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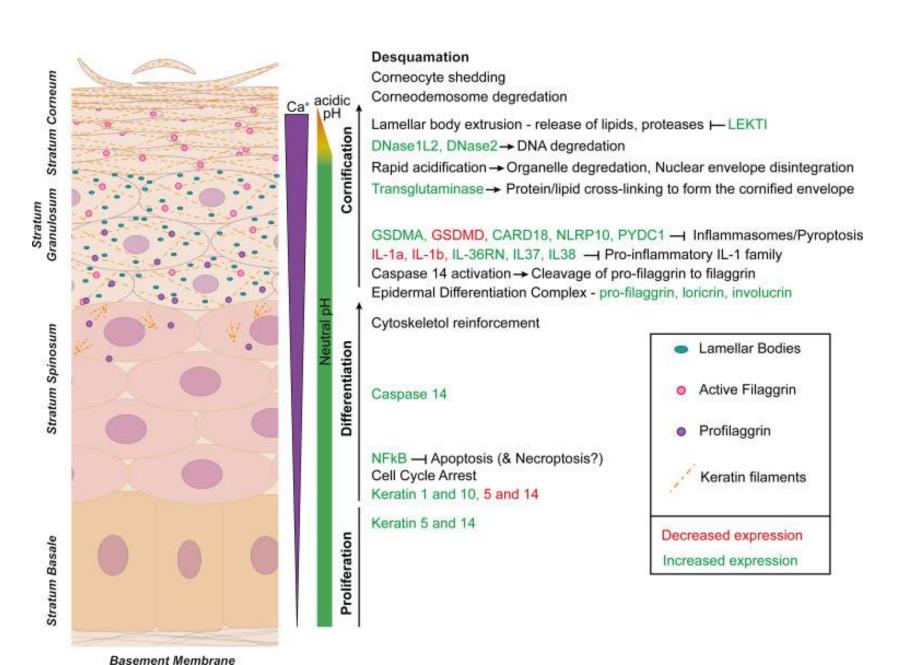
De standpunten die in deze slides worden weergegeven, zijn die van Hok Bing Thio

De informatie in deze slides kan afwijken van de huidige indicaties van de gepresenteerde geneesmiddelen. Raadpleeg de volledige SmPC's voor geldige voorschrijfinformatie.

Hok Bing Thio is/was consultant en gastspreker voor Astra Zeneca, Boehringer Ingelheim, Janssen, AbbVie, AMGEN, Galderma, LEO Pharma, Eli Lilly, Almirall, Kyowa Kirin, UCB en Novartis.

fineart america

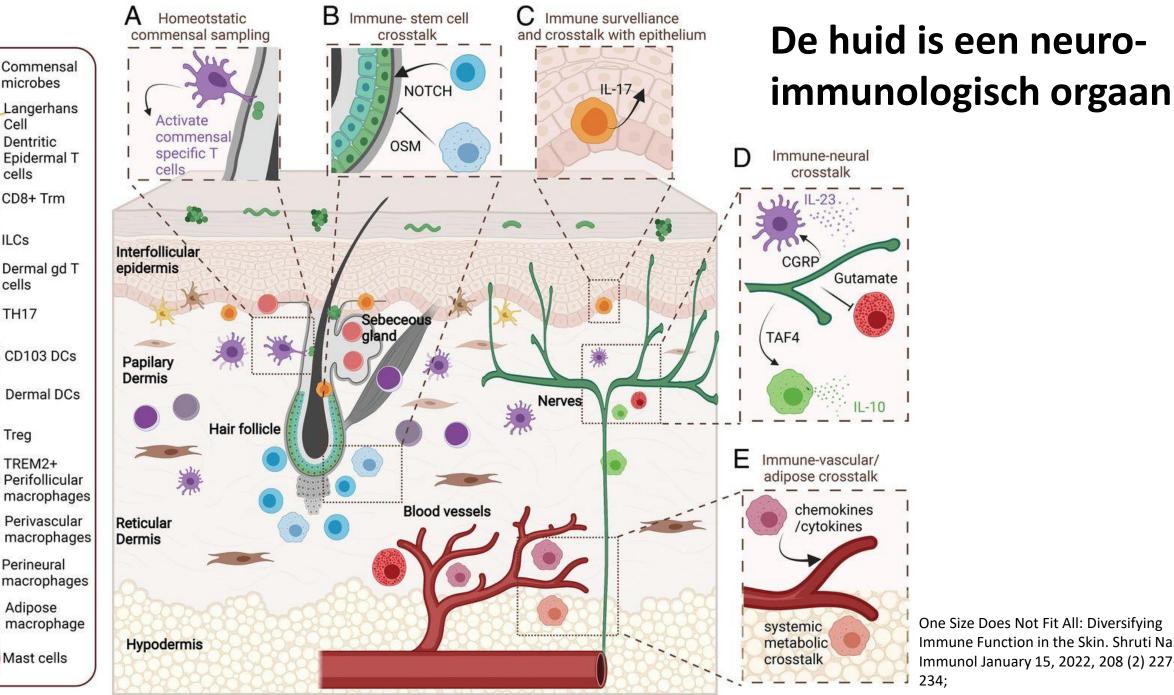




Opperhuid/ **Epidermis**

Anderton H, Algudah S. Cell death in skin function, inflammation, and disease. Biochem J. 2022 Aug 12;479(15):1621-1651. doi: 10.1042/BCJ20210606. PMID: 35929827;

PMCID: PMC9444075.



Commensal microbes

Langerhans

Epidermal T

Cell

cells

ILCs

cells

TH17

Treg

TREM2+

Perifollicular

Perivascular

Perineural

Adipose

Mast cells

Dentritic

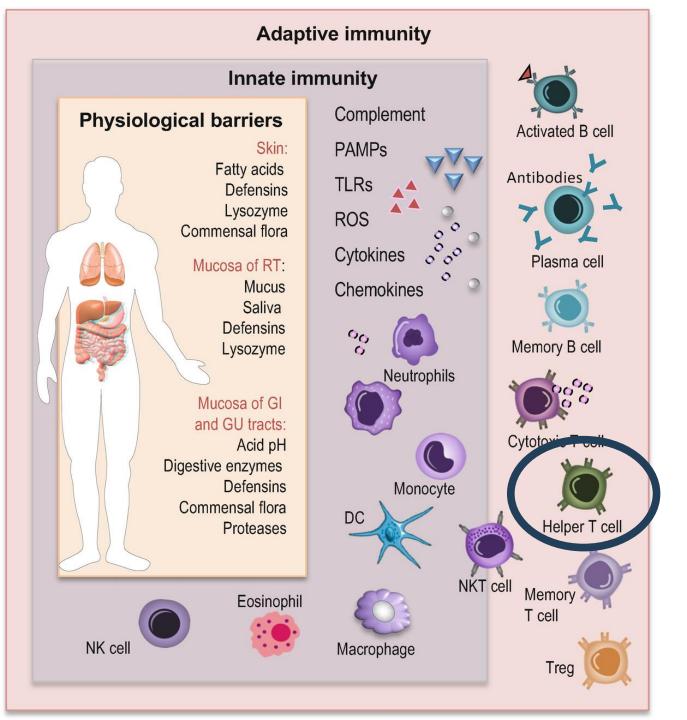
CD8+ Trm

Dermal gd T

CD103 DCs

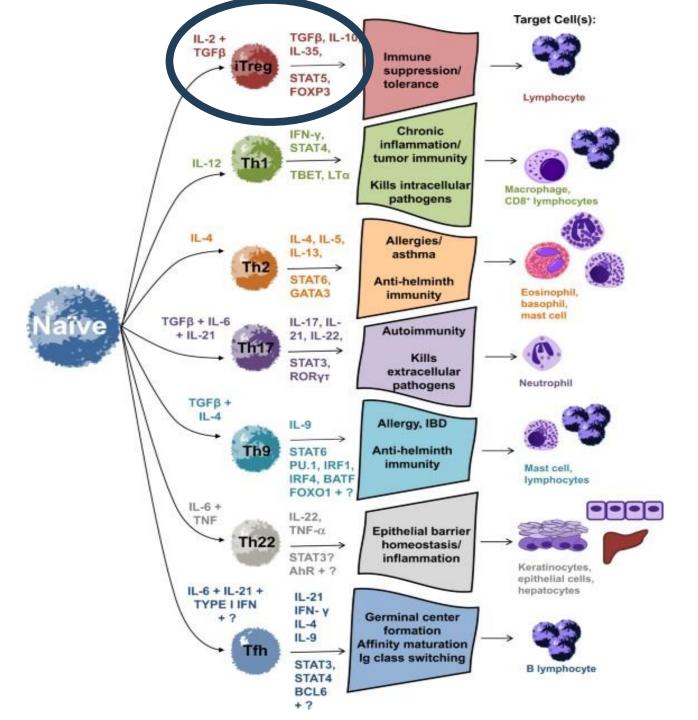
Dermal DCs

One Size Does Not Fit All: Diversifying Immune Function in the Skin, Shruti Naik, J Immunol January 15, 2022, 208 (2) 227-234;



Huid is een belangrijk onderdeel van het immuun systeem

Müller L., Di Benedetto S., Pawelec G. (2019) The Immune System and Its Dysregulation with Aging. In: Harris J., Korolchuk V. (eds) Biochemistry and Cell Biology of Ageing: Part II Clinical Science. Subcellular Biochemistry, vol 91. Springer, Singapore



Knochelmann, H.M., Dwyer, C.J., Bailey, S.R. et al. When worlds collide: Th17 and Treg cells in cancer and autoimmunity. Cell Mol Immunol 15, 458–469 (2018). https://doi.org/10.1038/s41423-018-0004-4

THE NOBEL PRIZE IN PHYSIOLOGY OR MEDICINE 2025

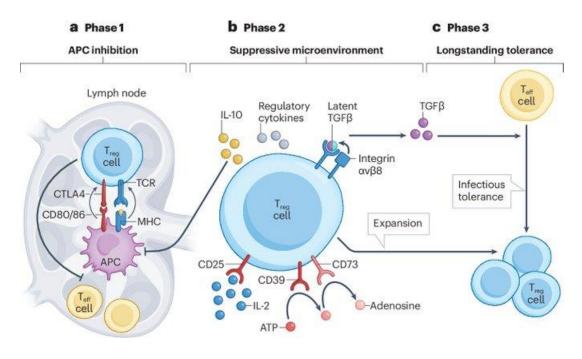


Mary E. Brunkow Fred Ramsdell Shimon Sakaguchi

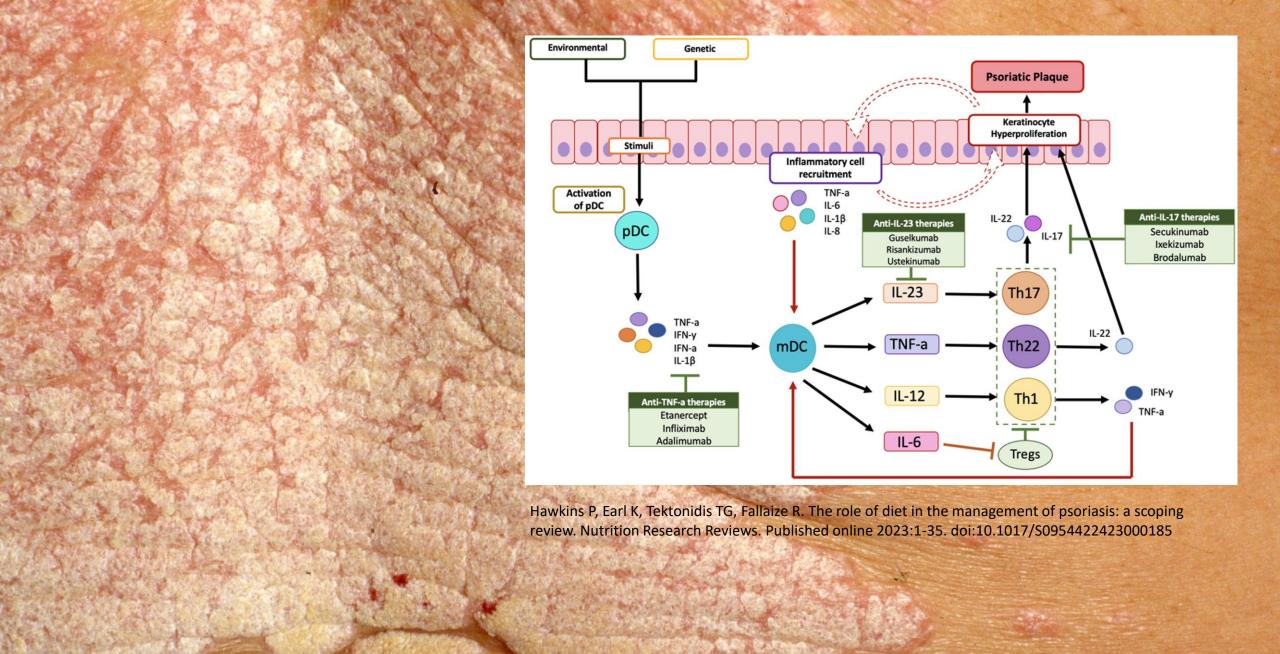
"for their discoveries concerning peripheral immune tolerance"

THE NOBEL ASSEMBLY AT KAROLINSKA INSTITUTET

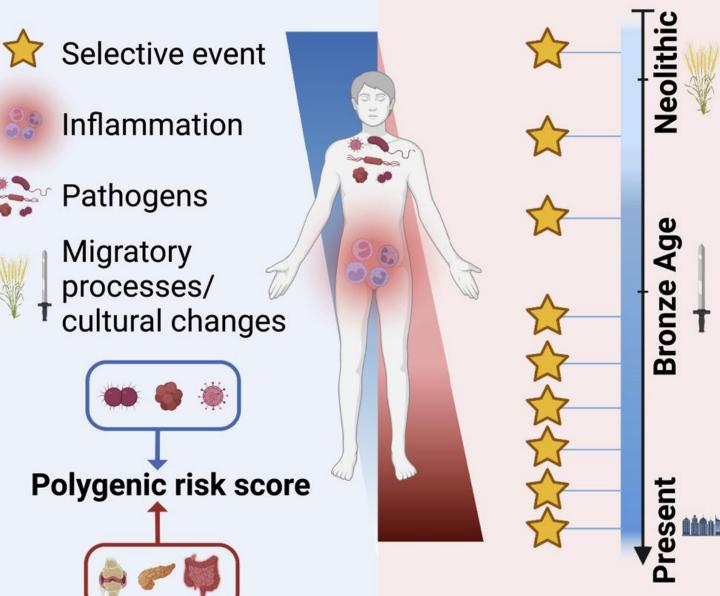




Wardell, C.M., Boardman, D.A. & Levings, M.K. Harnessing the biology of regulatory T cells to treat disease. Nat Rev Drug Discov 24, 93–111 (2025). https://doi.org/10.1038/s41573-024-01089-x



Infectious Autoimmune disease risk disorder risk



Genetic adaptation to pathogens and increased risk of inflammatory disorders in post-Neolithic Europe

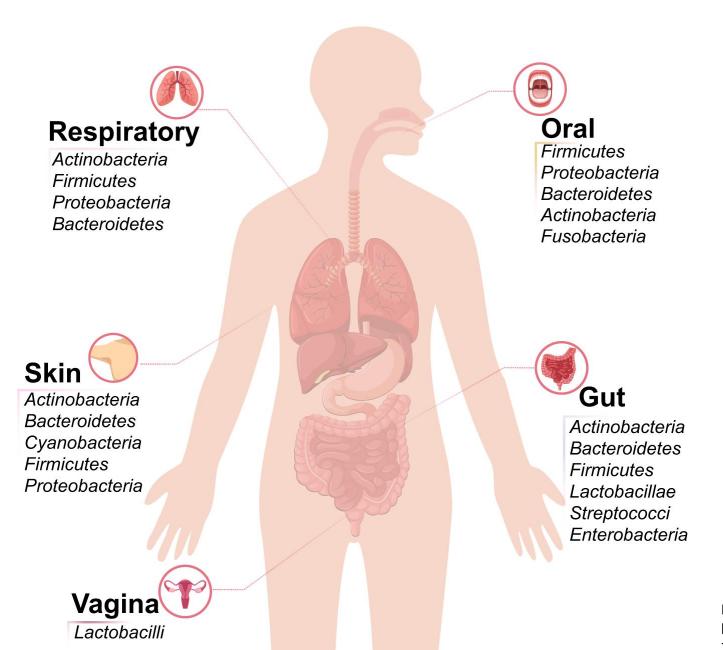
Ancient genomics studies allow detection of the extent of natural selection over time

- Genetic adaptation in Europe has mainly occurred after the start of the Bronze Age
- Immunity genes have been strongly affected by both positive and negative selection
- Resistance to infection has increased inflammatory disease risk in recent millennia

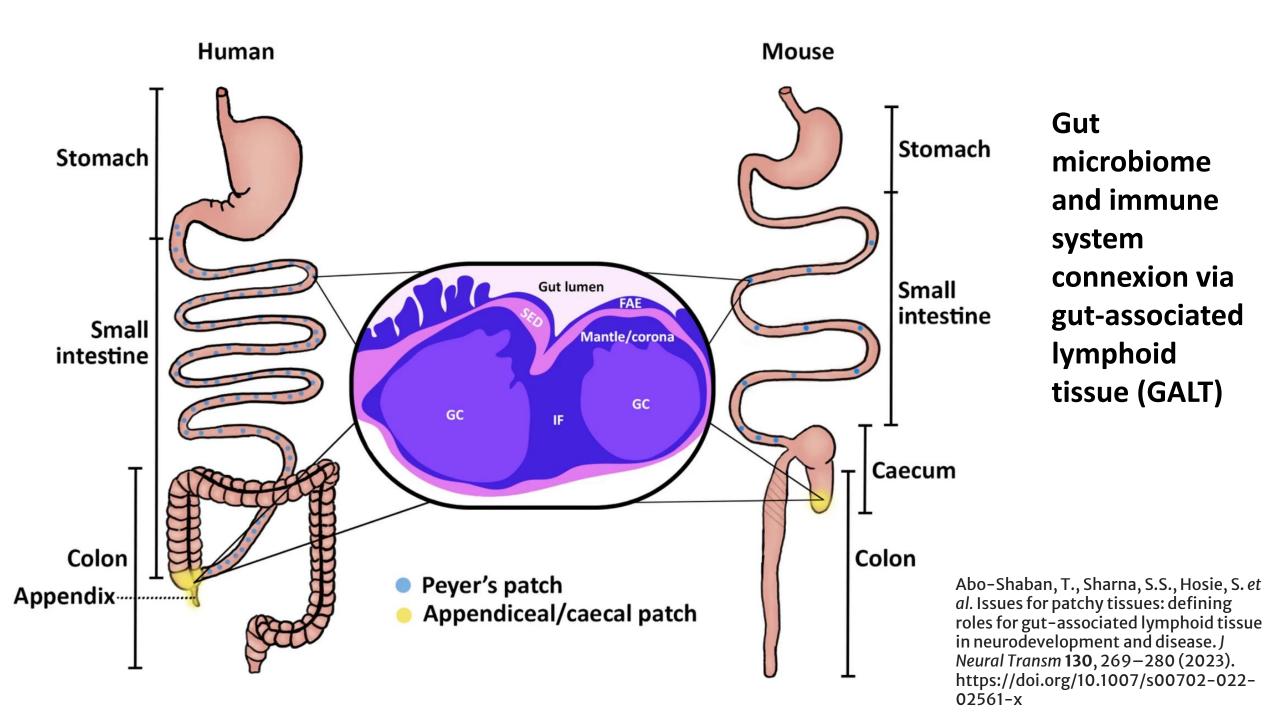
Kerner, Gaspard et al. Cell Genomics, 2023, Volume 3, Issue 2, 100248

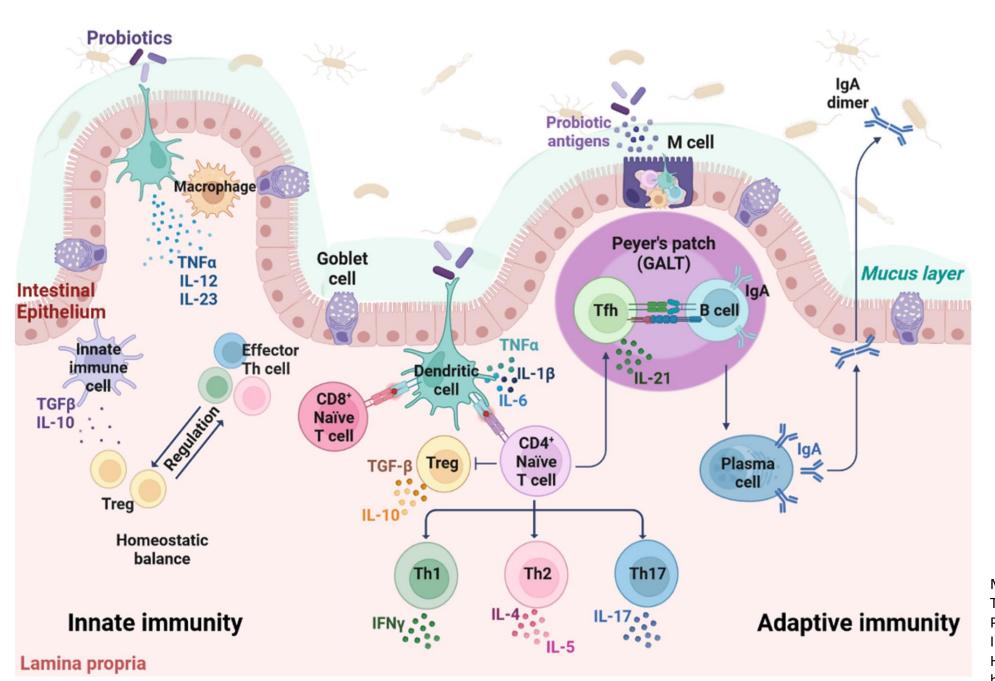


Microbiota composition in different regions

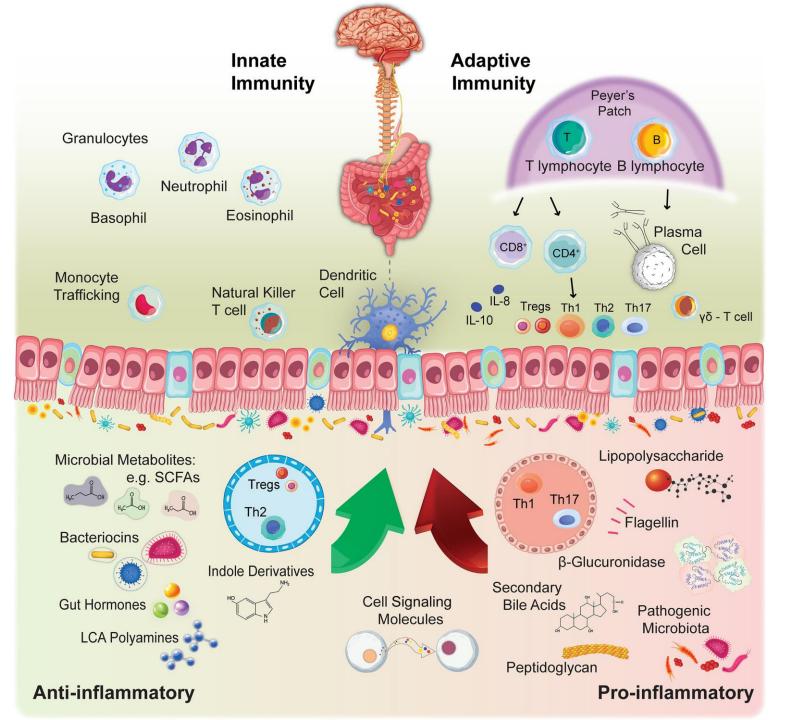


Hou, K., Wu, ZX., Chen, XY. et al. Microbiota in health and diseases. Sig Transduct Target Ther 7, 135 (2022). https://doi.org/10.1038/s41392-022-00974-4





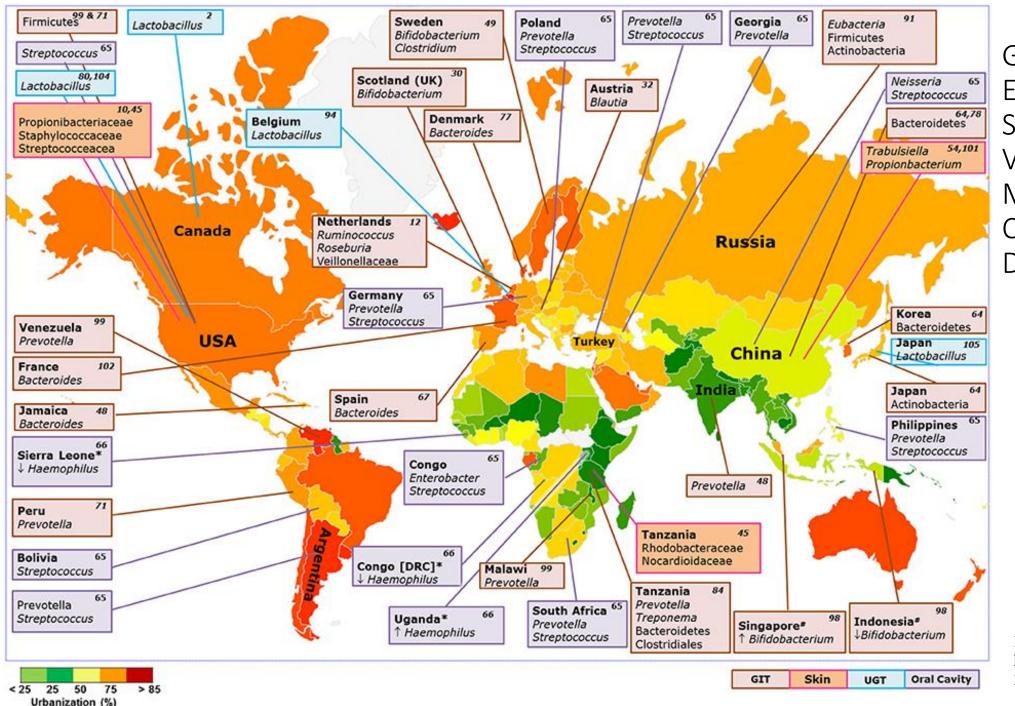
Mazziotta, C., Tognon, M., Martini, F., Torreggiani, E., & Rotondo, J. C. (2023). Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. Cells, 12(1), 184. https://doi.org/10.3390/cells12010184



Innate vs. adaptive immunity and the gut microbiome

The gut microbiota-immune-brain axis: Therapeutic implications O'Riordan, Kenneth J. et al.

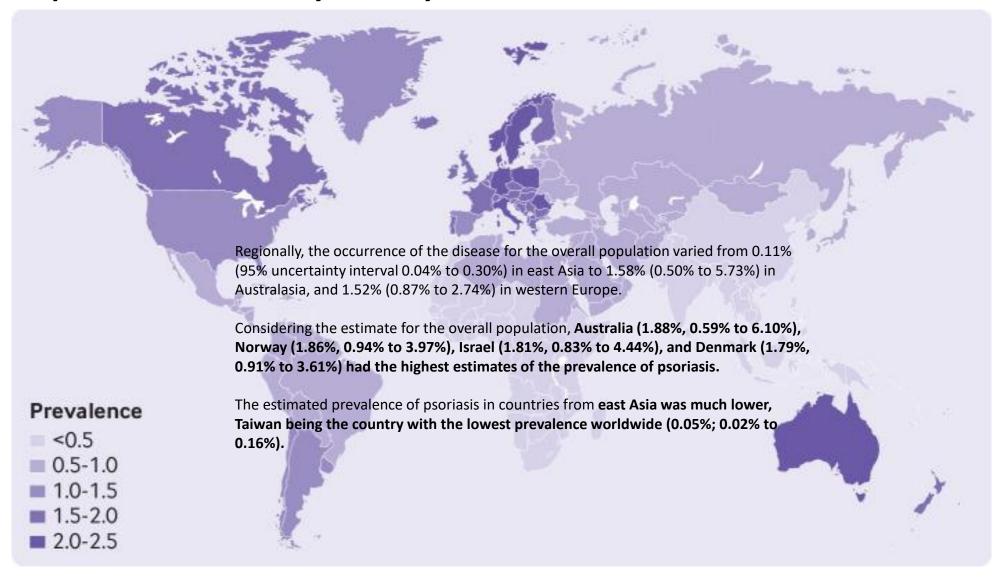
Cell Reports Medicine, 2025, Volume 6, Issue 3, 101982



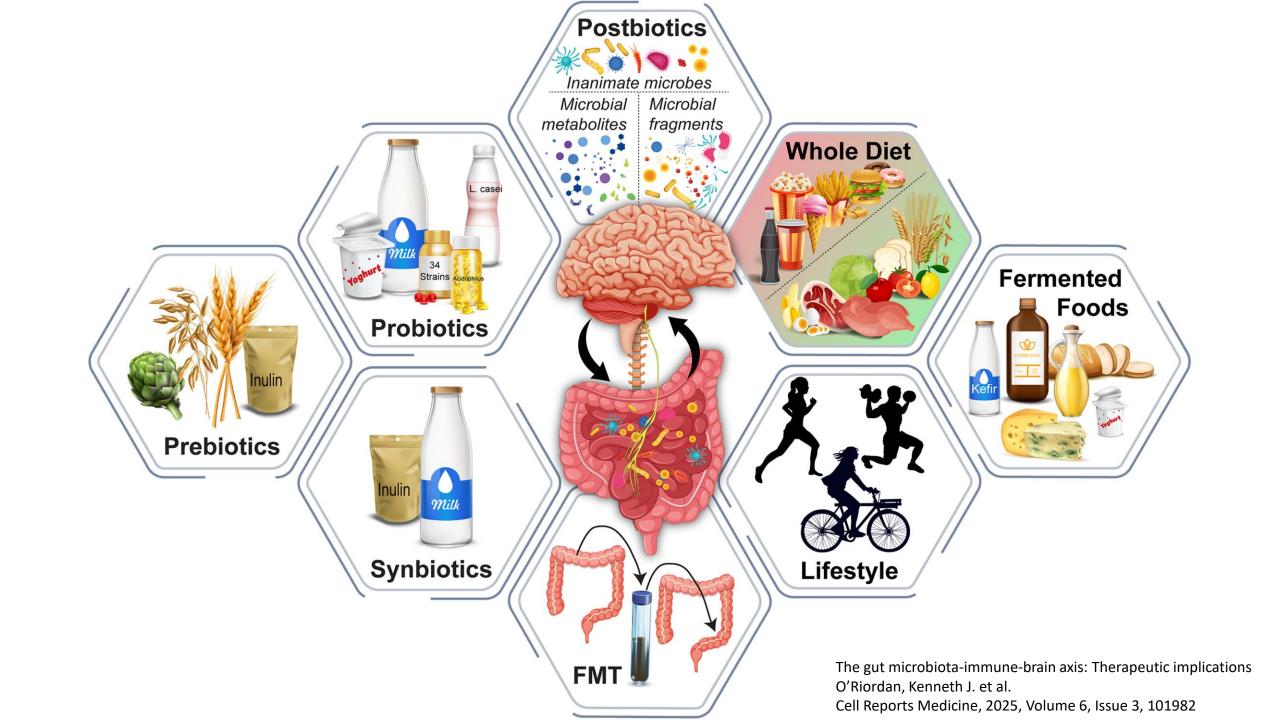
Geography,
Ethnicity or
Subsistence-Specific
Variations in Human
Microbiome
Composition and
Diversity

Front. Microbiol., 23 June 2017 | https://doi.org/10.3389/fmicb. 2017.01162

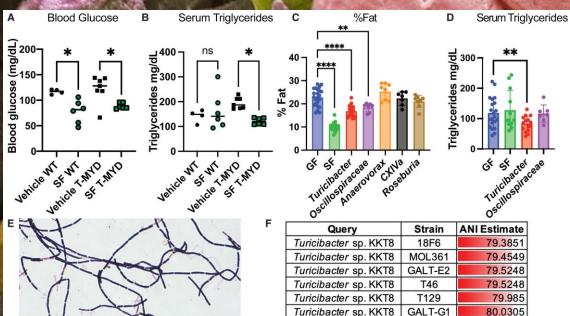
Lifetime (physician or dermatologist diagnosed) prevalence of psoriasis in adults by country.



Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM; Global Psoriasis Atlas. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020 May 28;369:m1590. doi: 10.1136/bmj.m1590. PMID: 32467098; PMCID: PMC7254147.







Turicibacter sp. KKT8

Turicibacter sp. KKT8

Turicibacter sp. KKT8

H121

TA25

1E2

80.3566

99.1095

99.017

Cell Metabolism



Article

Dietary fat disrupts a commensal-host lipid network that promotes metabolic health

Kendra Klag,¹ Darci Ott,¹ Trevor S. Tippetts,² Rebekah J. Nicolson,² Sean M. Tatum,² Kaylyn M. Bauer,¹ Emmanuel Stephen-Victor,¹ Allison M. Weis,¹ Rickesha Bell,¹ James Weagley,³ J. Alan Maschek,²,⁴ Dai Long Vu,⁵ Stacey Heaver,⁵ Ruth Ley,⁵ Ryan O'Connell,¹ William L. Holland,² Scott A. Summers,² W. Zac Stephens,¹ and June L. Round¹,⁶,⁺

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²Department of Nutrition and Integrative Physiology, College of Health, University of Utah, Salt Lake City, UT 84112, USA

³Department of Medicine, Division of Infectious Diseases, Edison Family Center for Genome Sciences & Systems Biology, Washington University School of Medicine, St. Louis, MO 63110, USA

Metabolomics Core Research Facility, University of Utah, Salt Lake City, UT 84112, USA

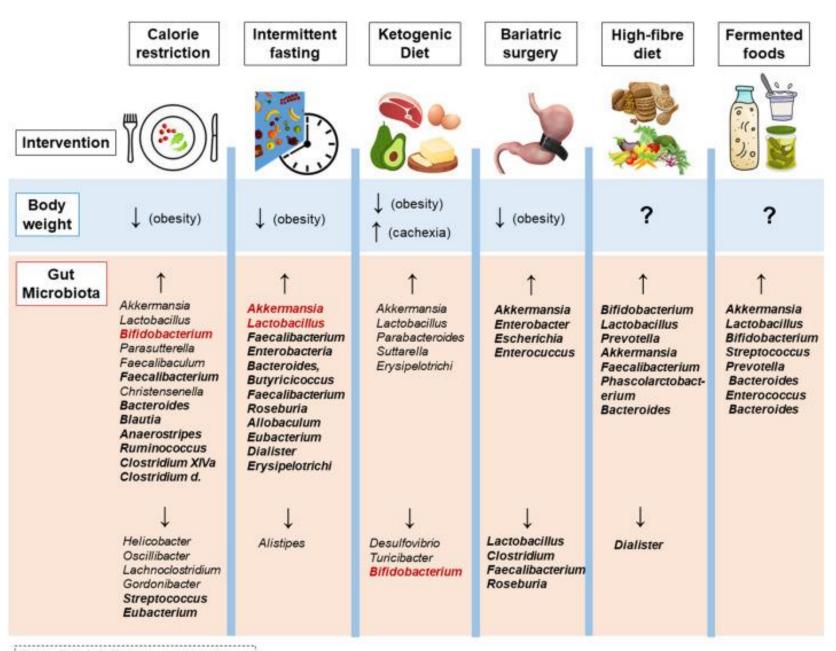
⁵Department of Microbiome Science, Max Planck Institute for Biology, Tübingen, Germany

6Lead contact

*Correspondence: june.round@path.utah.edu https://doi.org/10.1016/j.cmet.2025.10.007

SUMMARY

The microbiota influences metabolic health; however, few specific microbial molecules and mechanisms have been identified. We isolated a *Turicibacter* strain from a community of spore-forming bacteria that promotes leanness in mice. Human metagenomic analysis demonstrates reduced *Turicibacter* abundance in individuals with obesity. Similarly, a high-fat diet reduces *Turicibacter* colonization, preventing its weight-suppressive effects, which can be overcome with continuous *Turicibacter* supplementation. Ceramides accumulate during a high-fat diet and promote weight gain. Transcriptomics and lipidomics reveal that the spore-forming community and *Turicibacter* suppress host ceramides. *Turicibacter* produces unique lipids, which are reduced during a high-fat diet. These lipids can be transferred to host epithelial cells, reduce ceramide production, and decrease fat uptake. Treatment of animals with purified *Turicibacter* lipids prevents obesity, demonstrating that bacterial lipids can promote host metabolic health. These data identify a lipid metabolic circuit between bacteria and host that is disrupted by diet and can be targeted therapeutically.



Schellekens, John F. Cryan, Microbiota and body weight control: Weight watchers

García-Cabrerizo, Timothy Lipuma, Gerard Clarke, Harriët

Serena Boscaini, Sarah-Jane Leigh, Aonghus Lavelle, Rubén

within?.

Molecular Metabolism, Volume 57, 2022, 101427, ISSN 2212-8778, https://doi.org/10.1016/j.molmet.2021.101427.

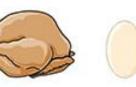
In preclinical studies In clinical studies In both preclinical and clinical studies

Lipids Proteins Carbohydrates











Animal-based

- ↓ Bacteroides
- ↑ Firmicutes, Proteobacteria
- ↓ Firmicutes (Roseburia, Eubacterium rectale, Ruminococcus bromii)
- ↑ Alistipes, Bilophila and Bacteroides

↑ Bifidobacterium, Lactobacillus









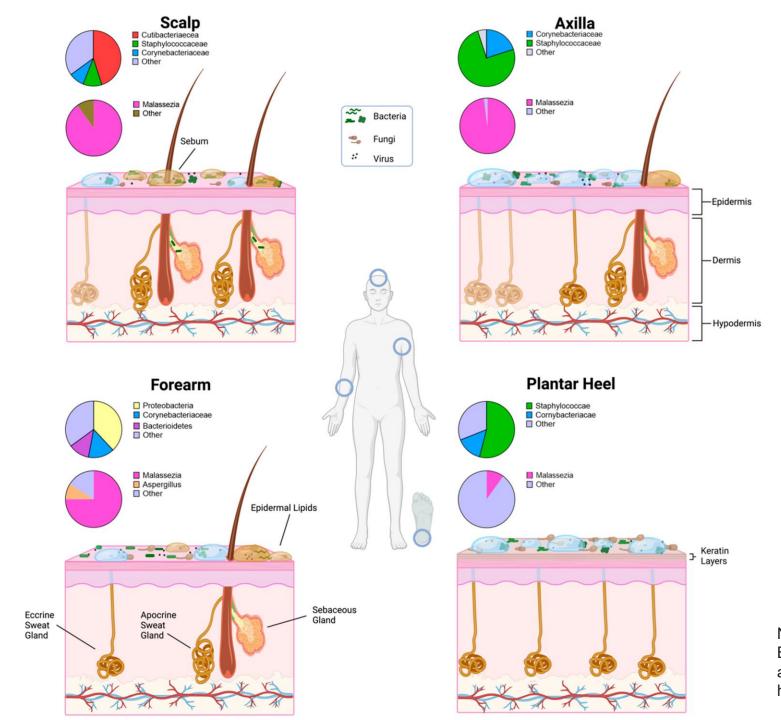


Plant-based

- ↑ Lactobacillus, Bifidobacteria, A. muciniphila
- ↓ Bacteroides fragilis and Clostridium perfringens and Ruminococcus bromii
- ↑ Bifidobacterium, Lactobacillus

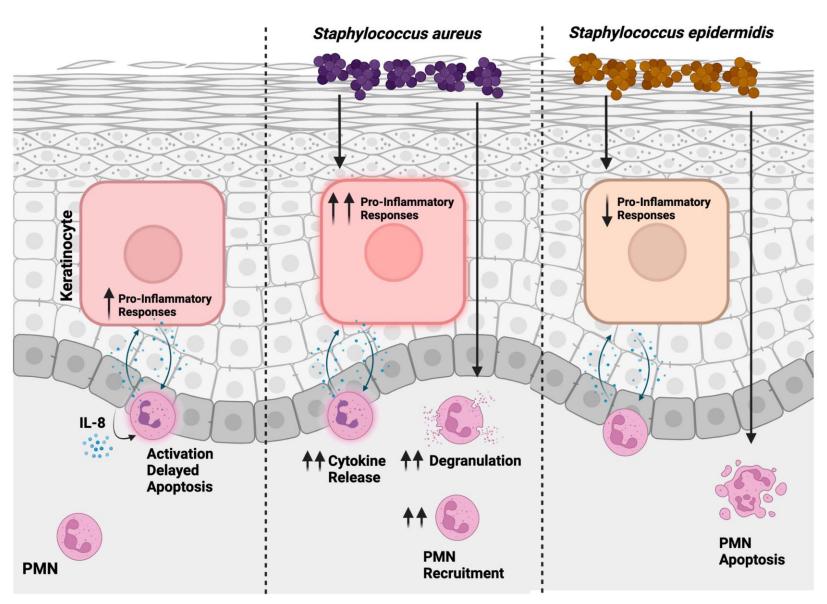
↑ Bifidobacterium Bacteroidetes

Front. Immunol., 09 June 2020 . Does an Apple a Day Also Keep the Microbes Away? The Interplay Between Diet, Microbiota, and Host Defense Peptides at the Intestinal Mucosal Barrier. Fabiola Puértolas-Balint and Bjoern O. Schroeder



Huidmicrobioom

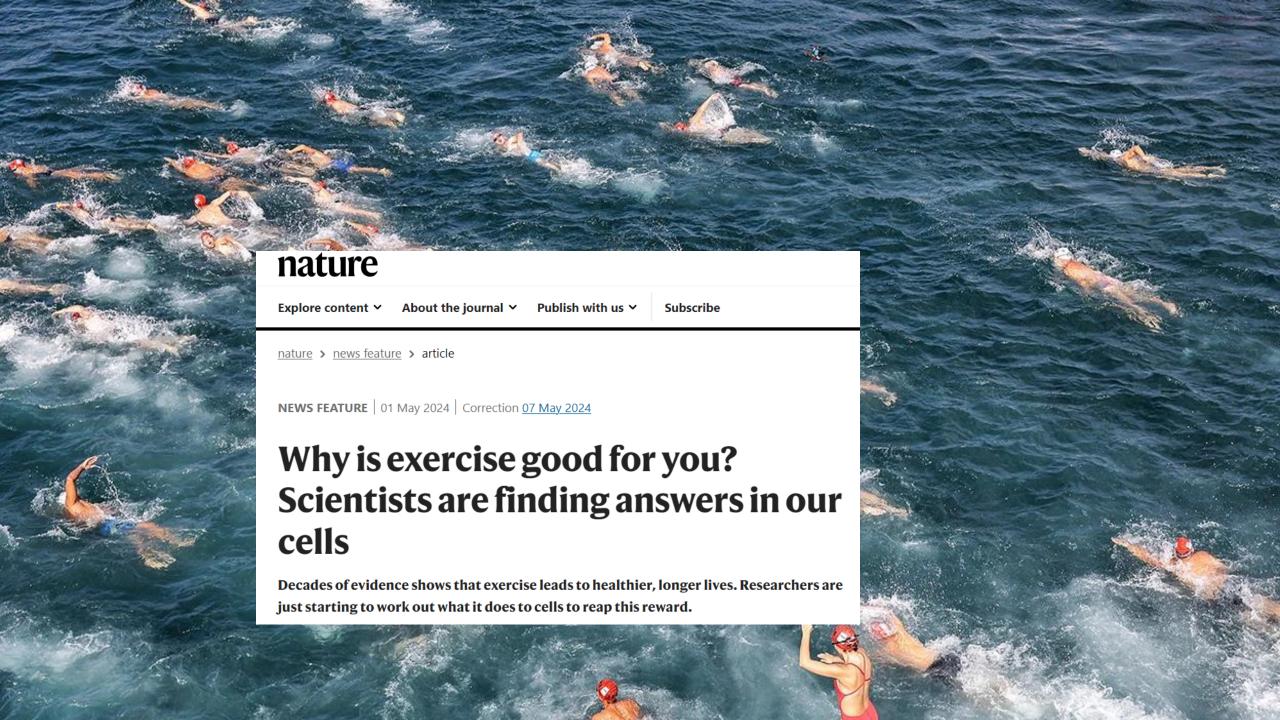
Nicholas-Haizelden, K.; Murphy, B.; Hoptroff, M.; Horsburgh, M.J. Bioprospecting the Skin Microbiome: Advances in Therapeutics and Personal Care Products. *Microorganisms* **2023**, *11*, 1899. https://doi.org/10.3390/microorganisms11081899



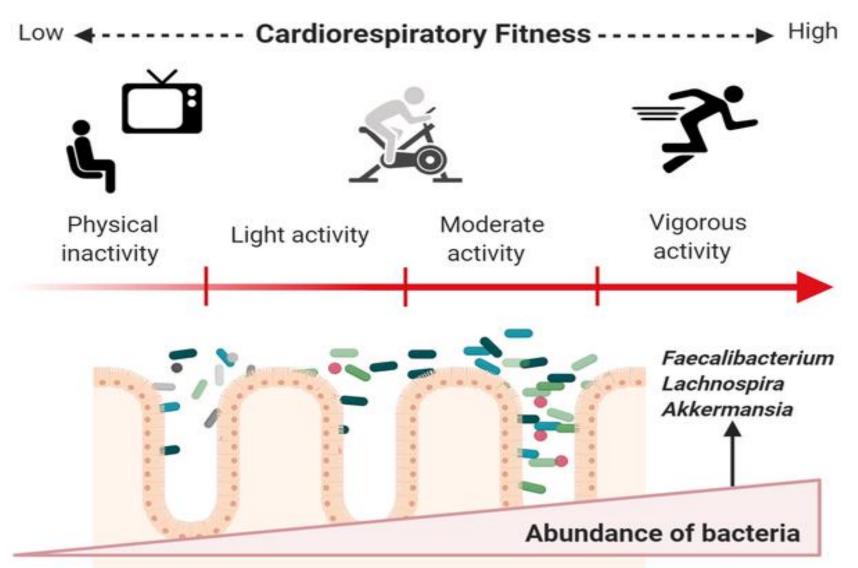
Front. Immunol., 16 February 2024
Volume 15 - 2024 |
https://doi.org/10.3389/fimmu.2024.127
5153
Crosstalk between keratinocytes and neutrophils shapes skin immunity against S. aureus infection

Jule Focken, Birgit Schittek

Polymorphonuclear neutrophils (PMNs)

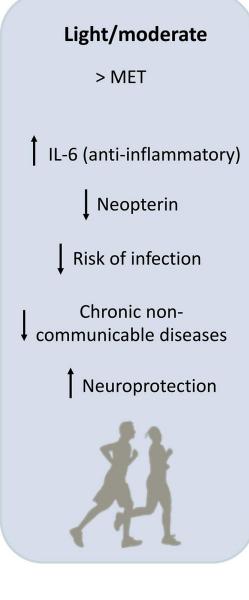


Progressive increase of physical activity level generates changes in the intestinal microbiota

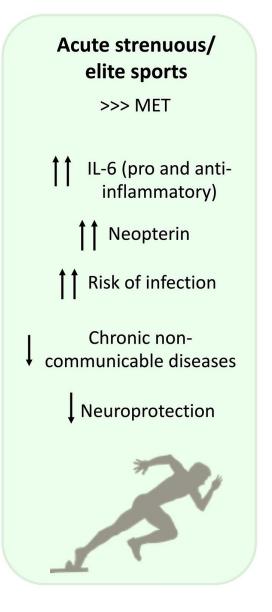


Aya V, Flórez A, Perez L, Ramírez JD (2021) Association between physical activity and changes in intestinal microbiota composition: A systematic review. PLOS ONE 16(2): e0247039.

Physical inactivity < 2 MET IL-6 (pro-inflammatory) Neopterin Risk of infection Chronic non-I I communicable diseases = Neuroprotection



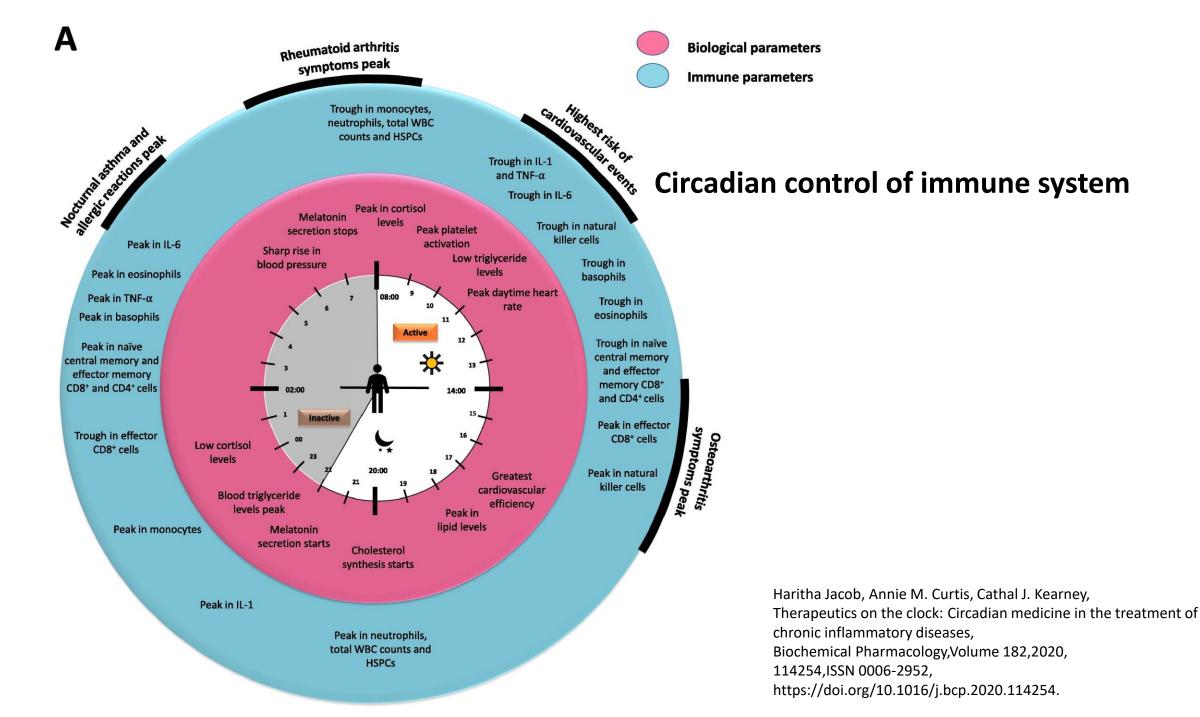
Regular training >> MET IL-6 (anti-inflammatory) Neopterin Risk of infection Chronic nontt communicable diseases Neuroprotection

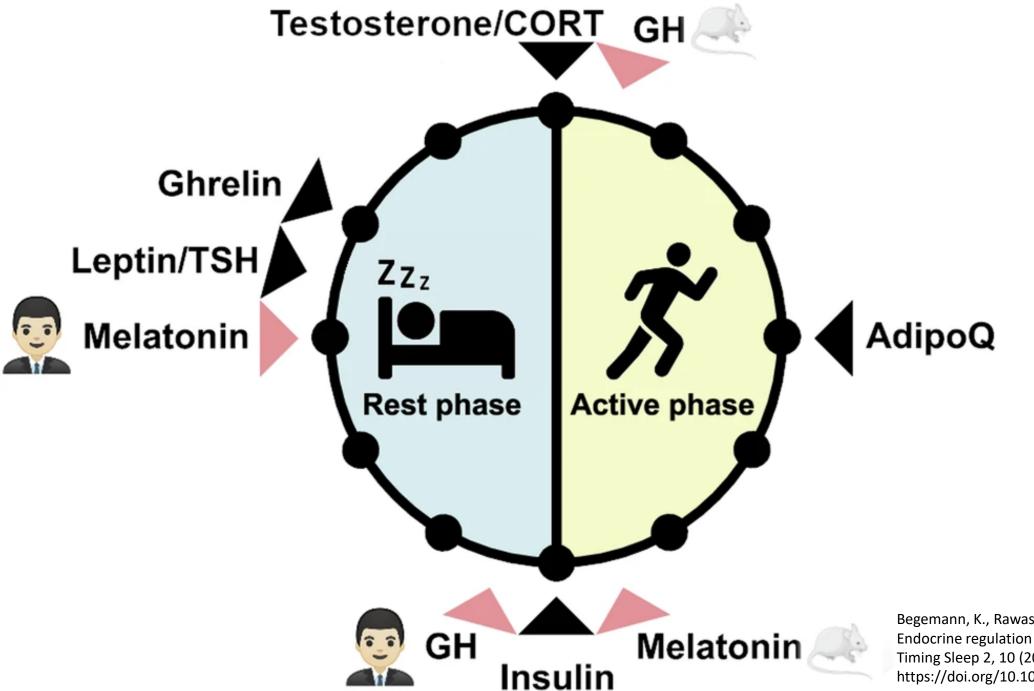


Débora da Luz Scheffer, Alexandra Latini, Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs, Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease, Volume 1866, Issue 10, 2020, 165823,

HEART RATE MODERATE EXERCISE VIGOROUS EXERCISE ACUTE EFFECTS Adenosine а Leukocytosis CD8+ T cell AMP **CD73** Non-classical Vitamin D b monocytes T_H1 O DAMPs T_H17 d k CHRONIC EFFECTS Non-classical and CXCR3 intermediate monocytes Preserving thymus output

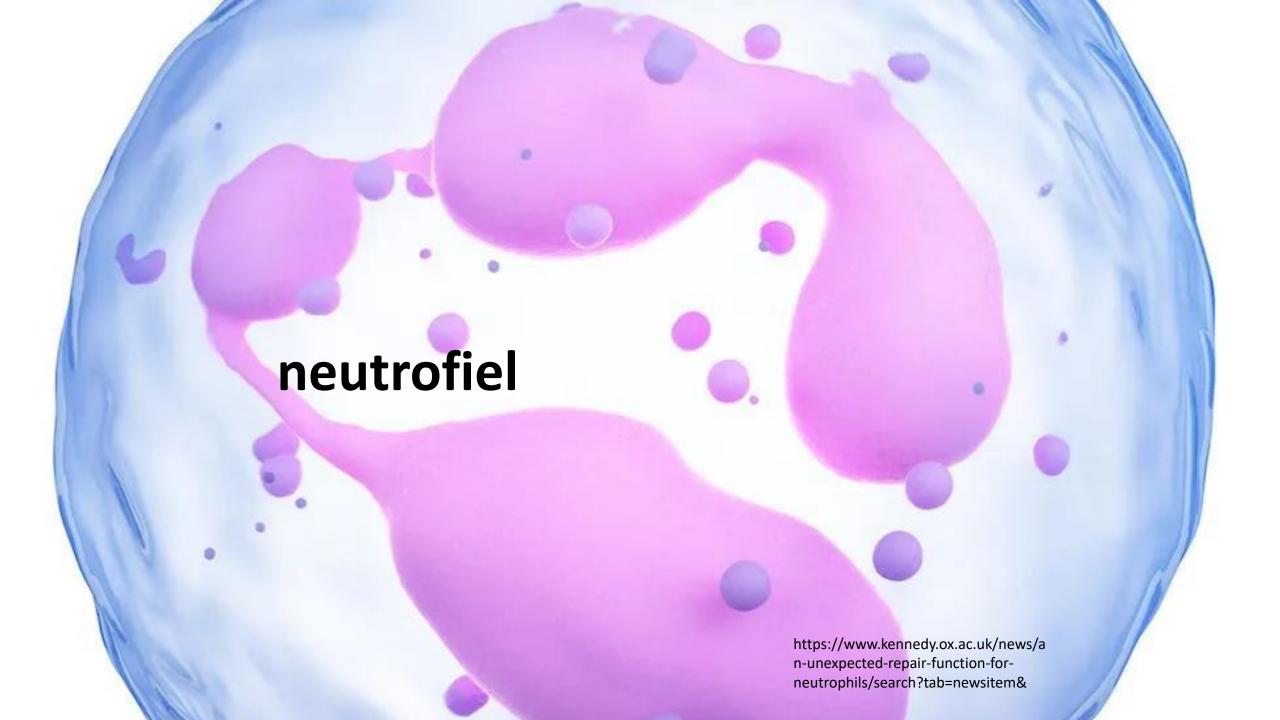
Meyer-Lindemann, U.; Moggio, A.; Dutsch, A.; Kessler, T.; Sager, H.B. The Impact of Exercise on Immunity, Metabolism, and Atherosclerosis. Int. J. Mol. Sci. 2023, 24, 3394. https://doi.org/10.3390/ijms24043394





Begemann, K., Rawashdeh, O., Olejniczak, I. et al. Endocrine regulation of circadian rhythms. npj Biol Timing Sleep 2, 10 (2025).

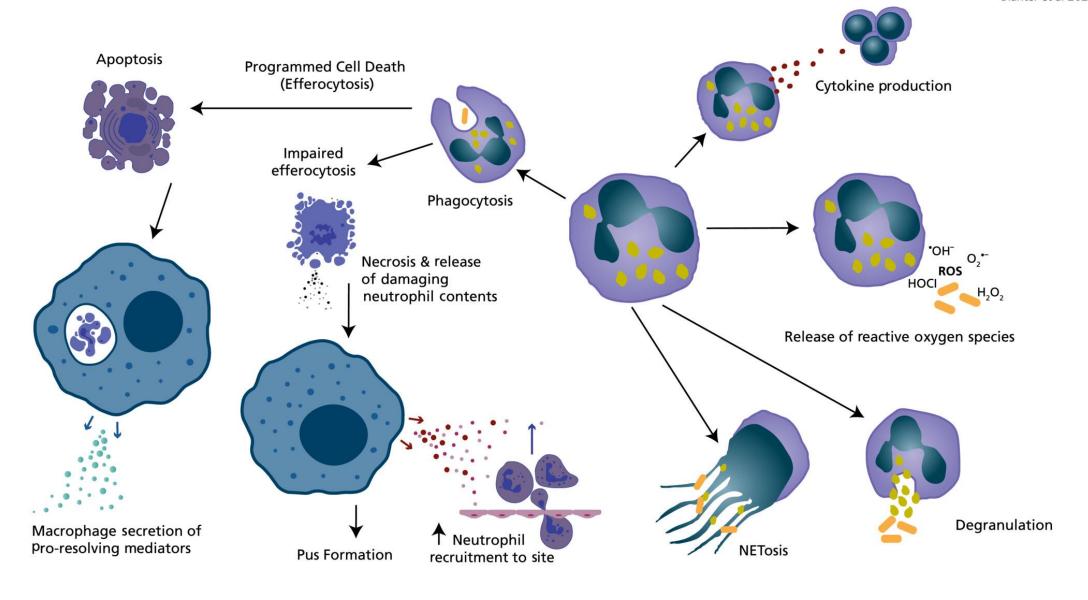
https://doi.org/10.1038/s44323-025-00024-6

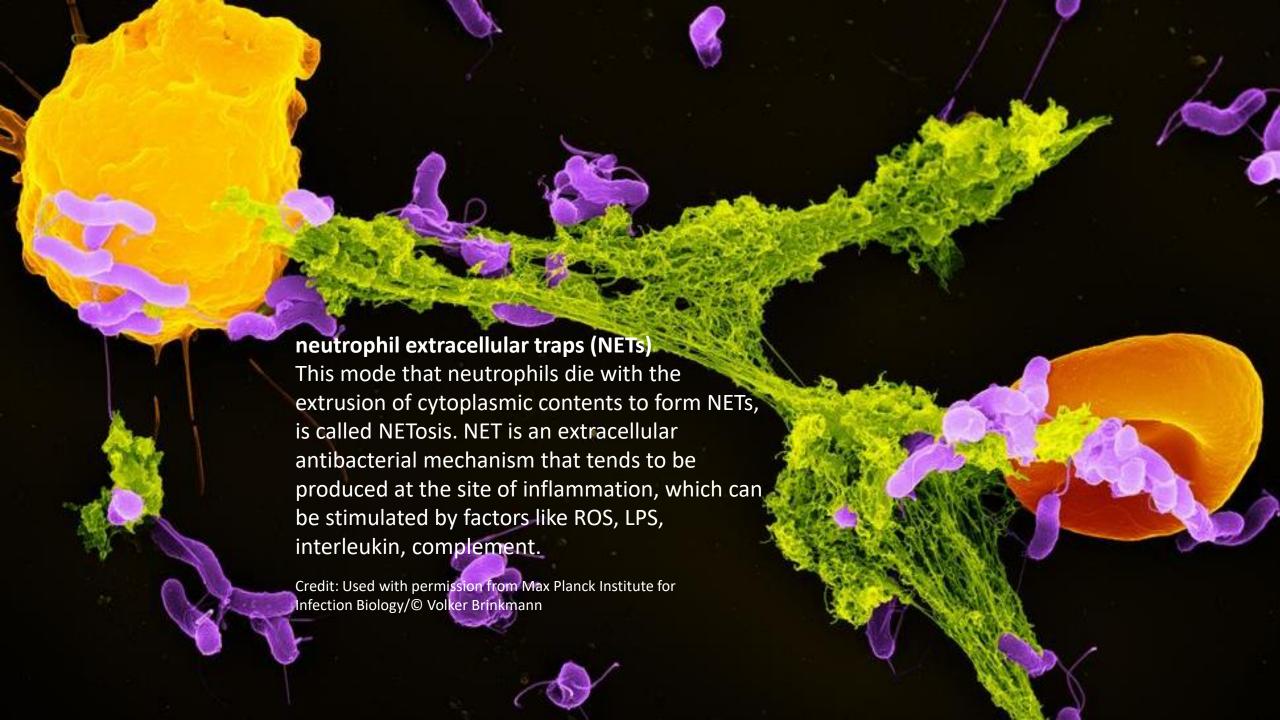


Myocardial Infarction Atherosclerosis Metabolic disease Stroke Clonal hematopoiesis Cancer Organismal aging Autoimmunity **NETs** ROS production Granule release (MPO, NE) Cytokine and alarmin production (IL-1b, IL-17A, CSF-1, S100A8/9) Interferon and inflammosome signaling (IFN, NLRP3) Neutrophil-WBC interaction (platelets, B and T cells, pDCs)

Neutrophils in Physiology and Pathology

Aroca-Crevillén A, Vicanolo T, Ovadia S, Hidalgo A. Neutrophils in Physiology and Pathology. Annu Rev Pathol. 2024 Jan 24;19:227-259. doi: 10.1146/annurev-pathmechdis-051222-015009. PMID: 38265879; PMCID: PMC11060889.





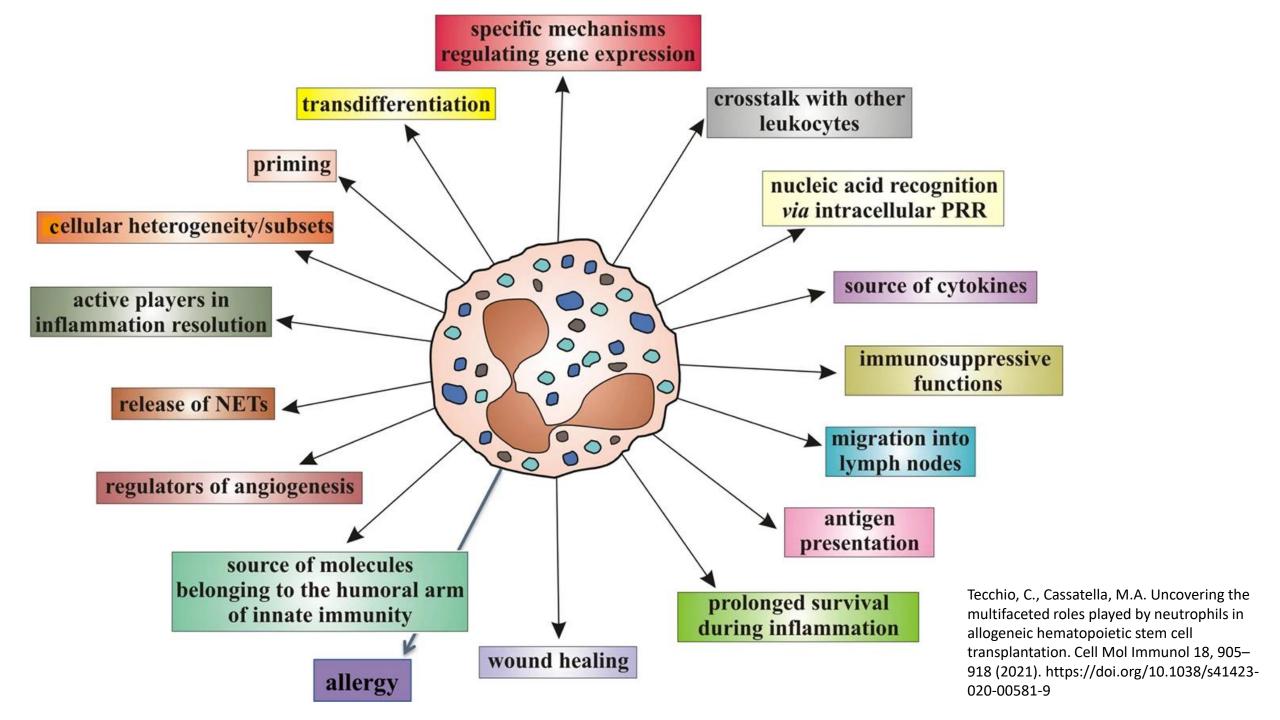


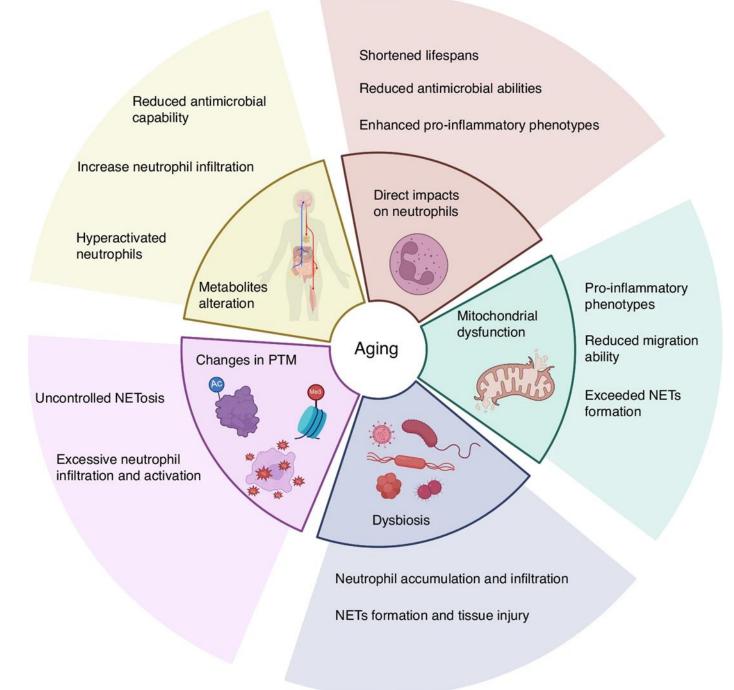
Skin Infections Caused by Staphylococcus aureus.

Skin Infections Caused by Staphylococcus aureus. Pascal del Giudice. Accepted Mar 19, 2020; Epub ahead of print Mar 24, 2020 Acta Derm Venereol 2020; 100: adv00110.



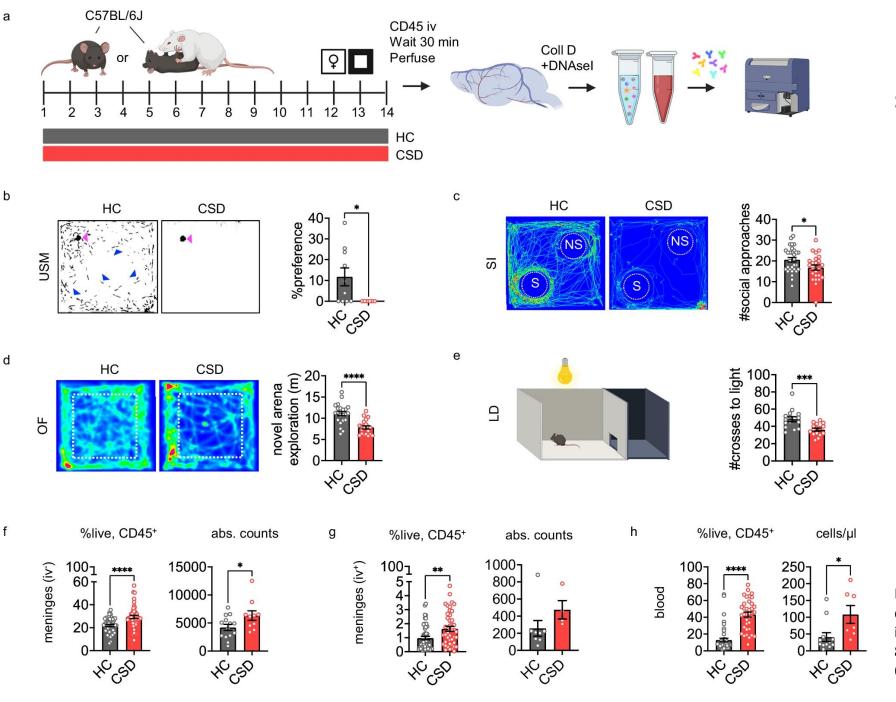
https://netec.org/2 024/07/11/mpoxin-2024-10takeaways-forfrontline-healthcare-staff/





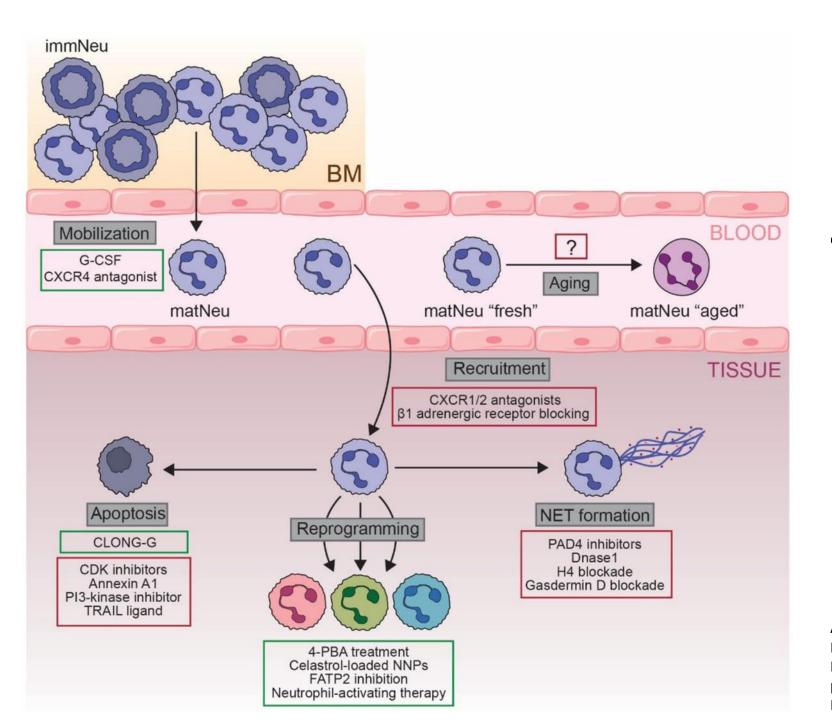
The effects of aging-induced changes on neutrophil functions

Wang, Z., Saxena, A., Yan, W. et al. The impact of aging on neutrophil functions and the contribution to periodontitis. Int J Oral Sci 17, 10 (2025). https://doi.org/10.1038/s41368-024-00332-w



stress induces meningeal neutrophilia via type I interferon signaling in male mice

Kigar, S.L., Lynall, ME., DePuyt, A.E. et al. Chronic social defeat stress induces meningeal neutrophilia via type I interferon signaling in male mice. Nat Commun 16, 8153 (2025). https://doi.org/10.1038/s41467-025-62840-5



Strategies to target neutrophils

Aroca-Crevillén A, Vicanolo T, Ovadia S, Hidalgo A. Neutrophils in Physiology and Pathology. Annu Rev Pathol. 2024 Jan 24;19:227-259. doi: 10.1146/annurevpathmechdis-051222-015009. PMID: 38265879; PMCID: PMC11060889.

Table 1. Uses and mechanisms of action of anti-neutrophilic drugs for dermatological and autoimmune disorders. Treatment Use Mechanism of Action Dermatitis herpetiformis Autoimmune bullous disorders Sweet syndrome and pyoderma gangrenosum Erythema elevatum diutinum Urticarial vasculitis Leukocytoclastic vasculitis Inhibits neutrophil chemotaxis. Dapsone Pustular psoriasis Reduces oxidative damage in tissues. Hidradenitis suppurativa Reduces tumor necrosis factor. Eosinophilic dermatoses: wells syndrome, granuloma faciale, eosinophilic annular erythema and chronic idiopathic urticaria Cutaneous lupus erythematosus Recurrent erythema multiforme Generalized granuloma annulare Rheumatoid papular eruption Autoimmune bullous disorders Sweet syndrome and pyoderma gangrenosum Disrupts microtubule formation. Colchicine Pustular psoriasis Reduces neutrophil migration and activity. Hidradenitis suppurativa Decreases inflammatory cytokines. Behçet's syndrome Acne Rosacea Autoimmune bullous disorders Sweet syndrome and pyoderma gangrenosum Inhibits neutrophil chemotaxis. Erythema elevatum diutinum Reduces cytokines. Tetracyclines Leukocytoclastic vasculitis Reduces matrix metalloproteinases.

Hidradenitis suppurativa

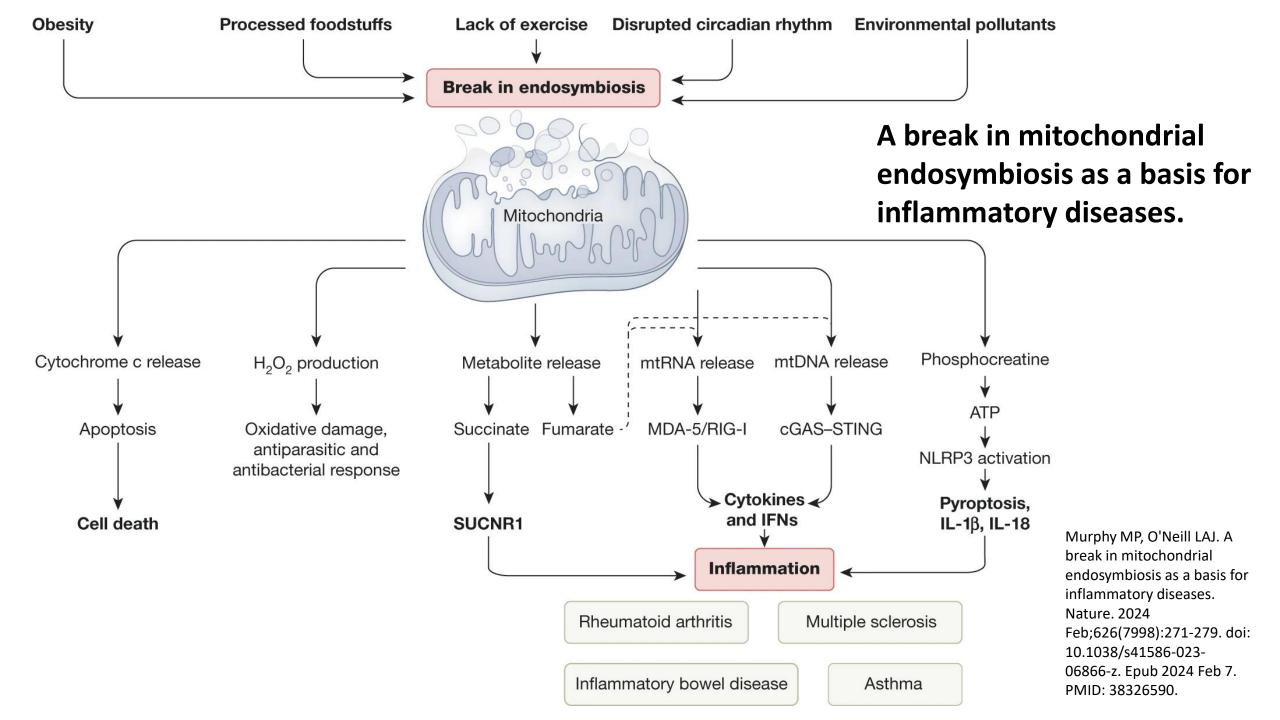
Pustular psoriasis

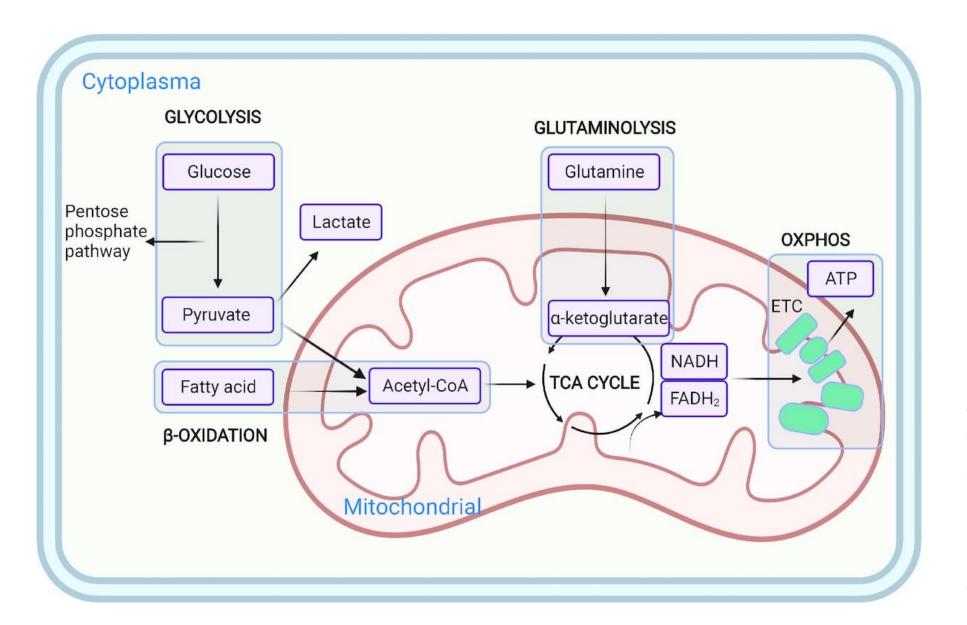
Wells syndrome
Lichen planus pilaris
Generalized granuloma annulare and cutaneous sarcoidosis

Francescnin, L., Guidotti, A., Miazzetto, K., Tartaglia, J., Ciolfi, C., Alaibac, M., & Sernicola, A. (2024). Repurposing Historic Drugs for Neutrophil-Mediated Inflammation in Skin Disorders. Biomolecules, 14(12), 1515. https://doi.org/10.3390/biom14121515

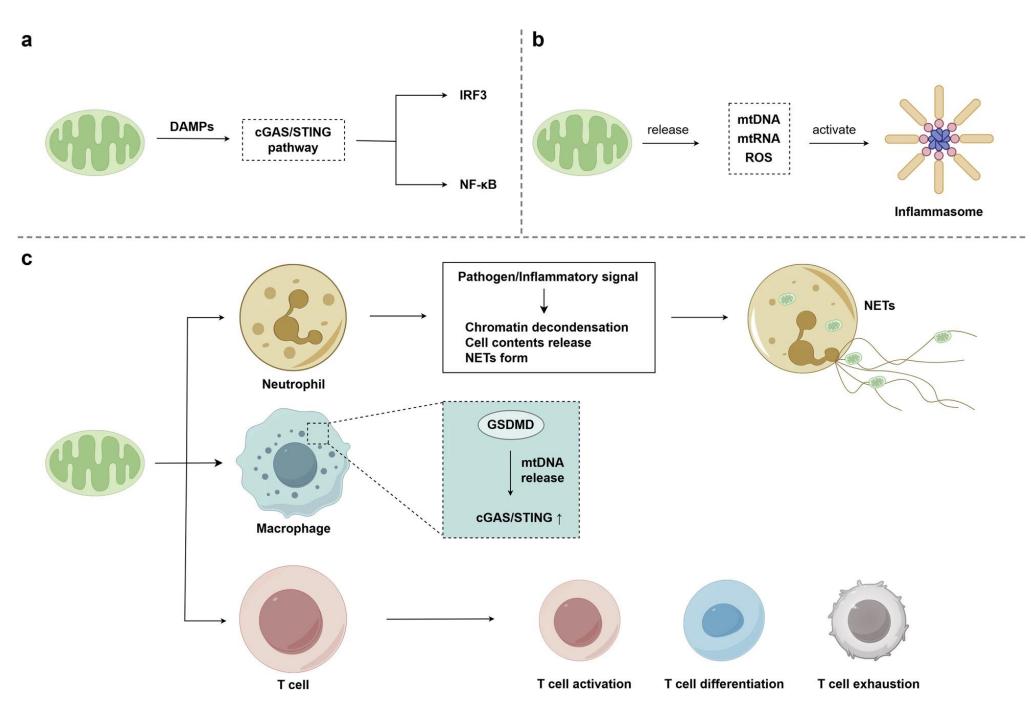
Prevents oxidative damage.

Anti-apoptotic effect.

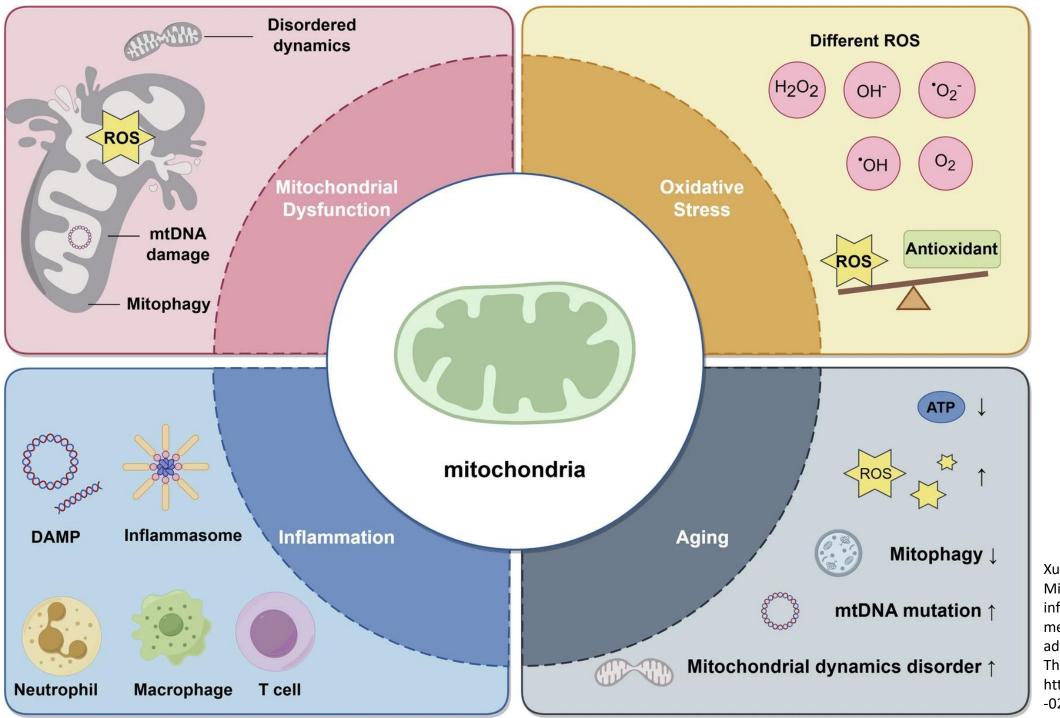




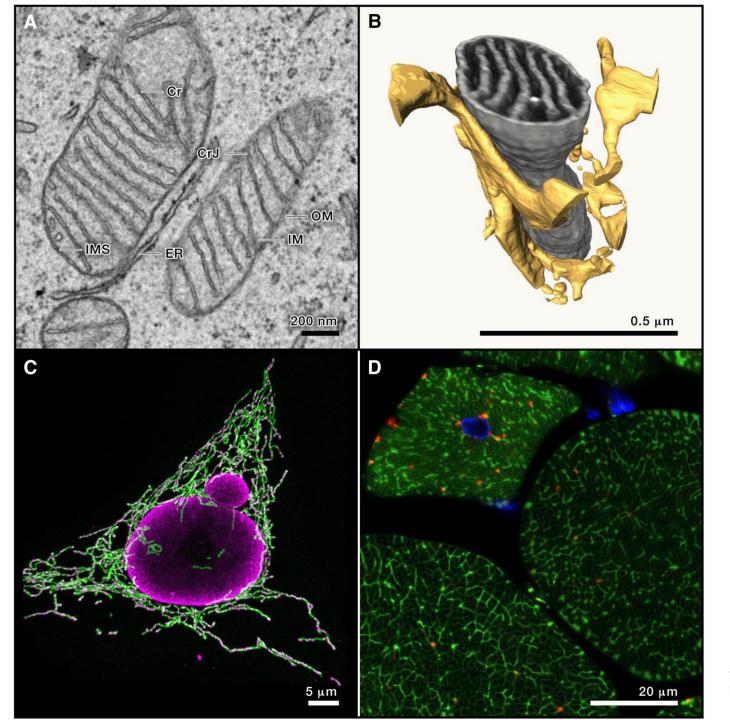
Wenjing Yang, Tianming Yu, Yingzi Cong, CD4+ T cell metabolism, gut microbiota, and autoimmune diseases: implication in precision medicine of autoimmune diseases, Precision Clinical Medicine, Volume 5, Issue 3, September 2022, pbac018, https://doi.org/10.1093/pcmedi/pba c018



Xu, X., Pang, Y. & Fan, X.
Mitochondria in oxidative stress, inflammation and aging: from mechanisms to therapeutic advances. Sig Transduct Target Ther 10, 190 (2025). https://doi.org/10.1038/s41392-025-02253-4



Xu, X., Pang, Y. & Fan, X.
Mitochondria in oxidative stress, inflammation and aging: from mechanisms to therapeutic advances. Sig Transduct Target Ther 10, 190 (2025). https://doi.org/10.1038/s41392-025-02253-4



Mitochondria at the crossroads of health and disease

Mitochondria at the crossroads of health and disease Suomalainen, Anu et al.

Cell, 2024, Volume 187, Issue 11, 2601 - 2627

mitochondrial signaling

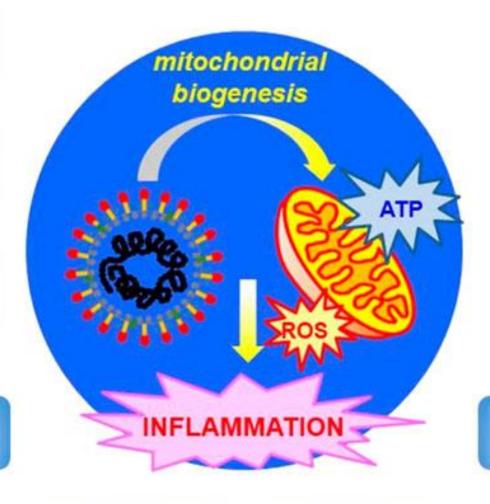
mitochondrial hormesis

mitochondrial senescence

mitochondrial dynamics

ncRNA

sgRNA in mitochondria



organ & tissue aberrations

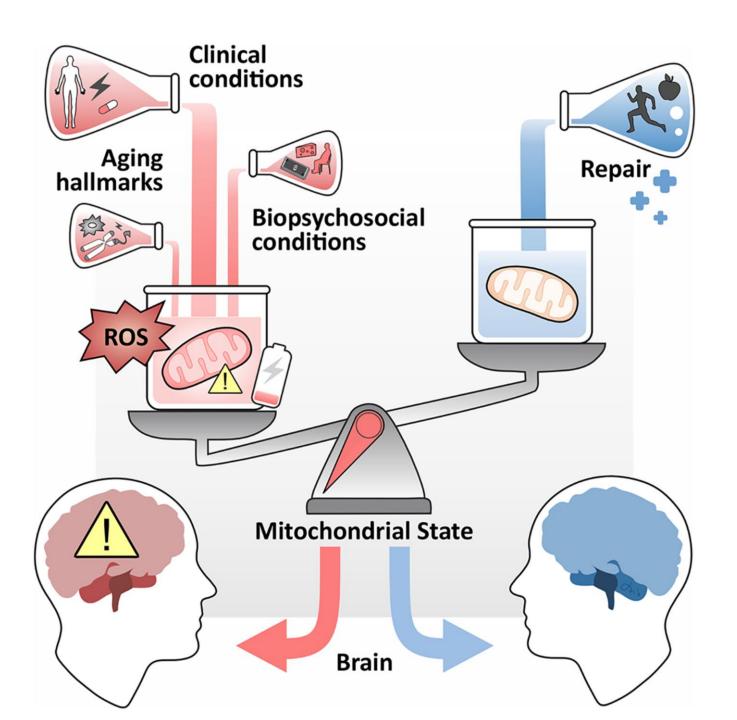
OXPHOS activity

protein-protein interactions

metabolic alterations

mitogenome sensing

diagnostic biomarkers Front. Physiol., 21 June 2024
Volume 15 - 2024 |
https://doi.org/10.3389/fphys.2024.1406635
Mitochondria in COVID-19: from cellular and molecular perspective
Michał Rurek



Ledo, A. and Rocha, B.S. (2024), Redox medicine: from cellular targets to systems physiology and therapeutics. FEBS Lett, 598: 2043-2046. https://doi.org/10.1002/1873-3468.15005

nature aging

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nature > nature aging > analyses > article

Analysis Published: 10 November 2025

Multilingualism protects against accelerated aging in cross-sectional and longitudinal analyses of 27 European countries

Lucia Amoruso, Hernan Hernandez, Hernando Santamaria-Garcia, Sebastian Moguilner, Agustina Legaz, Pavel Prado, Jhosmary Cuadros, Liset Gonzalez, Raul Gonzalez-Gomez, Joaquín Migeot, Carlos Coronel-Oliveros, Josephine Cruzat, Manuel Carreiras, Vicente Medel, Marcelo Adrián Maito, Claudia Duran-Aniotz, Enzo Tagliazucchi, Sandra Baez, Adolfo M. García & Agustin Ibanez

Nature Aging 5, 2340–2354 (2025) Cite this article

5571 Accesses | 2 Citations | 1424 Altmetric | Metrics

Abstract

Aging trajectories are influenced by modifiable risk factors, and prior evidence has hinted that multilingualism may have protective potential. However, reliance on suboptimal health markers, small samples, inadequate confounder control and a focus on clinical cohorts led to mixed findings and limited applicability to healthy populations. Here, we developed biobehavioral age gaps, quantifying delayed or accelerated aging in 86,149 participants across 27 European countries. National surveys provided individual-level positive (functional ability, education, cognition) and adverse (cardiometabolic conditions, female sex, sensory impairments) factors, while country-level multilingualism served as an aggregate exposure. Biobehavioral factors predicted age ($R^2 = 0.24$, r = 0.49, root mean squared error = 8.61), with positive factors linked to delayed aging and adverse factors to accelerated aging. Multilingualism emerged as a protective factor in cross-sectional (odds ratio = 0.46) and longitudinal (relative risk = 0.70) analyses, whereas monolingualism increased risk of accelerated aging (odds ratio = 2.11; relative risk = 1.43). Effects persisted after adjusting for linguistic, physical, social and sociopolitical exposomes. These results underscore the protective role of multilingualism and its broad applicability for global health initiatives.

nature reviews drug discovery

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Review Article Published: 04 March 2025

Thirty years of NRF2: advances and therapeutic challenges

Donna D. Zhang ☑

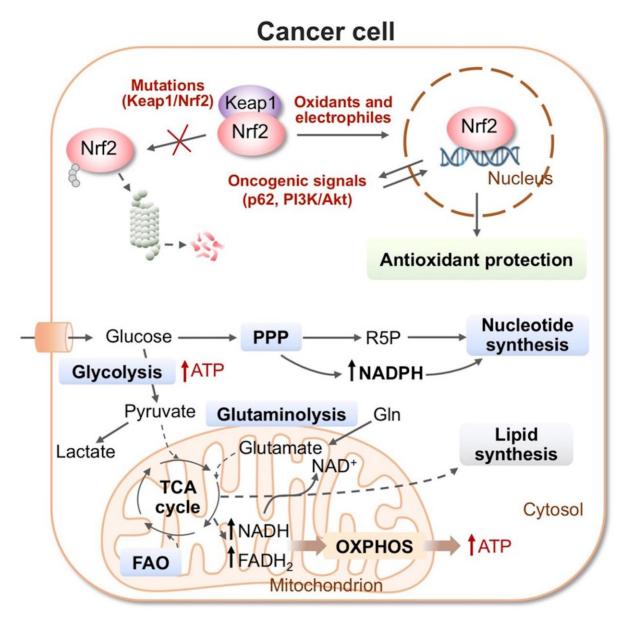
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Abstract

Over the last 30 years, NRF2 has evolved from being recognized as a transcription factor primarily involved in redox balance and detoxification to a well-appreciated master regulator of cellular proteostasis, metabolism and iron homeostasis. NRF2 plays a pivotal role in diverse pathologies, including cancer, and metabolic, inflammatory and neurodegenerative disorders. It exhibits a Janus-faced duality, safeguarding cellular integrity in normal cells against environmental insults to prevent disease onset, whereas in certain cancers, constitutively elevated NRF2 levels provide a tumour survival advantage, promoting progression, therapy resistance and metastasis. Advances in understanding the mechanistic regulation of NRF2 and its roles in human pathology have propelled the investigation of NRF2-targeted therapeutic strategies. This Review dissects the mechanistic intricacies of NRF2 signalling, its cross-talk with biological processes and its far-reaching implications for health and disease, highlighting key discoveries that have shaped innovative therapeutic approaches targeting NRF2.

Nuclear factor erythroid 2-related factor 2 (NRF2)



Luchkova, A., Mata, A. and Cadenas, S. (2024), Nrf2 as a regulator of energy metabolism and mitochondrial function. FEBS Lett, 598: 2092-2105. https://doi.org/10.1002/1873-3468.14993

A Probiotic-Derived Topical Strategy to Strengthen Cutaneous Defense Against UV-Related Environmental Stress Through Nrf-2 Activation

Brief Title: Cutaneous Defense Against Environmental Stress

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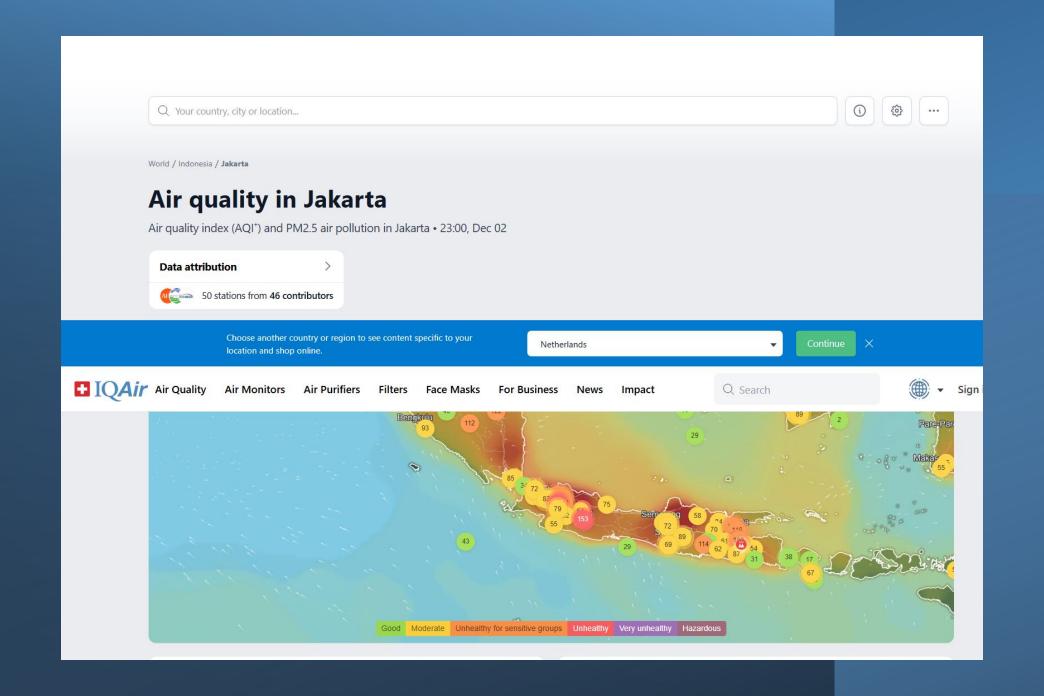
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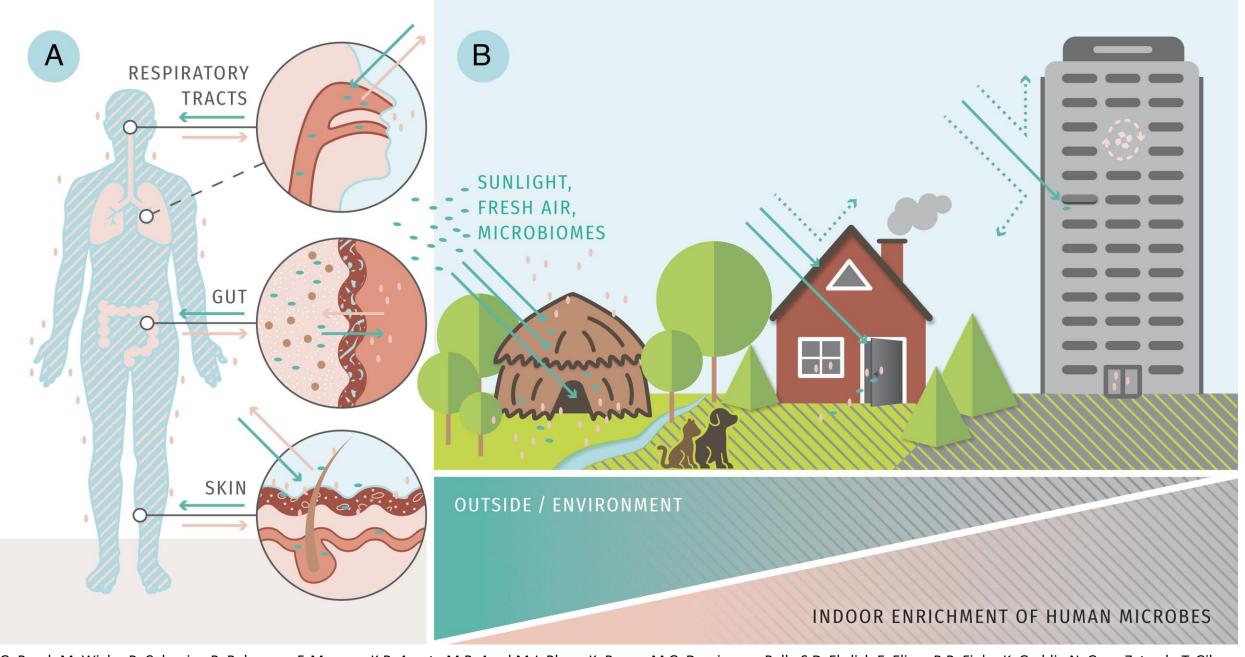
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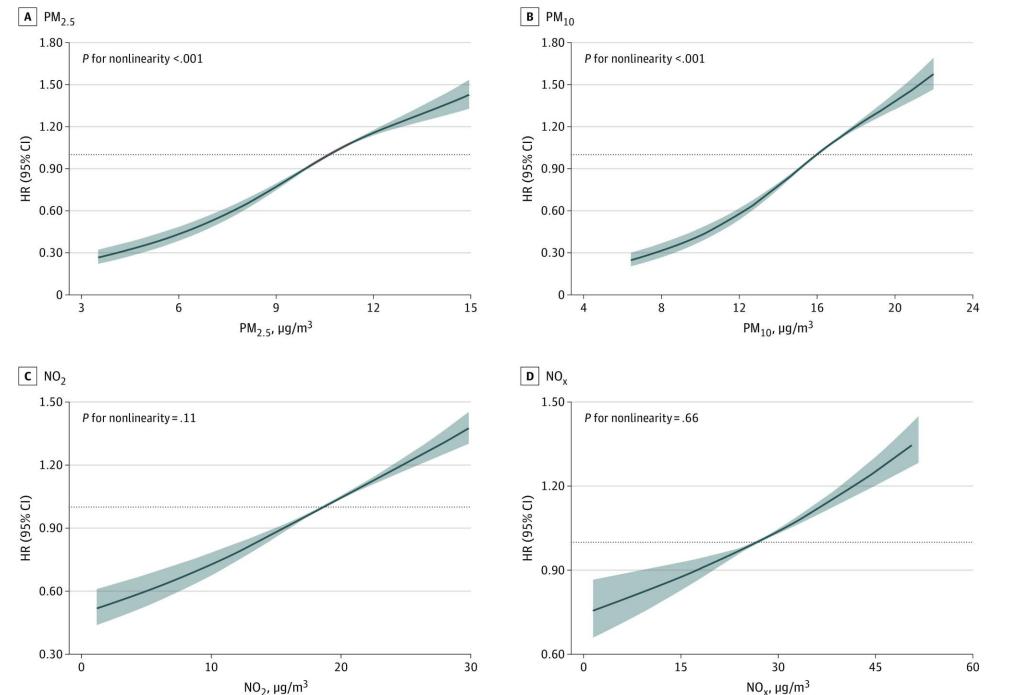
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Psoriasis vulgaris

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Exposure to Air Pollution,
Genetic
Susceptibility,
and Psoriasis
Risk in the UK

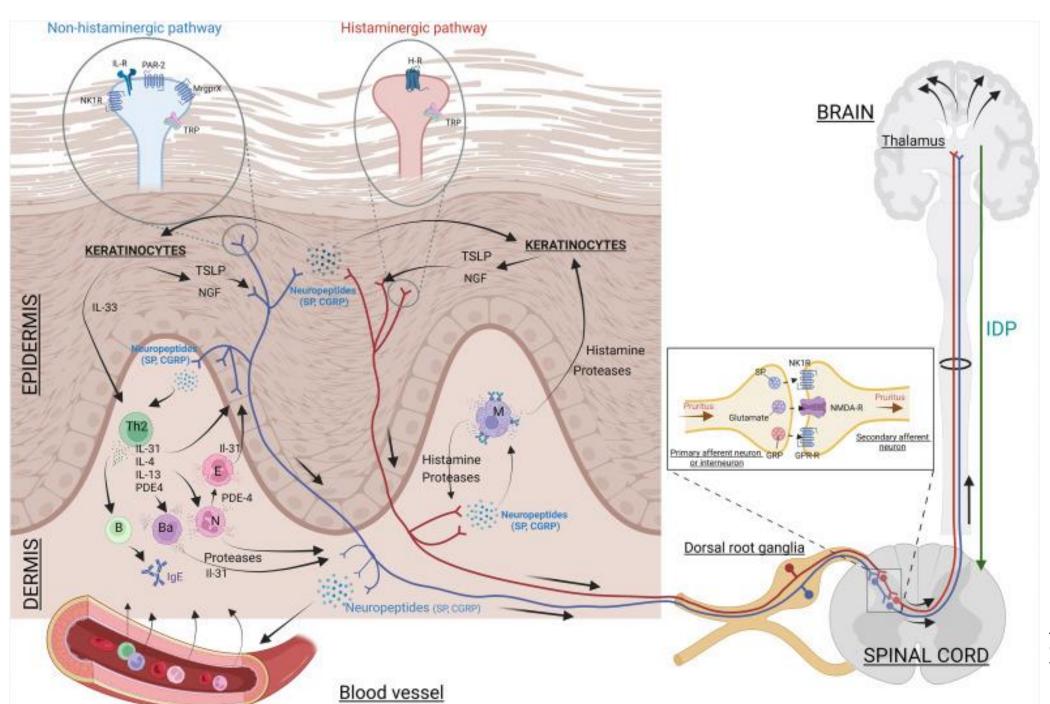
Wu J, Ma Y, Yang J, Tian Y. Exposure to Air Pollution, Genetic Susceptibility, and Psoriasis Risk in the UK. JAMA Netw Open. 2024;7(7):e2421665. doi:10.1001/jamanetworkopen. 2024.21665



9 October 2025

Data from more than 300,000 UK Biobank participants show that air pollution can raise older people's risk of a condition causing unbearably itchy skin.

UK Biobank participants living in areas with high air pollution are more likely to develop atopic eczema late in life. Almost 16% of late-life eczema cases could be prevented by cutting air pollution in the worst-affected areas, the researchers estimate. They suggest that studies such as this one should be a wake-up call for politicians and policymakers to push for cleaner air solutions.



Basic mechanisms of itch Misery, Laurent et al. Journal of Allergy and Clinical Immunology, 2023 Volume 152, Issue 1, 11 - 23

