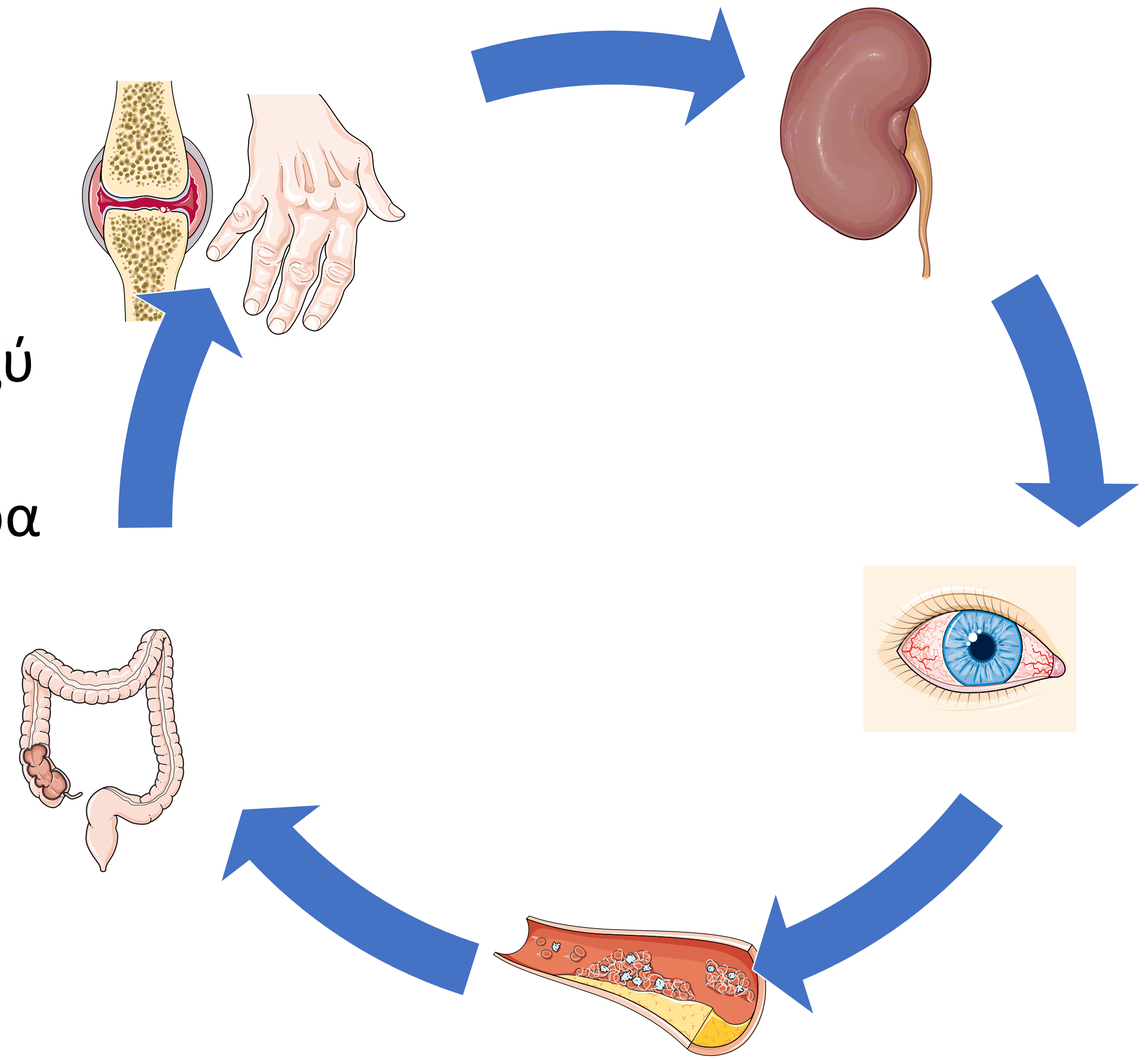
Χρόνια φλεγμονή και εκπαιδευόμενη ανοσία

Συστηματική επίδραση της φλεγμονής



Ferguson, Nat Rev Rheum 2019

Υπάρχει σύνδεση μεταξύ των φλεγμονωδών εκδηλώσεων σε διάφορα όργανα?



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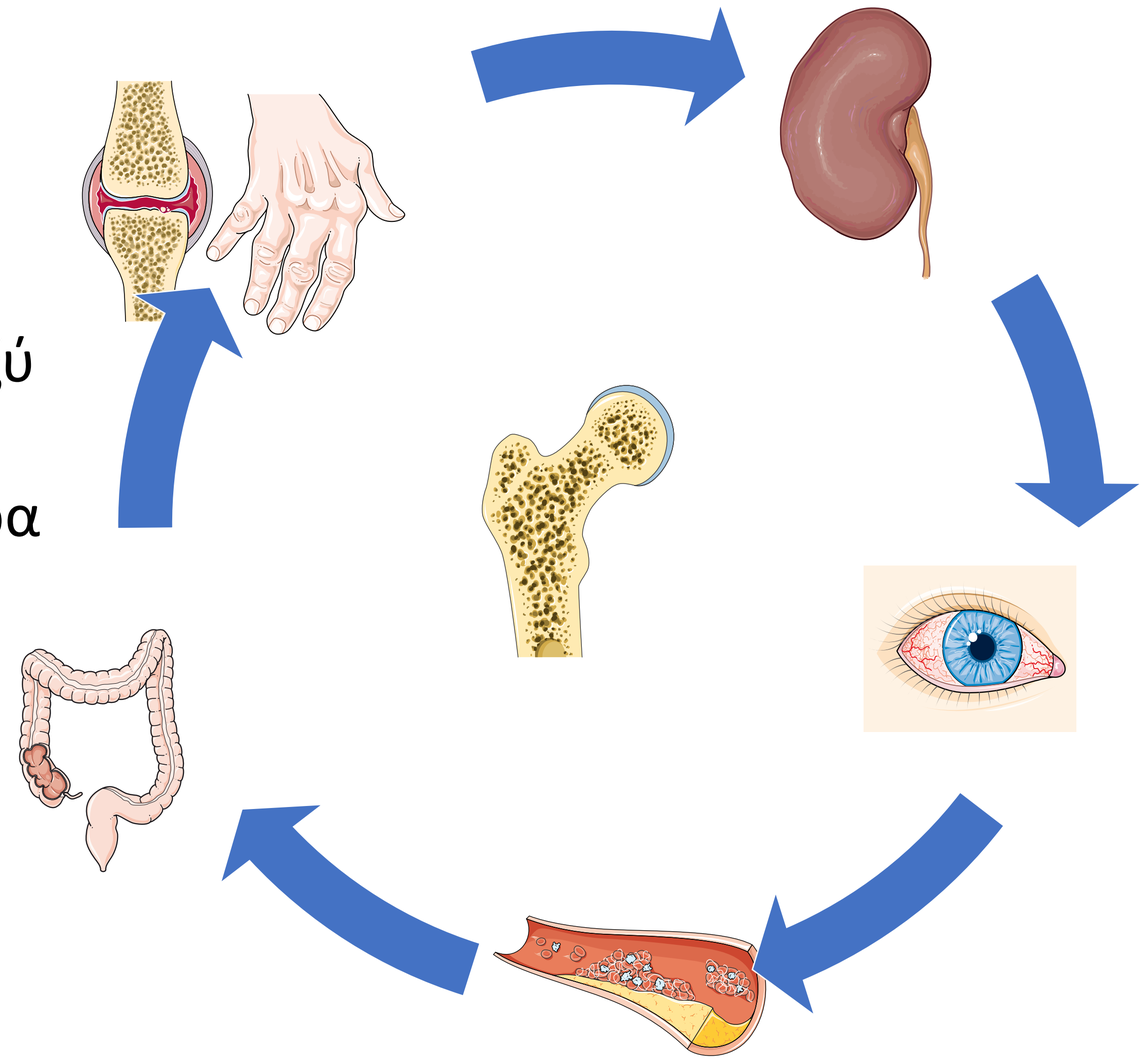
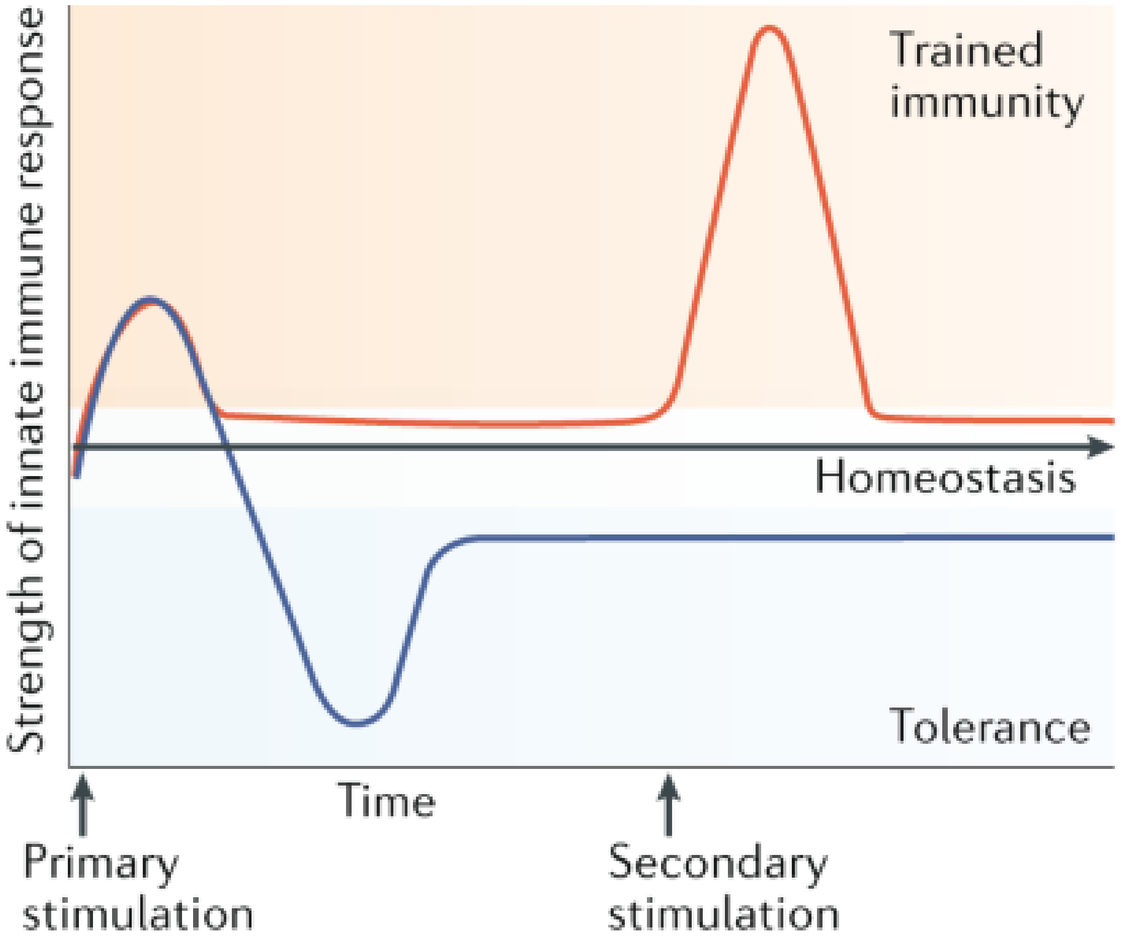
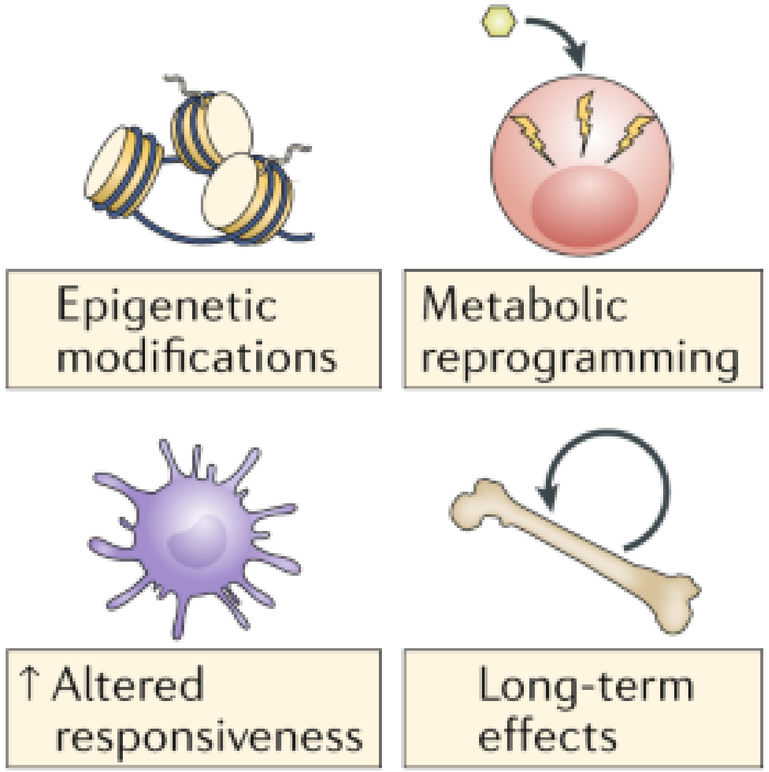


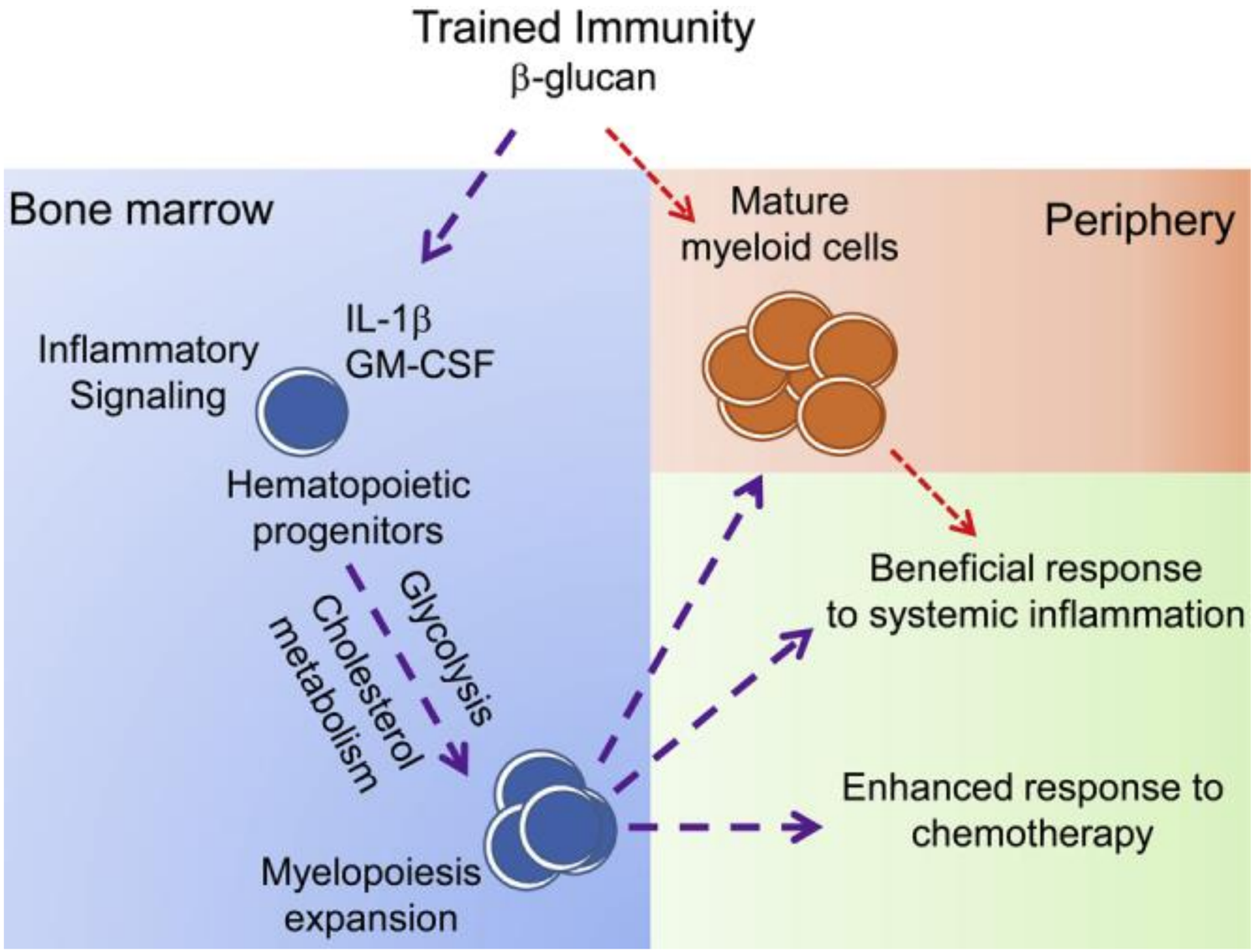
Εκπαιδευόμενη ανοσία





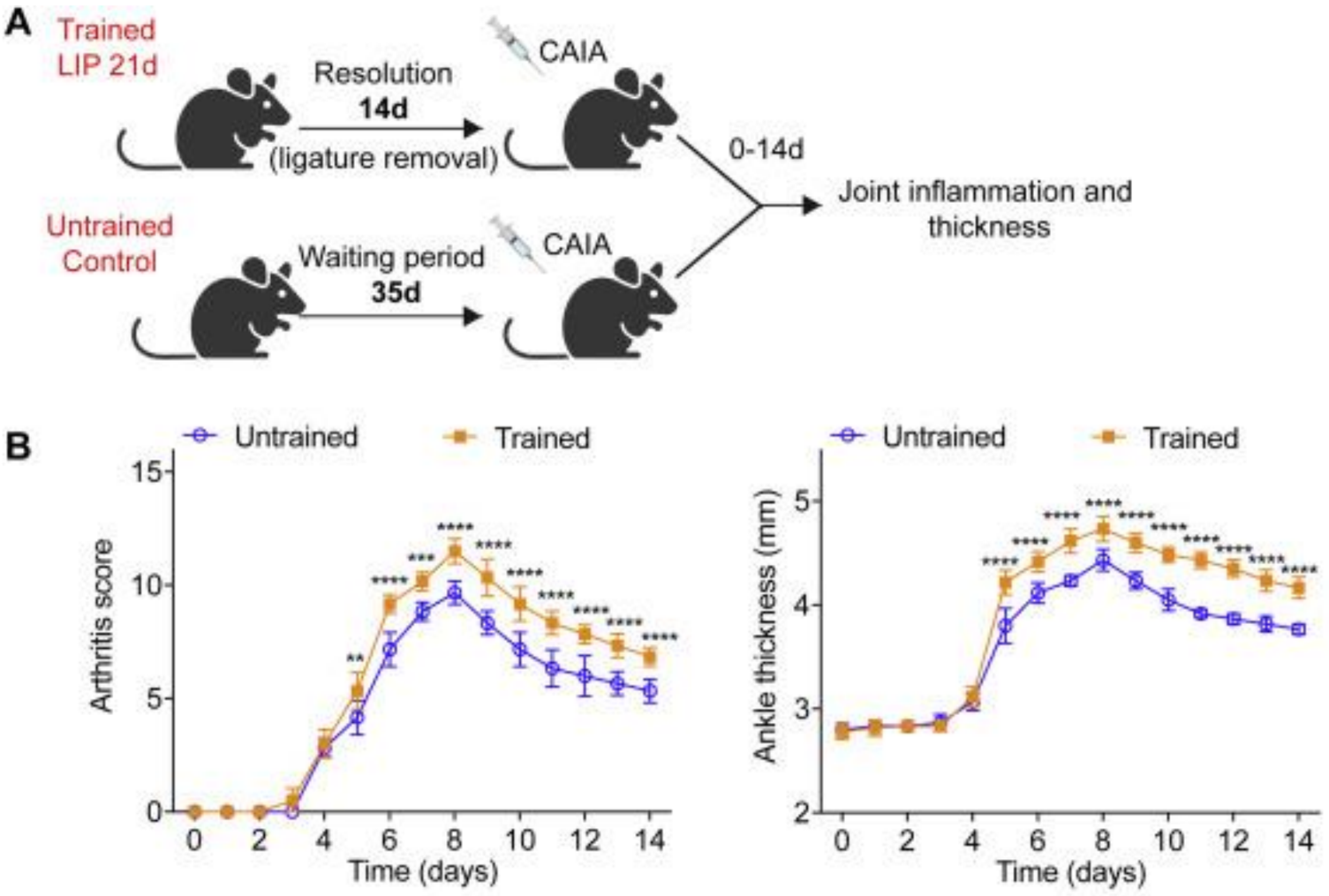
Netea et al, Nat Rev Immunol, 2020

Η IL-1β προκαλεί μακροχρόνιες μεταβολές στα προγονικά κύτταρα



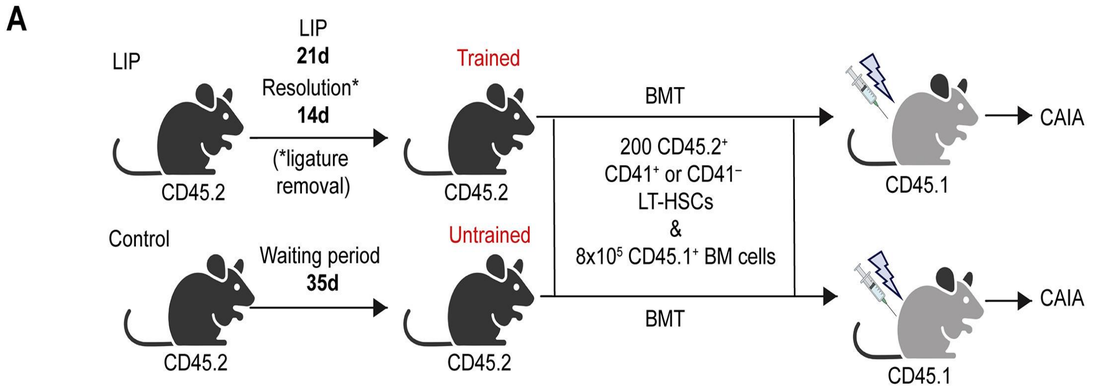
Mitroulis et al, Cell, 2018

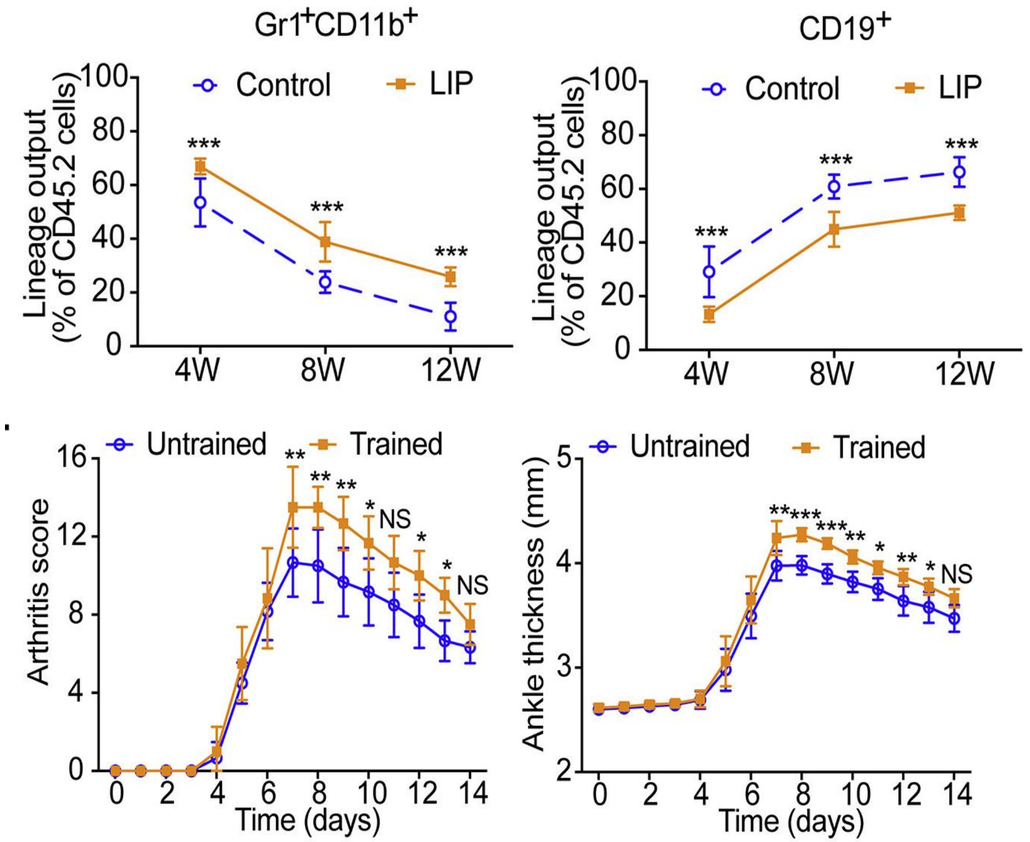
Η ενεργοποίηση της μυελοποίησης οδηγεί στην παραγωγή φλεγμονωδών κυττάρων που ενισχύουν τη φλεγμονή σε όργανα στόχους



Li et al, Cell 2022

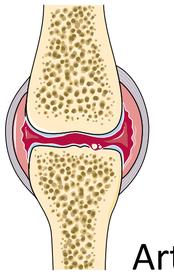
Εκπαίδευση των αρχέγονων αιμοποιητικών κυττάρων σε ρευματικά νοσήματα



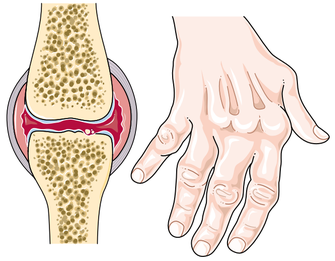


Li et al, Cell 2022

Ο μυελός των οστών ως σταυροδρόμι για τη σύνδεση φλεγμονωδών εκδηλώσεων



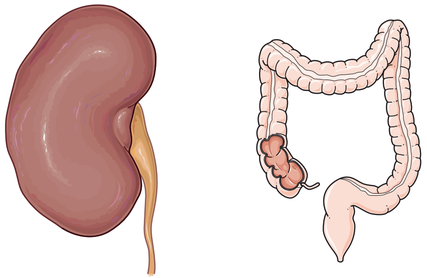
Arthritis



Cytokines (IL-1, TNF, IL6)

Growth factors

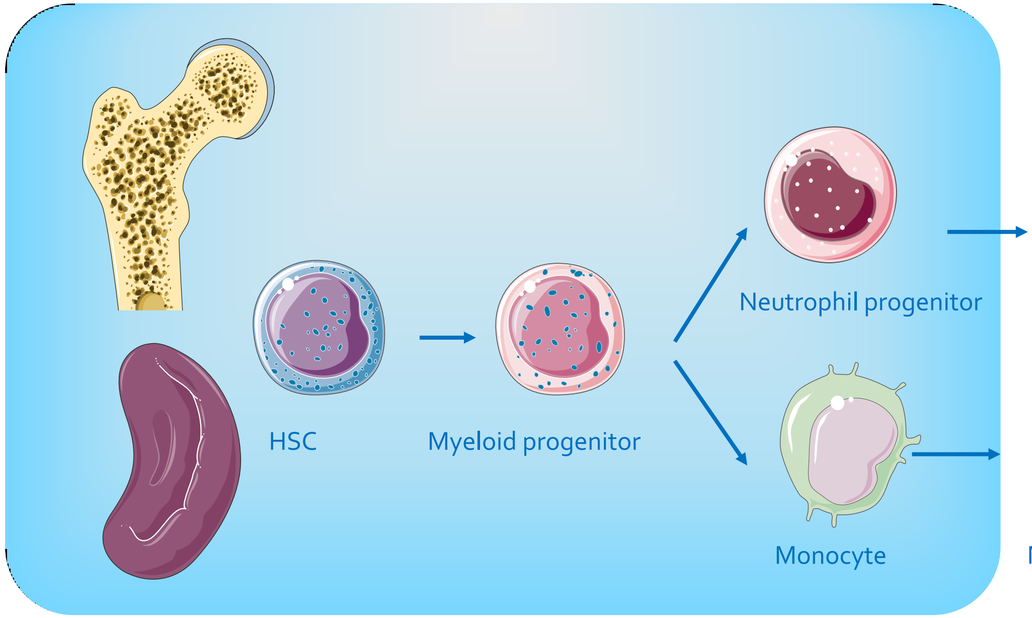
(M-CSF, GM-CSF, G-CSF)

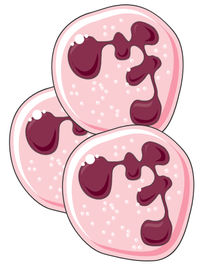


Inflammatory

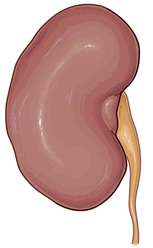
and

autoimmune disorders

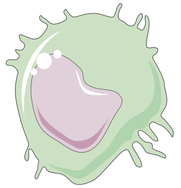




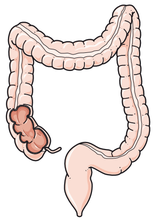
Neutrophil granulocyte



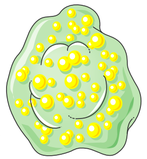
Renal manifestations



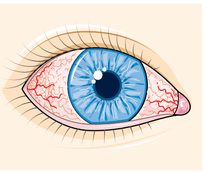
Macrophage



Colitis

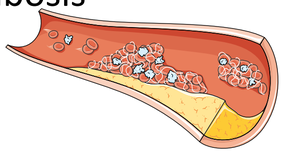


Foam cell

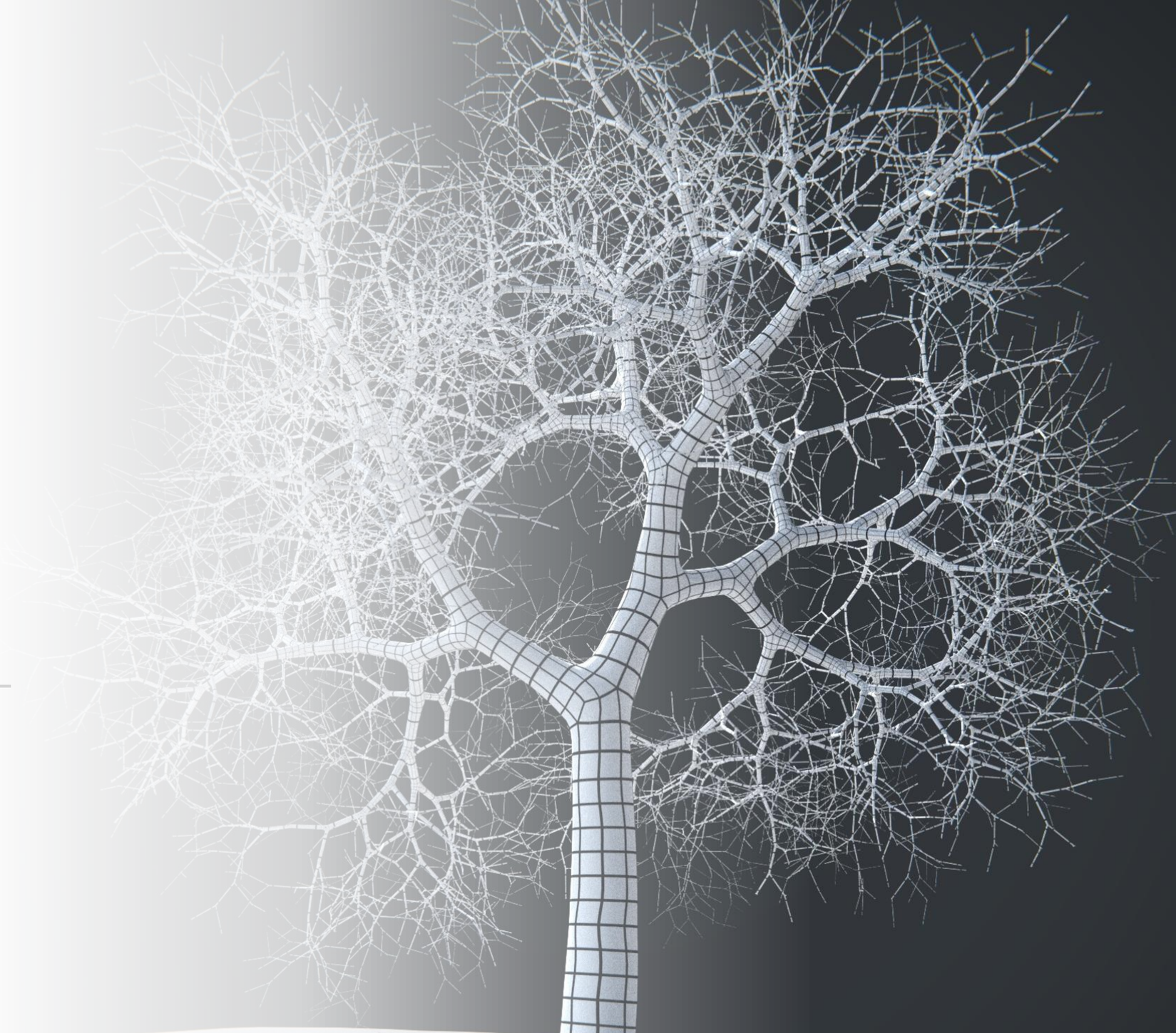


Ocular manifestations

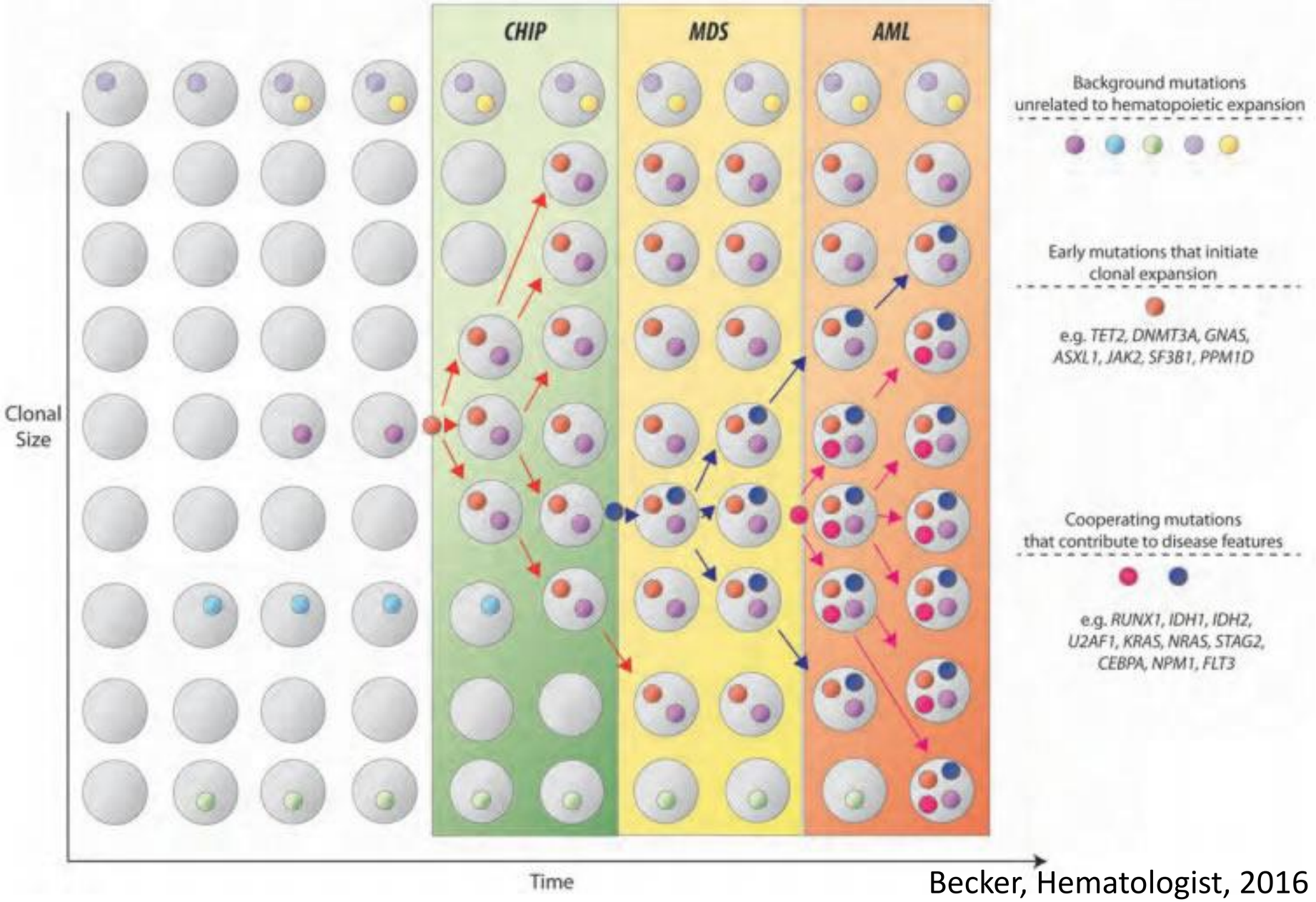
Atherothrombosis



Κλωνική Αιμοποίηση



A Model of Clonal Expansion and Clonal Evolution from Normal Hematopoeisis to Myelodysplasia and Myeloid Leukemia

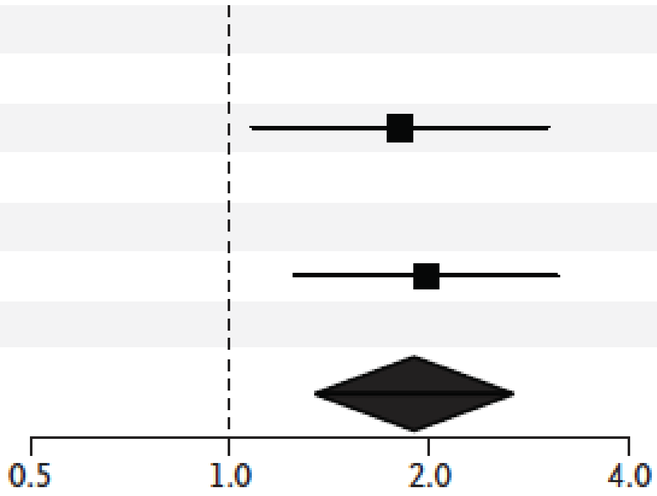


Becker, Hematologist, 2016

CHIP και καρδιαγγειακός κίνδυνος

A CHIP and Coronary Heart Disease

Subgroup	No. of Participants with Coronary Heart Disease/ No. at Risk	Hazard Ratio (95% CI)	P Value
BioImage			
No mutation (reference)	94/326		
Mutation	19/44	1.8 (1.1–2.9)	0.03
MDC			
No mutation (reference)	299/607		
Mutation	21/33	2.0 (1.2–3.1)	0.003
Fixed-effects meta-analysis		**1.9 (1.4–2.7)**	**<0.001**

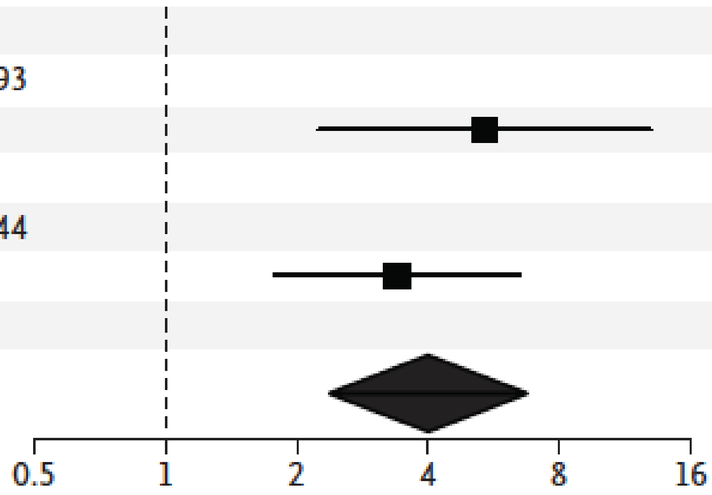


Jaiswal et, NEJM, 2017

CHIP και καρδιαγγειακός κίνδυνος

B CHIP and Early-Onset Myocardial Infarction

Subgroup	No. of Participants with Myocardial Infarction/ No. at Risk	Odds Ratio (95% CI)	P Value
ATVB			
No mutation (reference)	1716/3293		
Mutation	37/43	5.4 (2.3–13.0)	<0.001
PROMIS			
No mutation (reference)	2488/3844		
Mutation	52/65	3.4 (1.8–6.5)	<0.001
Fixed-effects meta-analysis		**4.0 (2.4–6.7)**	**<0.001**

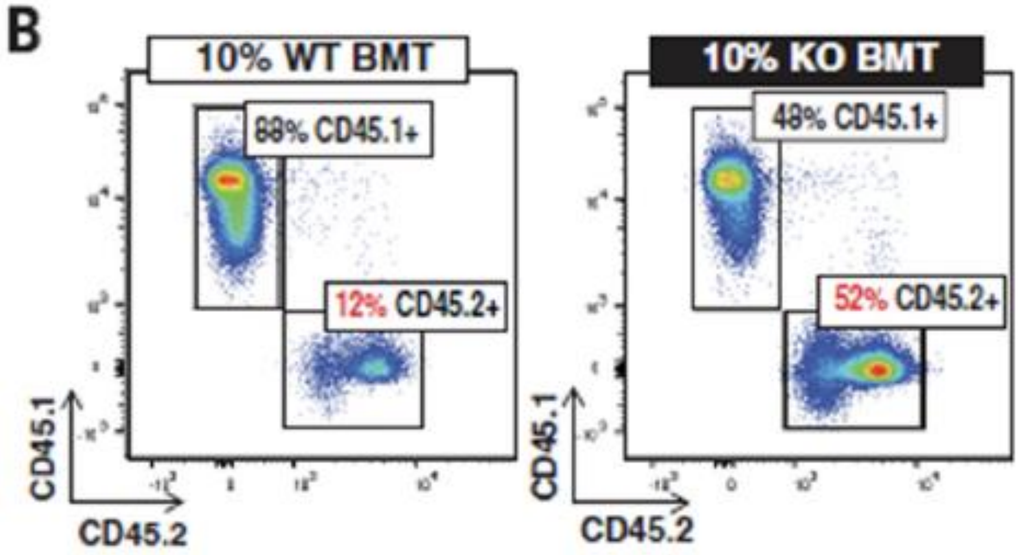


Jaiswal et, NEJM, 2017

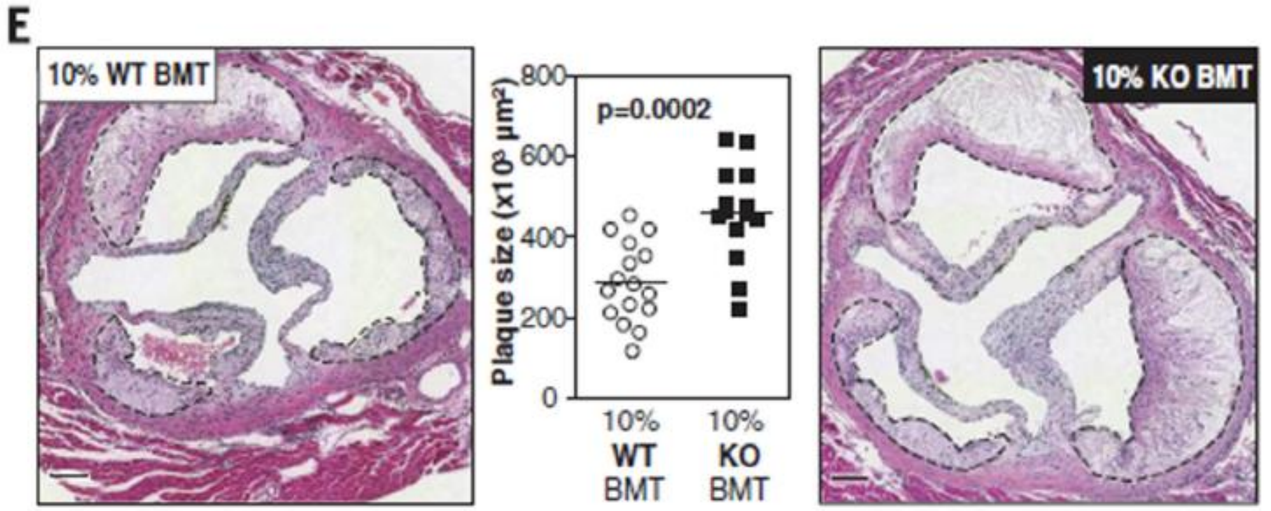
When primary pathogenetic events are unknown, control of inflammation is sometimes the next best option.

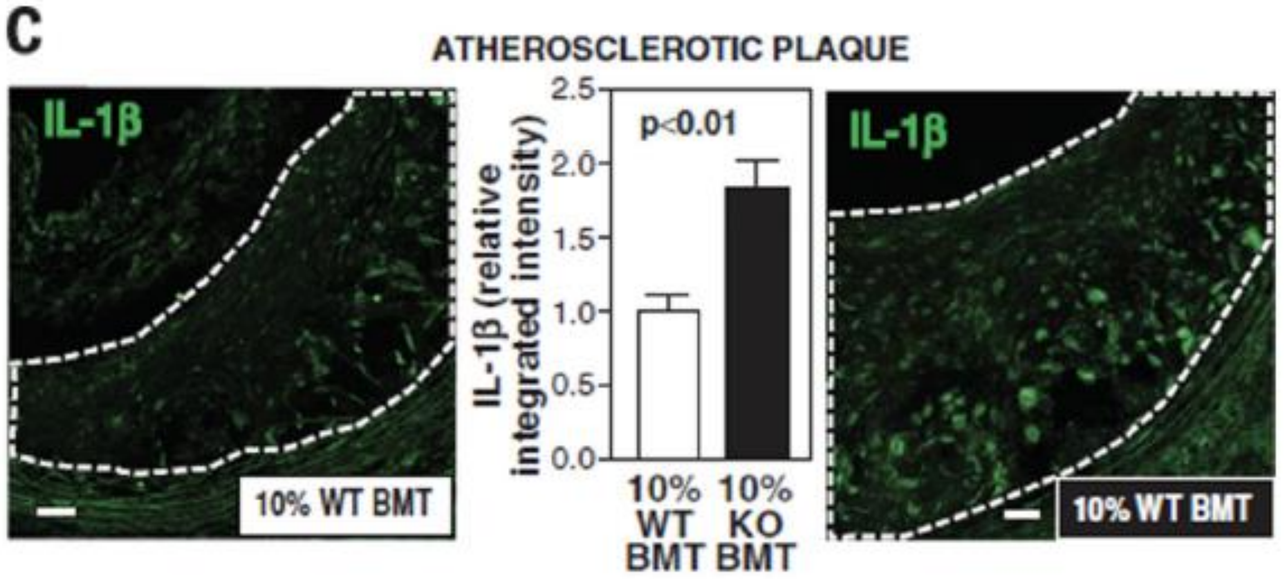
Carl Nathan, 2002

Η IL-1β ευθύνεται για την επιταχυνόμενη αθηρωμάτωση στην CHIP



chimeric Ldlr-/- mice

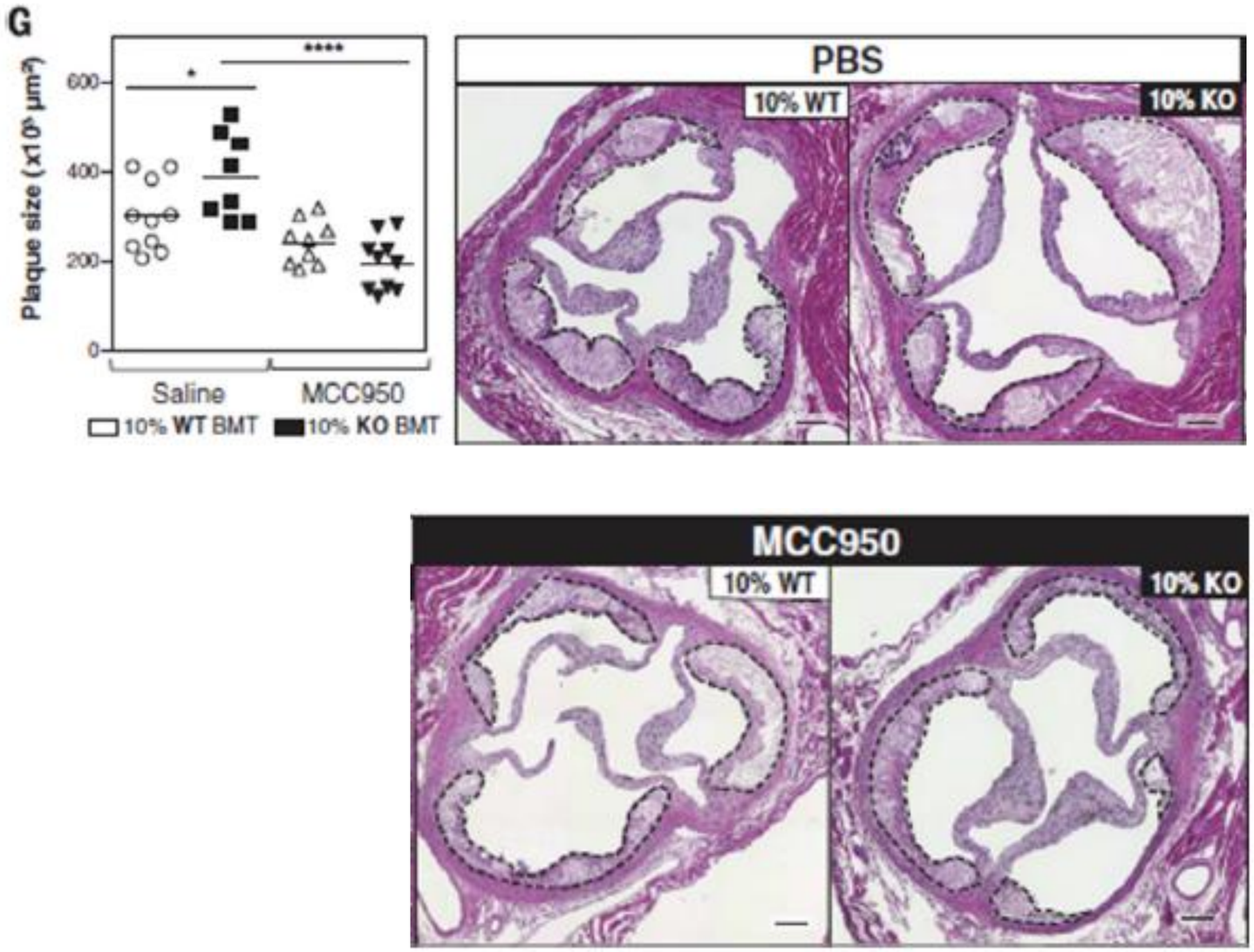




Αυξημένη παραγωγή IL-1β

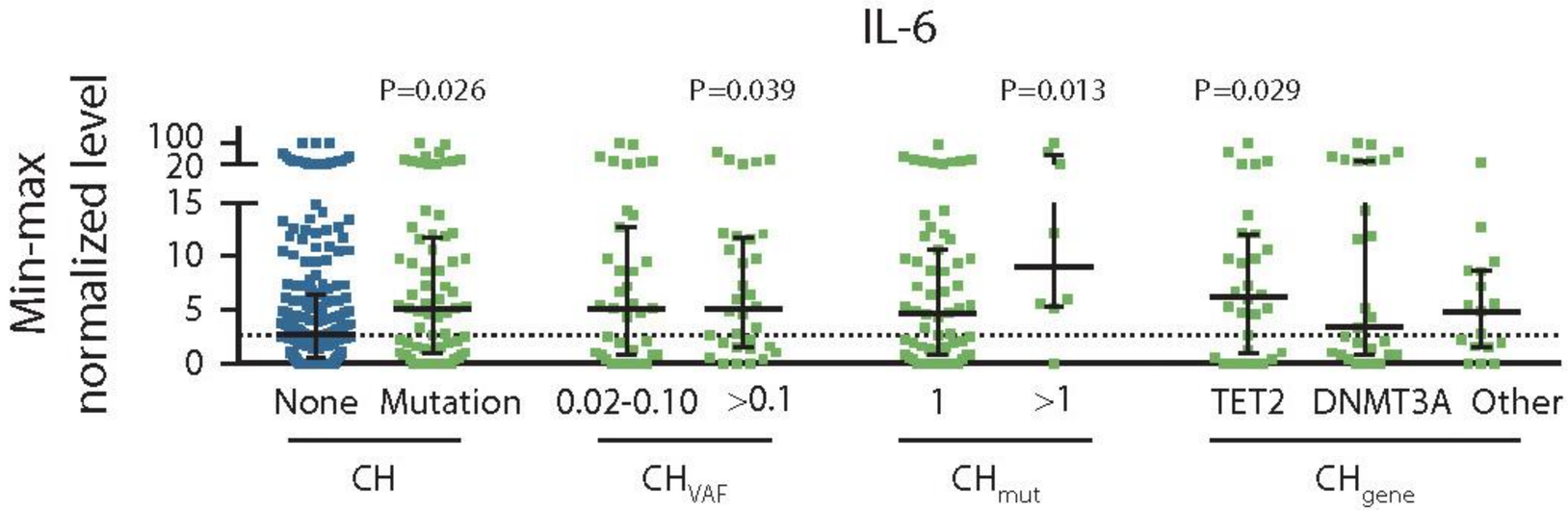
Fuster et al, Science 2017

Η IL-1β ευθύνεται για την επιταχυνόμενη αθηρωμάτωση στην CHIP



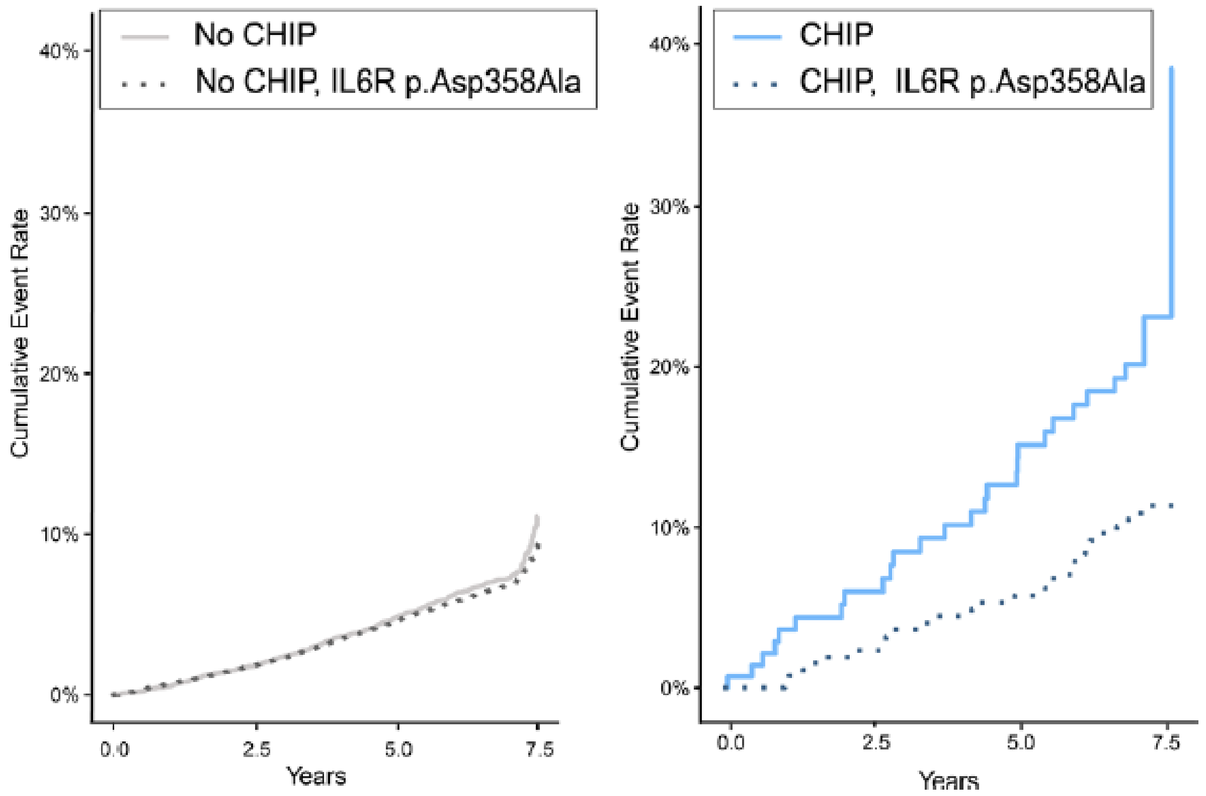
Fuster et al, Science 2017

Ο ρόλος της IL-6

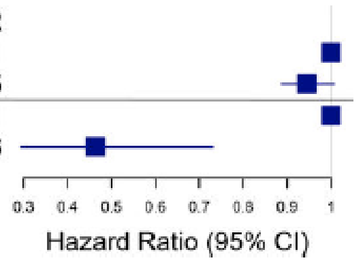


Cook et al, Blood Adv, 2021

Πολυμορφισμοί στον IL-6R ελαττώνουν τον καρδιαγγειακό κίνδυνο σε ασθενείς CHIP

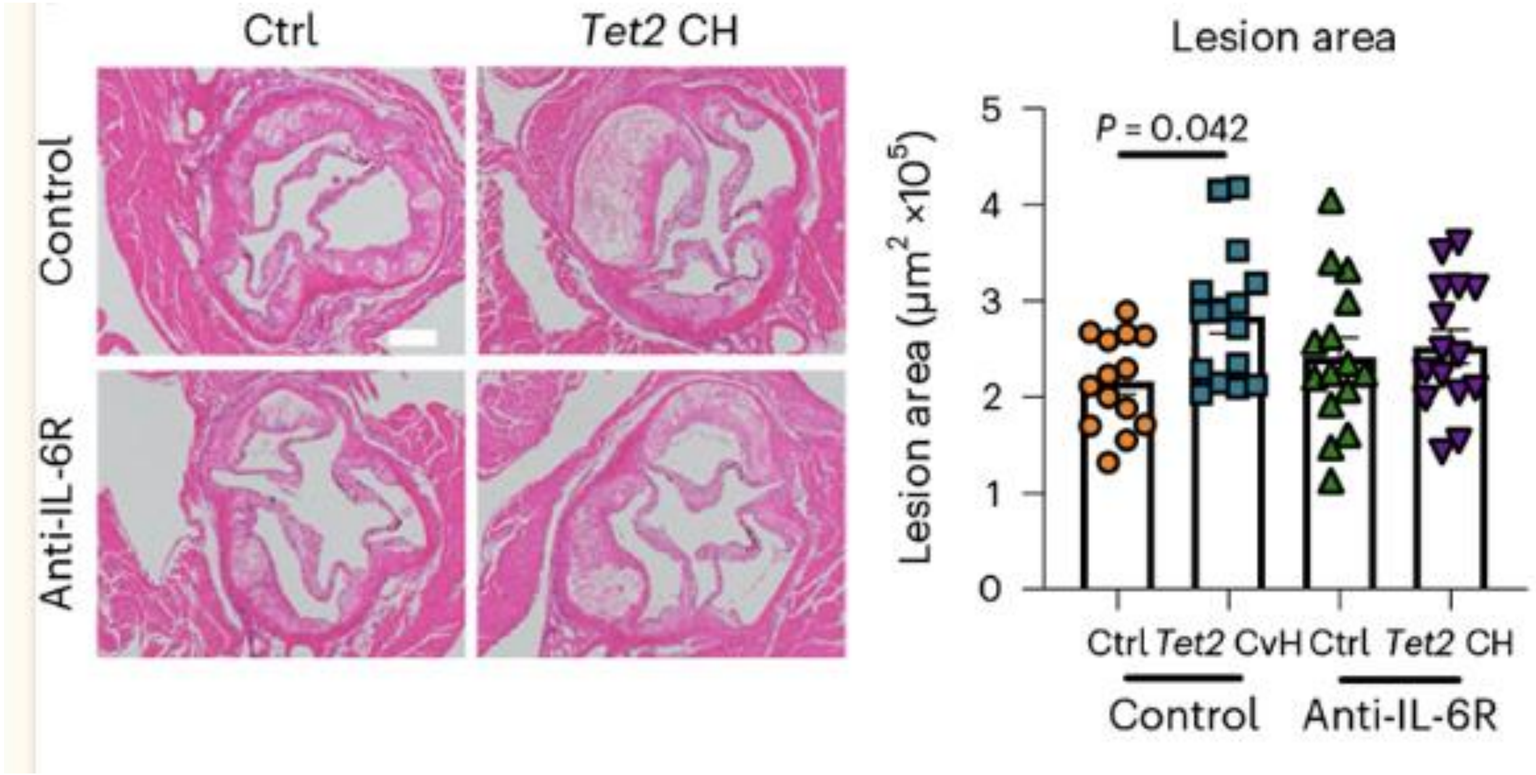


Group	At risk	Incident Events	P−value	HR
No CHIP	11874	703		1
No CHIP, IL6R p.Asp358Ala	22463	1248	0.083	0.95
CHIP	143	27		1
CHIP, IL6R p.Asp358Ala	289	26	0.00095	0.46



Pick et al, Circulation 2020

Αναστολή της IL6 ελαττώνει το ρυθμό εξέλιξης της αθηρωμάτωσης σε μοντέλο CHIP



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Published online 2023 Jun 8. doi: 10.1038/s44161-023-00281-3

PMCID: PMC10399458
NIHMSID: NIHMS1907595
PMID: 37539077

Blockade of IL-6 signaling alleviates atherosclerosis in *Tet2*-deficient clonal hematopoiesis

Wenli Liu,[1,11,✉] Mustafa Yalcinkaya,[1] Inés Fernández Maestre,[2,3] Malgorzata Olszewska,[4,5,6] Patrick B. Ampomah,[7] J. Brett Heimlich,[8] Ranran Wang,[1] Pablo Sánchez Vela,[2] Tong Xiao,[1] Alexander G. Bick,[9] Ross Levine,[2] Eirini P. Papapetrou,[4,5,6] Peter Libby,[10] Ira Tabas,[1] Nan Wang,[1,11,✉] and Alan R. Tall[1,11,✉]

CHIP and gout: trained immunity?

Tony R. Merriman[1] and Leo A. B. Joosten[2] | [1]University of Alabama at Birmingham and [2]Iuliu Haieganu University of Medicine and Pharmacy

In this issue of *Blood*, Agrawal et al[1] identified clonal hematopoiesis of indeterminate potential (CHIP) as a risk factor for gout, a common inflammatory arthritis that is defined by an NLRP3-inflammasome and an interleukin-1β (IL-1β)–dependent innate immune system response to monosodium urate (MSU) crystals.

Savola et al. *Blood Cancer Journal* (2018)8:69
DOI 10.1038/s41408-018-0107-2

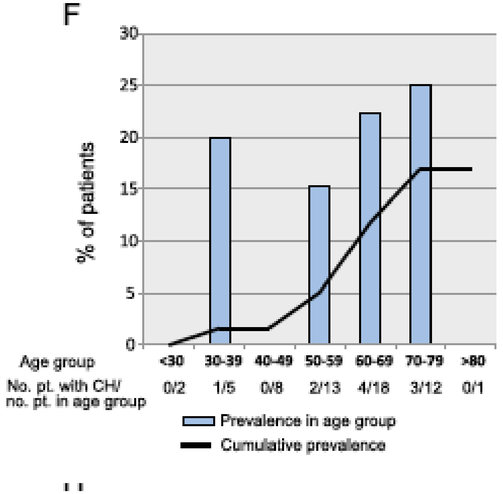
Blood Cancer Journal

CORRESPONDENCE Open Access

Clonal hematopoiesis in patients with rheumatoid arthritis

Paula Savola[1,2], Sofie Lundgren[1,2], Mikko A. I. Keränen[1], Henrikki Almusa[3], Pekka Ellonen[3], Marjatta Leirisalo-Repo[4], Tiina Kelkka[1,2] and Satu Mustjoki[1,2]

F



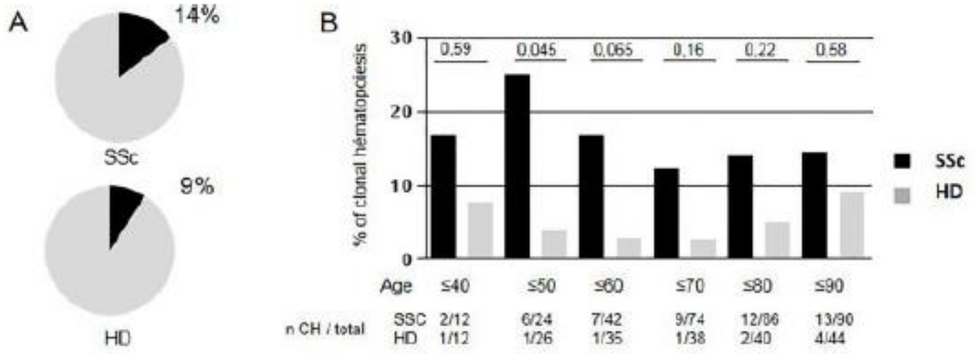
RHEUMATOLOGY

Rheumatology 2020;59:3499–3504
doi:10.1093/rheumatology/keaa282
Advance Access publication 5 August 2020

Concise report

Clonal haematopoiesis is increased in early onset in systemic sclerosis

Laure Ricard[1,2,*], Pierre Hirsch[1,3,*], Laëtitia Largeaud[1,3], Caroline Deswarte[1], Vincent Jachiet[1,2], Mohamad Mohty[1,4], Sébastien Rivière[2], Florent Malard[1,4], Maxime Tenon[1], Frédéric de Vassoigne[5], Olivier Fain[1,2], Béatrice Gaugler[1,4], Julien Rossignol[6], François Delhommeau[1,3] and Arsène Mekinian[1,2]; on behalf MINHEMON (French Network of dysimmune disorders associated with



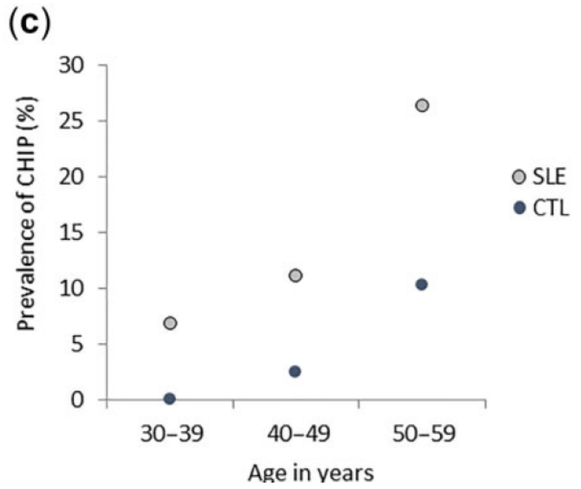
RHEUMATOLOGY

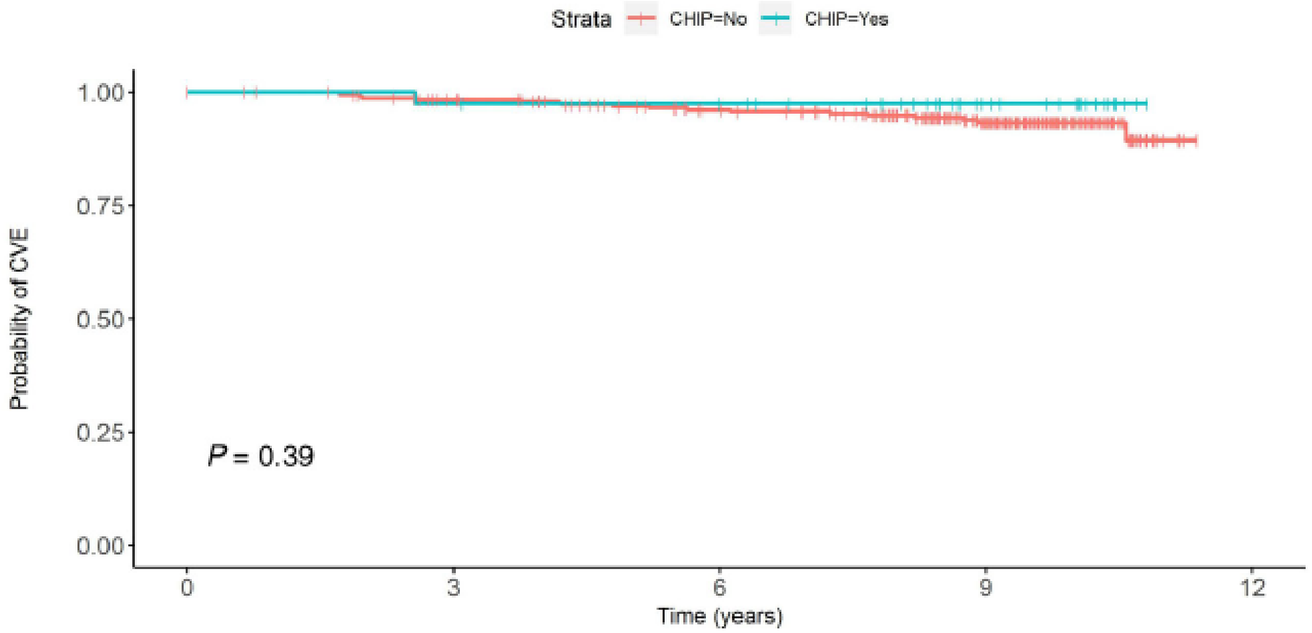
Rheumatology 2022;61:4355–4363
https://doi.org/10.1093/rheumatology/keac108
Advance access publication 17 February 2022

Original article

Clonal haematopoiesis of indeterminate potential and cardiovascular events in systemic lupus erythematosus (HEMATOPLUS study)

Αυξημένη συχνότητα CHIP στον SLE χωρίς επίπτωση στην εμφάνιση καρδιαγγειακών επεισοδίων





RHEUMATOLOGY

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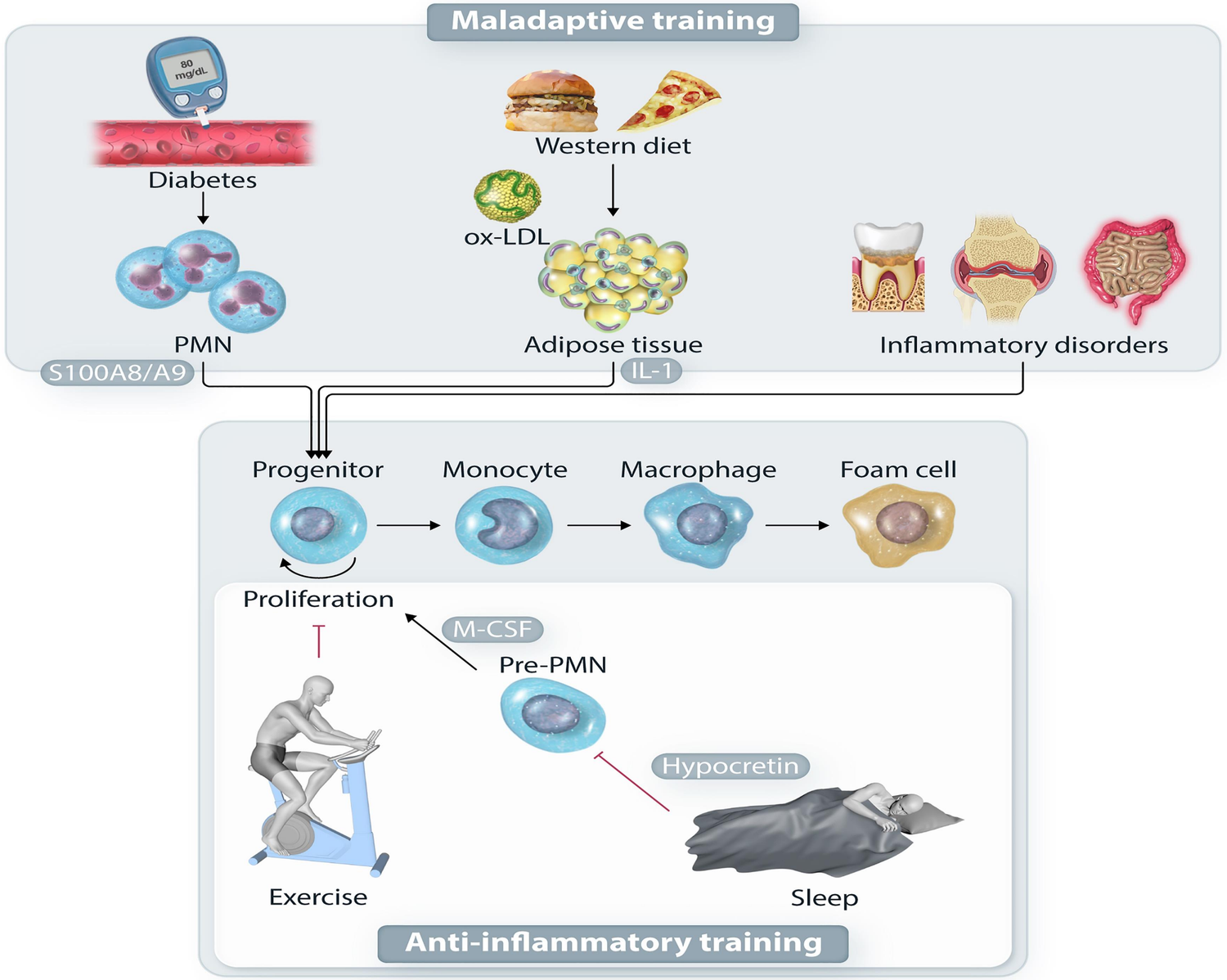
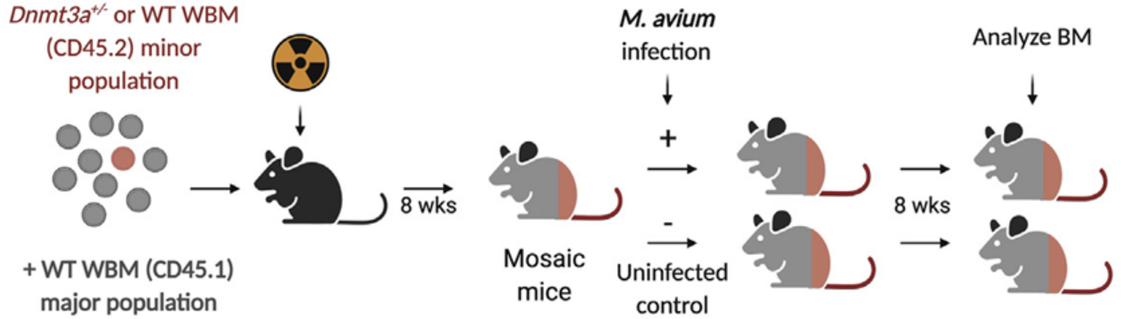
Clonal haematopoiesis of indeterminate potential and cardiovascular events in systemic lupus erythematosus (HEMATOPLUS study)

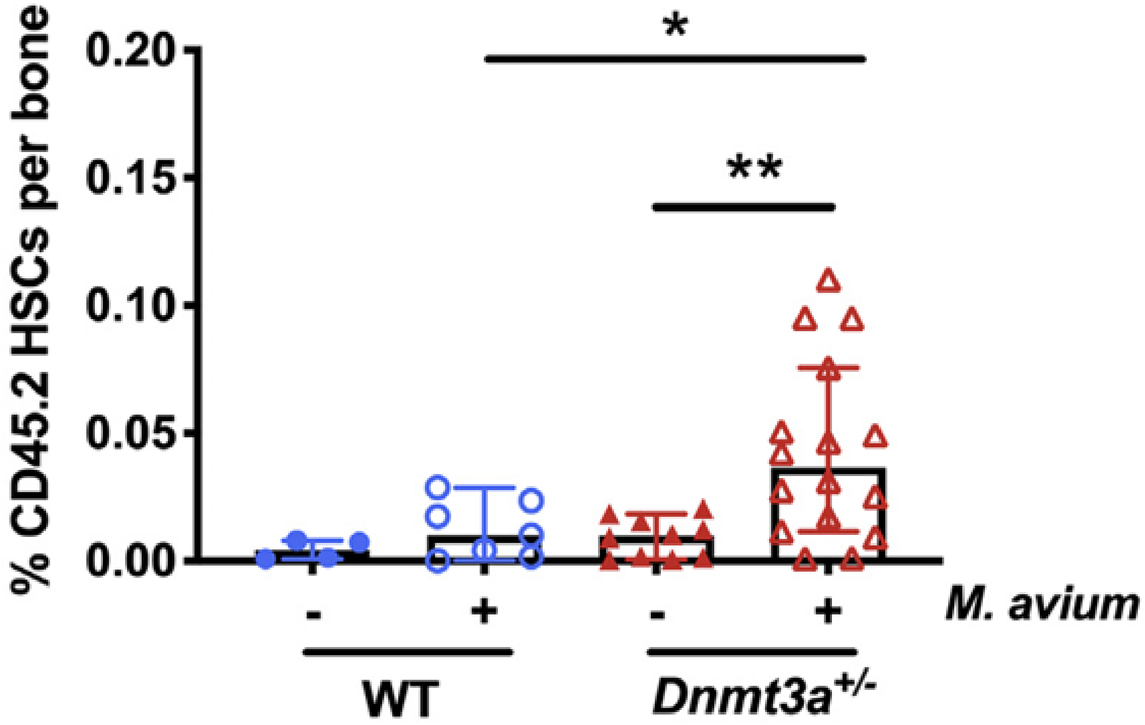
Η σχετιζόμενοι με καρδιαγγειακό κίνδυνο παράγοντες επηρεάζουν την αιμοποίηση



Mitroulis, Hajishengallis, Chavakis Cardiovasc Res 2023

Η φλεγμονή διευκολύνει την επικράτηση κλώνων





CellPress

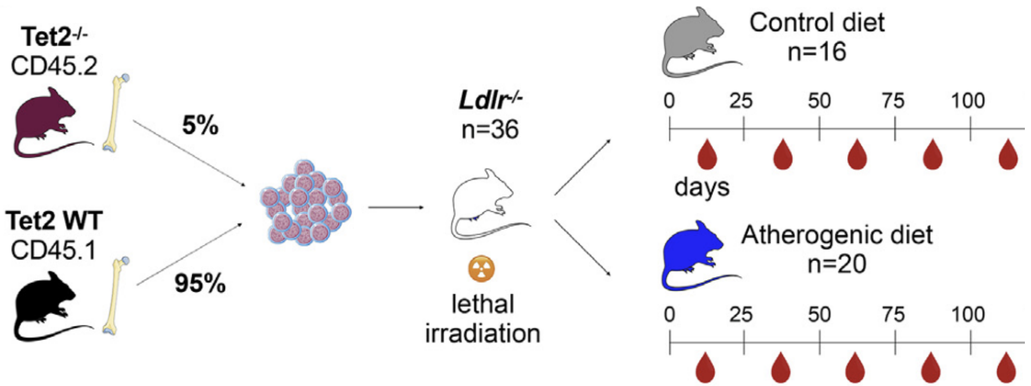
Cell Stem Cell

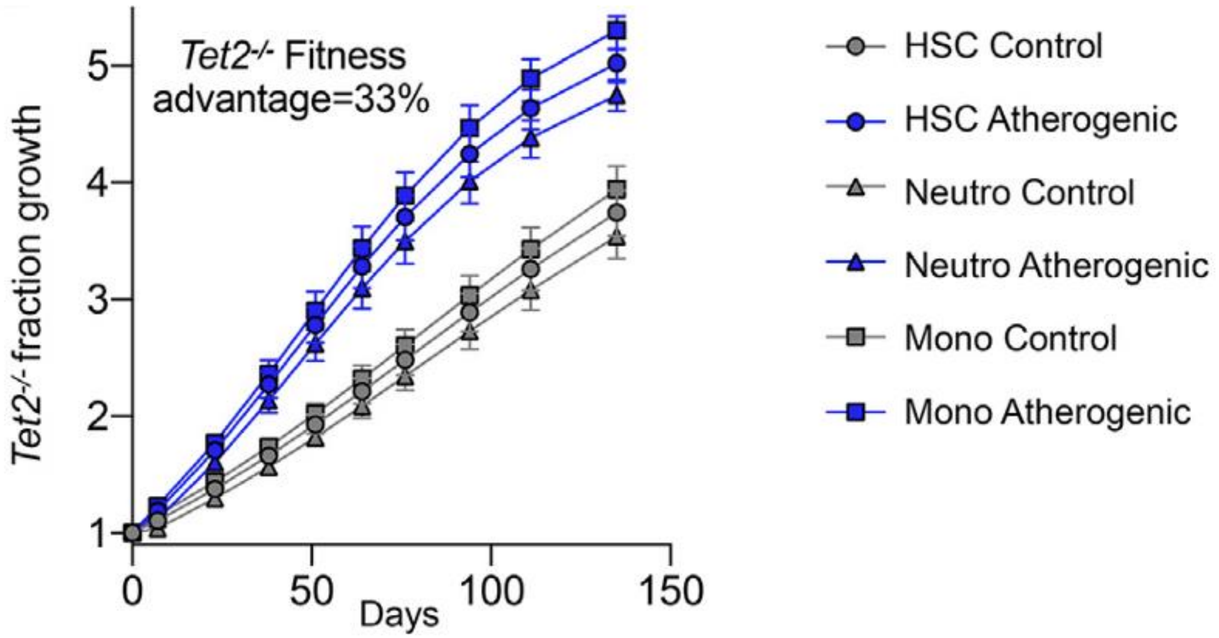
Article

Chronic infection drives Dnmt3a-loss-of-function clonal hematopoiesis via IFNγ signaling

Daniel Hormaechea-Agulla,[1,8] Katie A. Matatall,[1,8] Duy T. Le,[2] Bailee Kain,[3] Xiaochen Long,[4] Pawel Kus,[5] Roman Jaksik,[5] Grant A. Challen,[6] Marek Kimmel,[4,5] and Katherine Y. King[1,2,3,7,9,*]

Η σχετιζόμενη με το μεταβολικό σύνδρομο φλεγμονή διευκολύνει την ανάπτυξη κλώνων





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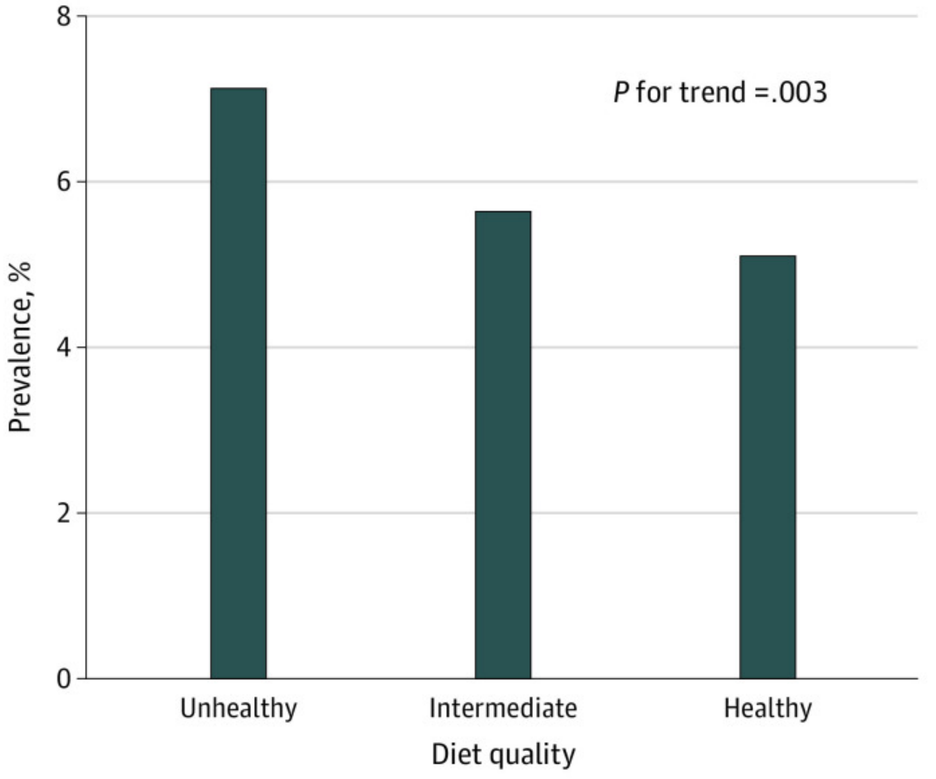
Cell

Theory

Increased stem cell proliferation in atherosclerosis accelerates clonal hematopoiesis

Alexander Heyde,[1,8] David Rohde,[2,8] Cameron S. McAlpine,[2,8] Shuang Zhang,[2] Friedrich F. Hoyer,[2] Jeffrey M. Gerold,[1] David Cheek,[2] Yoshiko Iwamoto,[2] Maximilian J. Schloss,[2] Katrien Vandoorne,[2] Oriol Iborra-Egea,[3] Christian Muñoz-Guijosa,[3] Antoni Bayes-Genis,[3] Johannes G. Reiter,[4] Morgan Craig,[5] Filip K. Swirski,[2] Matthias Nahrendorf,[2,6] Martin A. Nowak,[1,7] and Kamila Naxerova[2,9,*]

Δίαιτα και CHIP



Bhattacharya et al, JAMA Cardiol, 2021

Συσχέτιση μεταξύ παχυσαρκίας και CHIP

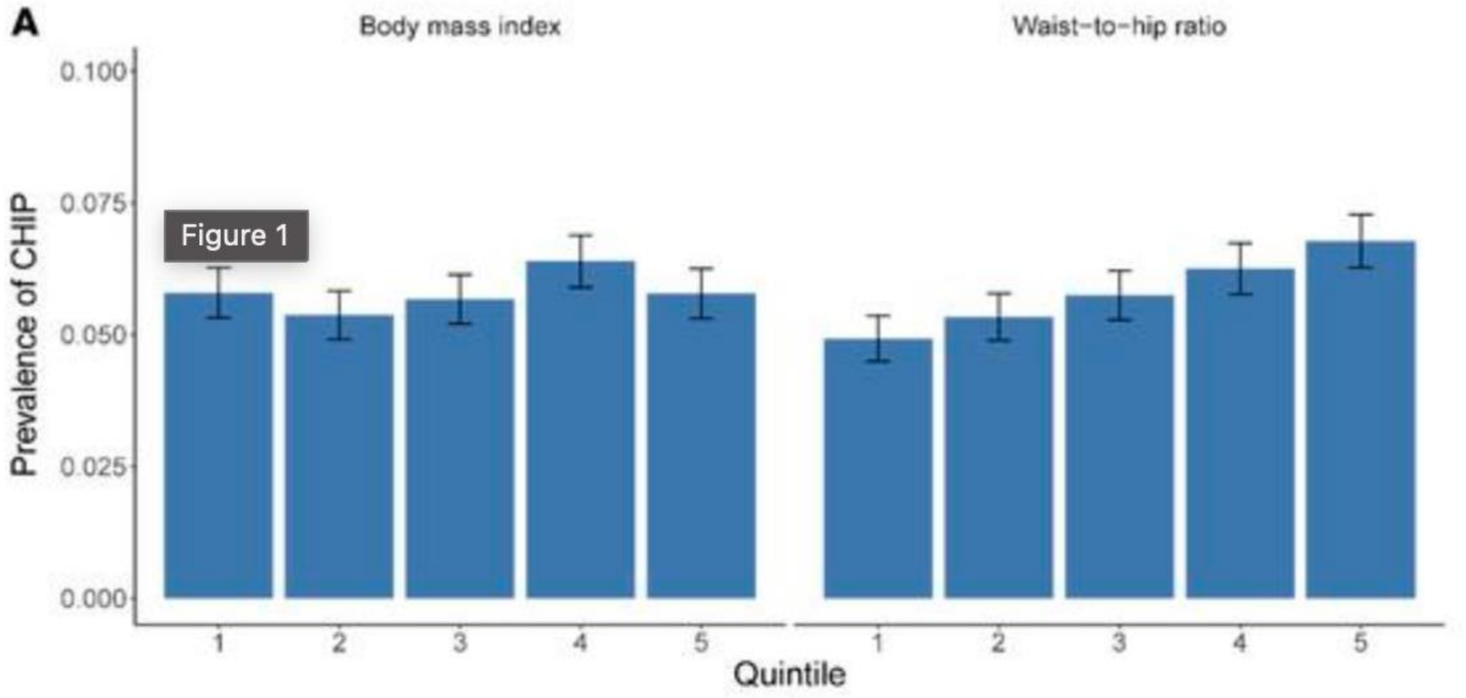


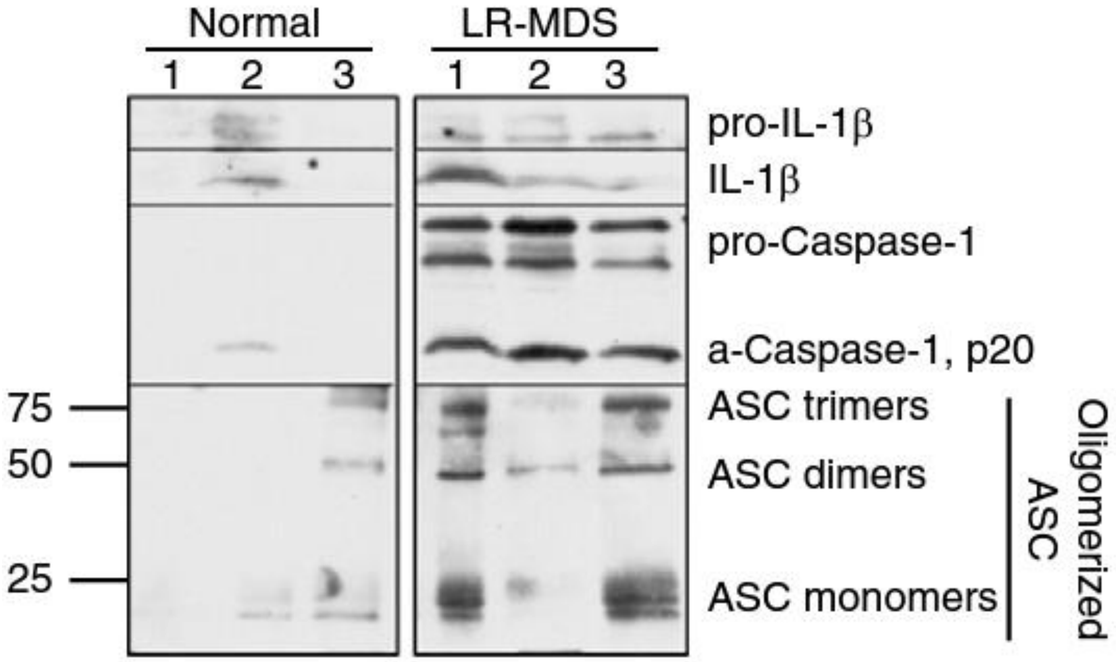
Figure 1

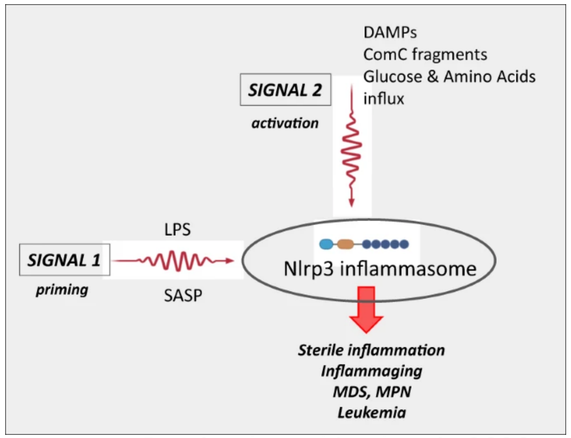
)besity-induced inflammation exacerbates lonal hematopoiesis

Santhosh Kumar Pasupuleti,[1] Baskar Ramdas,[1] Sarah S. Burns,[1] Lakshmi Reddy Palam,[1] Rahul Kanumuri,[1] Ramesh Kumar,[1] Taruni Reddy Pandhiri,[1] Utpal P. Dave,[2] Nanda Kumar Yellapu,[3] Xinyu Zhou,[4] Chi Zhang,[4] George E. Sandusky,[5] Zhi Yu,[6,7] Michael C. Honigberg,[6] Alexander G. Bick,[8] Gabriel K. Griffin,[9,10] Abhishek Niroula,[7] Benjamin L. Ebert,[11] Sophie Paczesny,[12] Pradeep Natarajan,[6,7,13] and Reuben Kapur[1,14]

Published April 18, 2023 - More info

Ενεργοποίηση του φλεγμονοσώματος στο μυελοδυσπλαστικό σύνδρομο





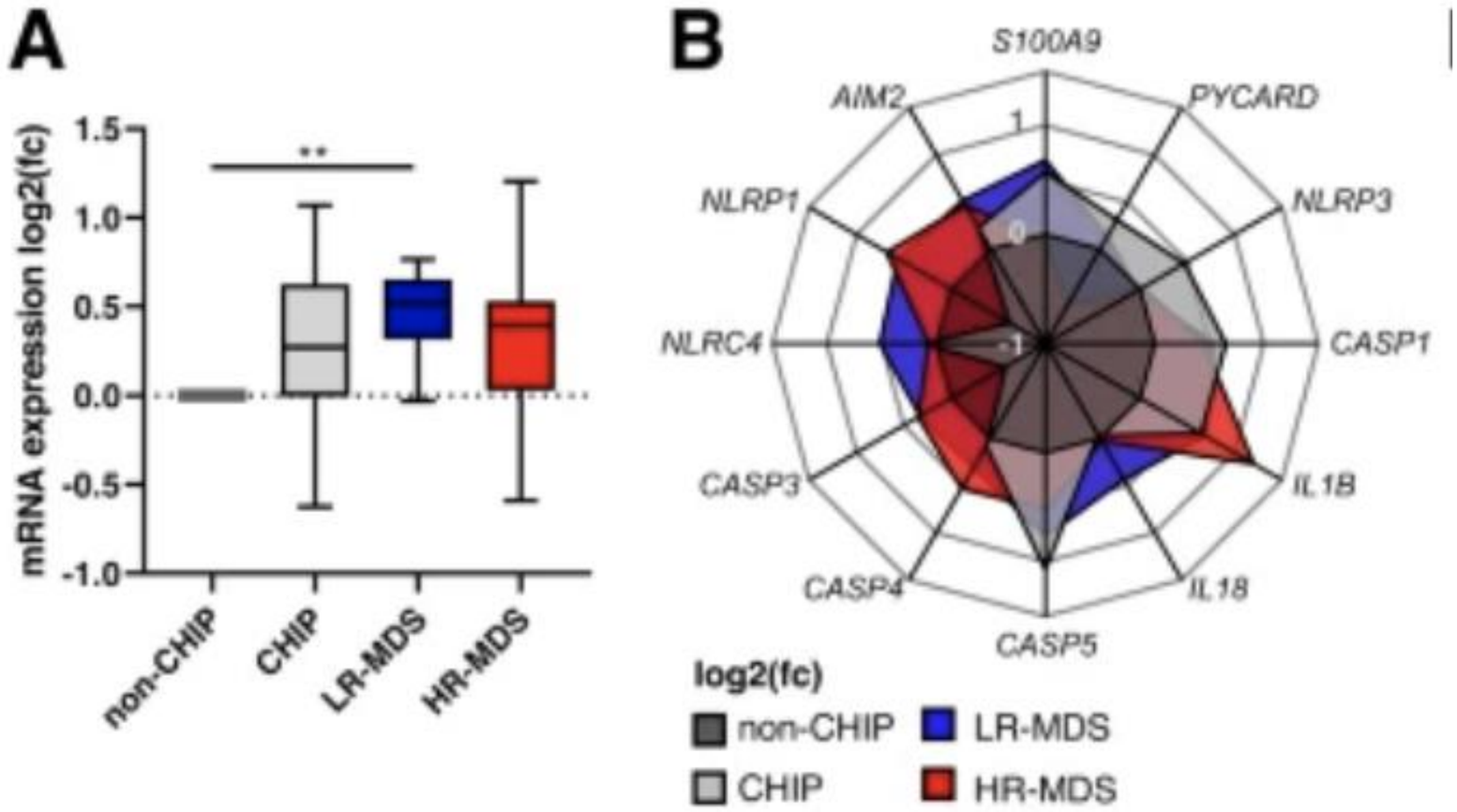
Ratajczak et al Leukemia 2020

MYELOID NEOPLASIA

The NLRP3 inflammasome functions as a driver of the myelodysplastic syndrome phenotype

Ashley A. Basiorka,[1] Kathy L. McGraw,[2] Erika A. Eksioglu,[3] Xianghong Chen,[3] Joseph Johnson,[4] Ling Zhang,[5] Qing Zhang,[2] Brittany A. Irvine,[2] Thomas Cluzeau,[6-9] David A. Sallman,[2] Eric Padron,[2] Rami Komrokji,[2] Lubomir Sokol,[2] Rebecca C. Coll,[10] Avril A. B. Robertson,[10] Matthew A. Cooper,[10] John L. Cleveland,[11] Luke A. O'Neill,[12] Sheng Wei,[3] and Alan F. List[2]

Αυξημένη έκφραση των γονιδίων που σχετίζονται με το φλεγμονόσωμα στο ΜΔΣ



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MYELODYSPLASTIC NEOPLASM

Activation of distinct inflammatory pathways in subgroups of LR-MDS

Marie Schneider, Clara Rolfs, Matthias Trumpp, Susann Winter, Luise Fischer, Mandy Richter, Victoria Menger, Kolja Nenoff, Nora Grieb, Klaus H. Metzeler, Anne Sophie Kubasch, Katja Sockel, Christian Thiede, Jincheng Wu, Janghee Woo, Andreas Brüderle, Lorenz C. Hofbauer, Jörg Lützner, Andreas Roth, Michael Cross & Uwe Platzbecker

Leukemia **37**, 1709–1718 (2023) | Cite this article

VEXAS syndrome: αυτοφλεγμονή και ΜΔΣ

- **V** Vacuoles
- **E** E1 ubiquitin activating enzyme
- **X** X-linked
- **A** Autosomal
- **S** Somatic

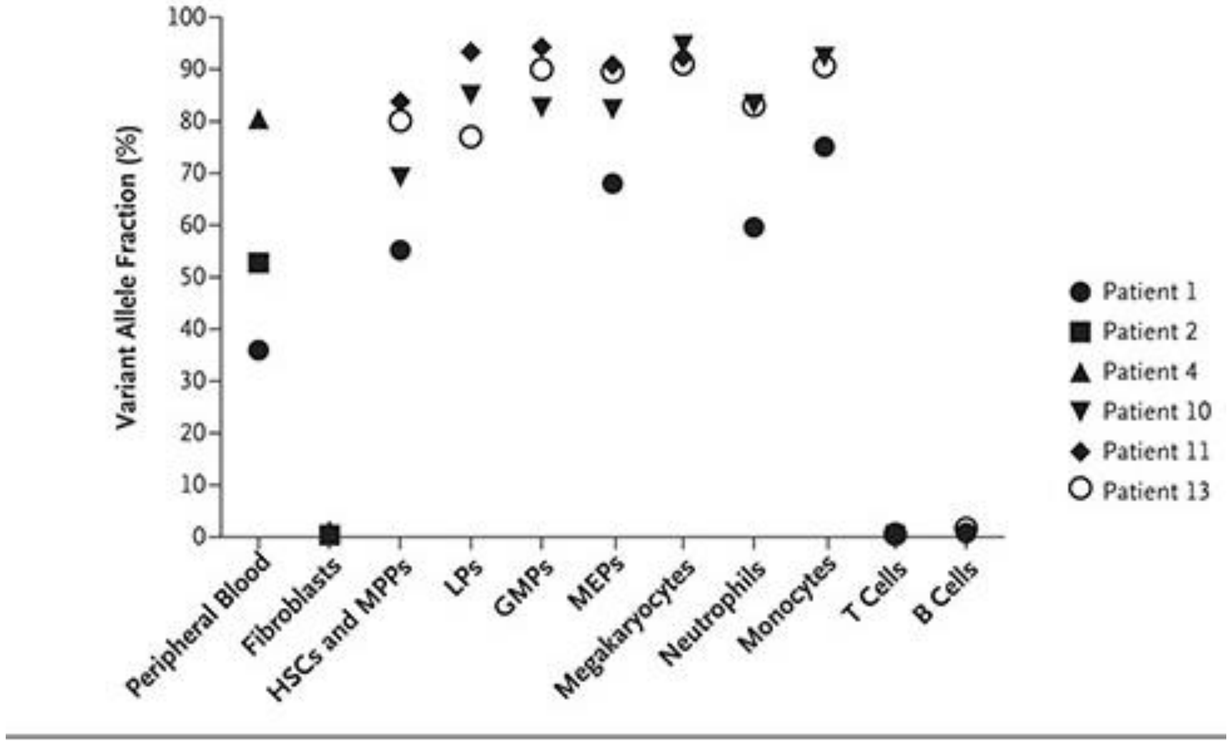
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

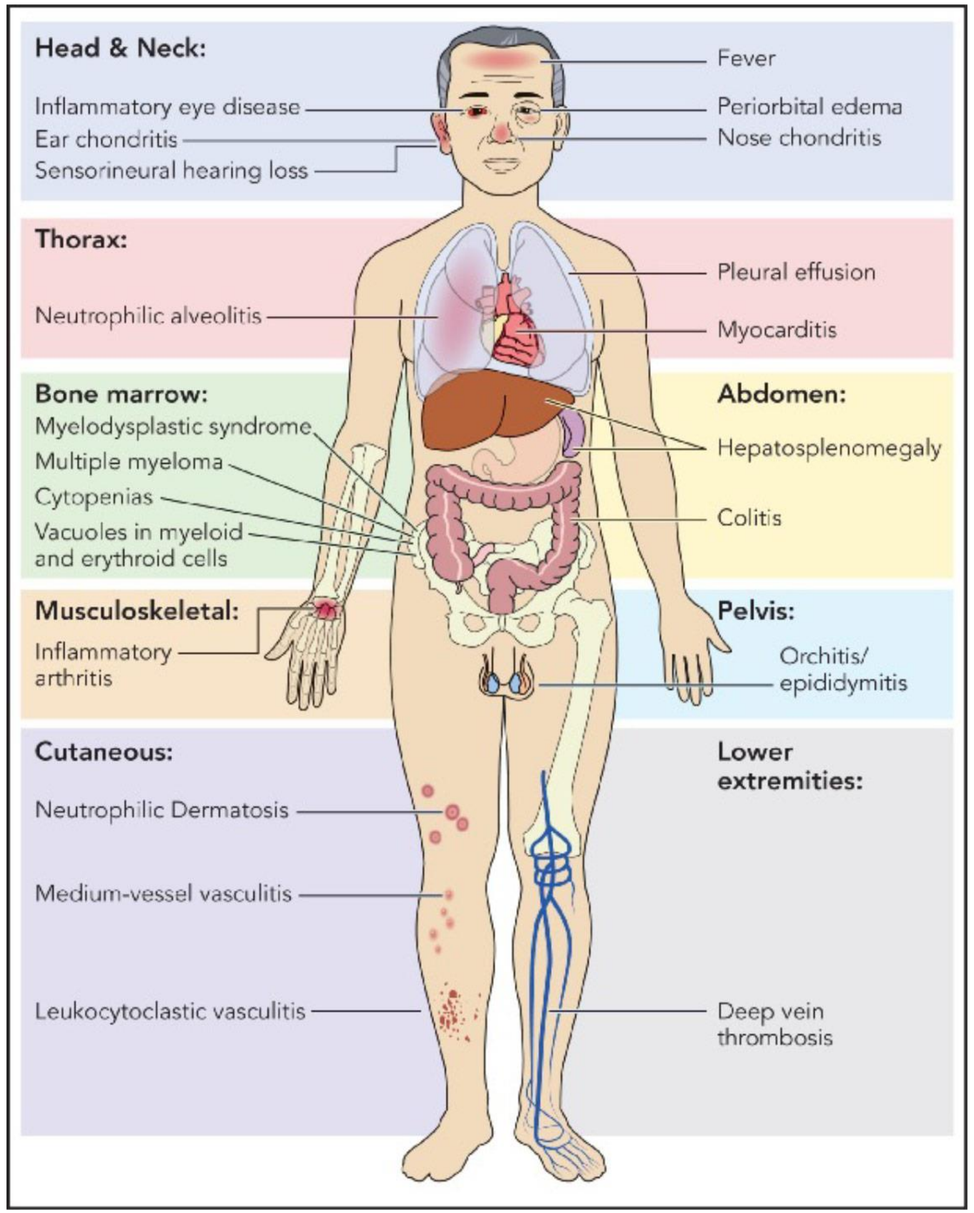
Somatic Mutations in *UBA1* and Severe Adult-Onset Autoinflammatory Disease

D.B. Beck, M.A. Ferrada, K.A. Sikora, A.K. Ombrello, J.C. Collins, W. Pei, N. Balanda, D.L. Ross, D. Ospina Cardona, Z. Wu, B. Patel, K. Manthiram, E.M. Groarke, F. Gutierrez-Rodrigues, P. Hoffmann, S. Rosenzweig, S. Nakabo, L.W. Dillon, C.S. Hourigan, W.L. Tsai, S. Gupta, C. Carmona-Rivera, A.J. Asmar, L. Xu, H. Oda, W. Goodspeed, K.S. Barron, M. Nehrebecky, A. Jones, R.S. Laird, N. Deuitch, D. Rowczenio, E. Rominger, K.V. Wells, C.-C.R. Lee, W. Wang, M. Trick, J. Mullikin, G. Wigerblad, S. Brooks, S. Dell'Orso, Z. Deng, J.J. Chae, A. Dulau-Florea, M.C.V. Malicdan, D. Novacic, R.A. Colbert, M.J. Kaplan, M. Gadina, S. Savic, H.J. Lachmann, M. Abu-Asab, B.D. Solomon, K. Retterer, W.A. Gahl, S.M. Burgess, I. Aksentijevich, N.S. Young, K.R. Calvo, A. Werner, D.L. Kastner, and P.C. Grayson

Σωματική μετάλλαξη της μυελικής σειράς

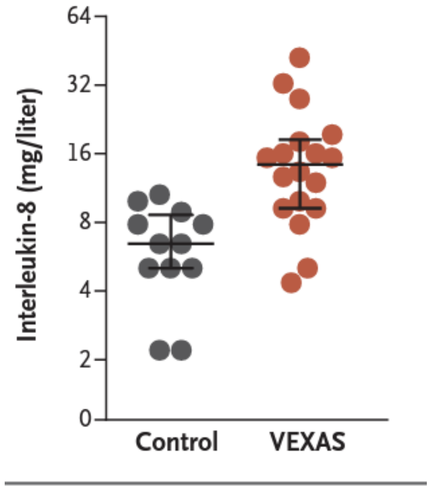


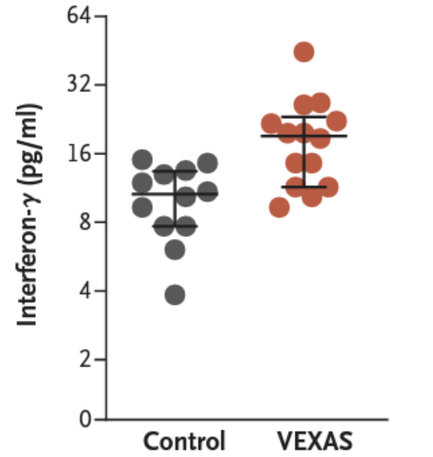
VEXAS syndrome: κλινική εικόνα

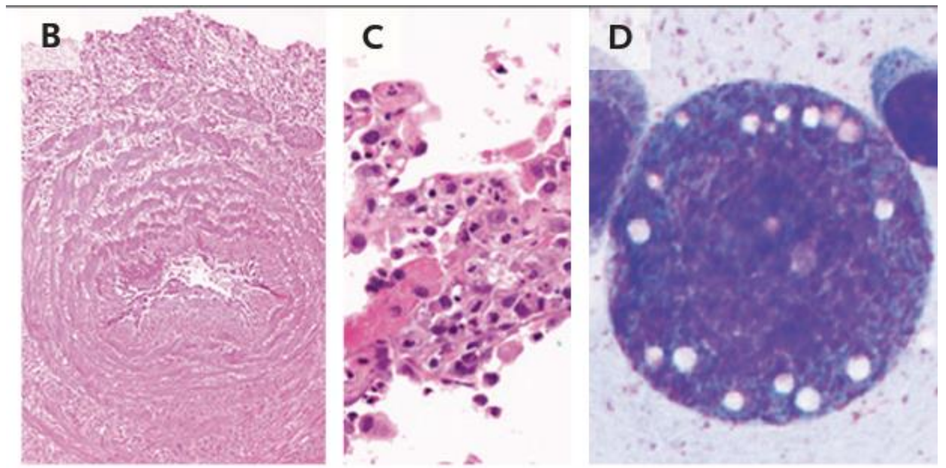


Grayson et al, Blood , 2021

VEXAS syndrome: αυτοφλεγμονή και ΜΔΣ







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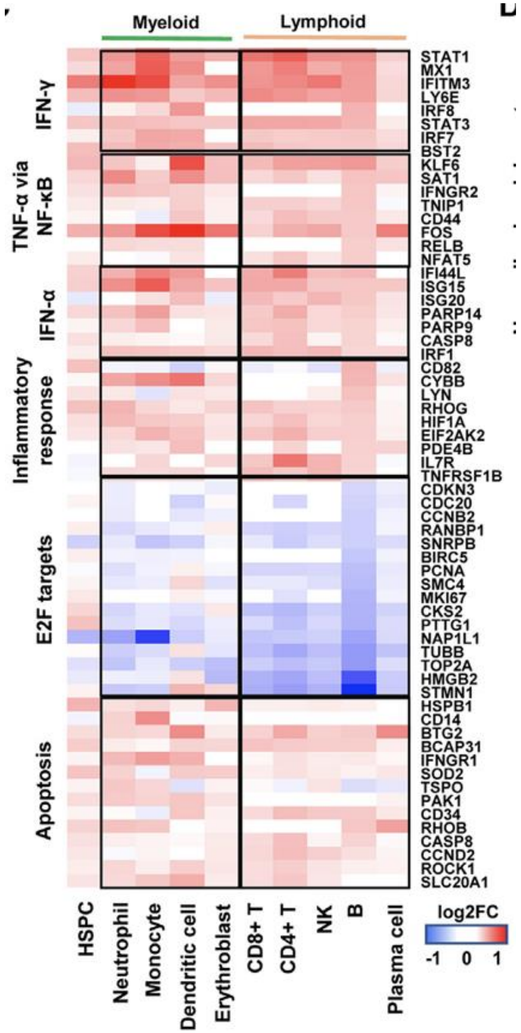
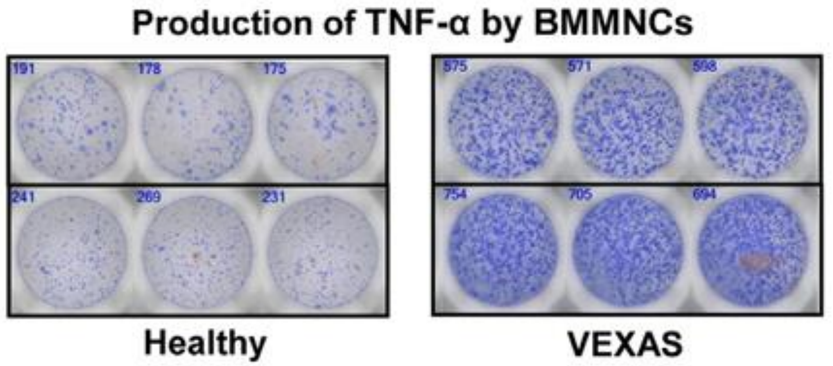
PET-CT με αυξημένο μεταβολισμό στο μυελό των οστών

Grayson et al, Blood , 2021

Ενεργοποίηση φλεγμονώδους προγράμματος στα προγονικά κύτταρα στο σύνδρομο VEXAS





Cell Reports Medicine

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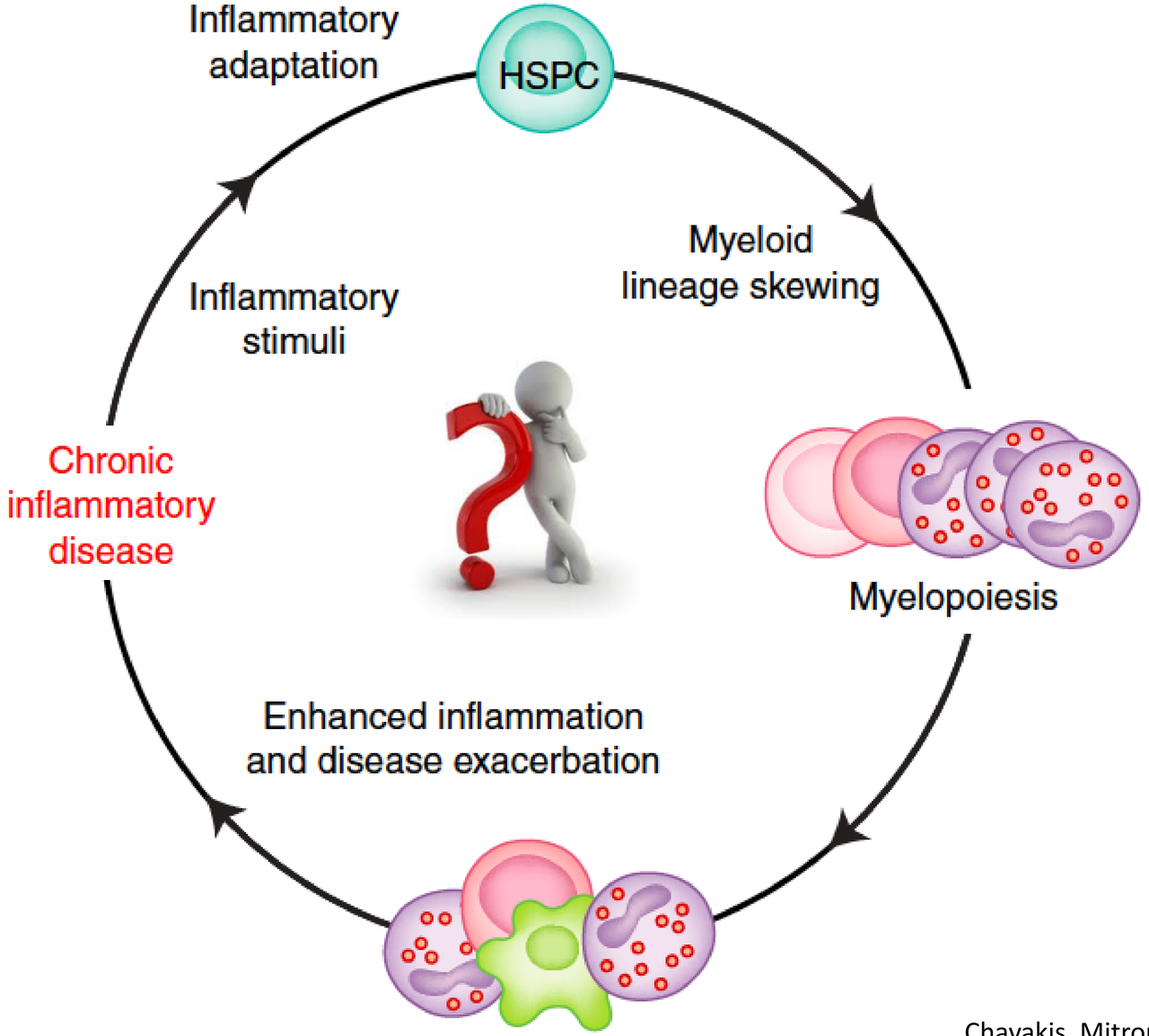
Article

Early activation of inflammatory pathways in *UBA1*-mutated hematopoietic stem and progenitor cells in VEXAS

Zhijie Wu,[1,7,9,*] Shouguo Gao,[1,7] Qingyan Gao,[1] Bhavisha A. Patel,[1] Emma M. Groarke,[1] Xingmin Feng,[1] Ash Lee Manley,[1] Haoran Li,[1] Daniela Ospina Cardona,[2,5,6] Sachiko Kajigaya,[1] Lemlem Alemu,[1] Diego Quinones Raffo,[1] Amanda K. Ombrello,[2] Marcela A. Ferrada,[3] Peter C. Grayson,[3] Katherine R. Calvo,[4] Daniel L. Kastner,[2] David B. Beck,[2,5,6,8,*] and Neal S. Young[1,8]



Chavakis, Mitroulis, Hajishengallis, Nat Immunol, 2019

Thank you for your attention