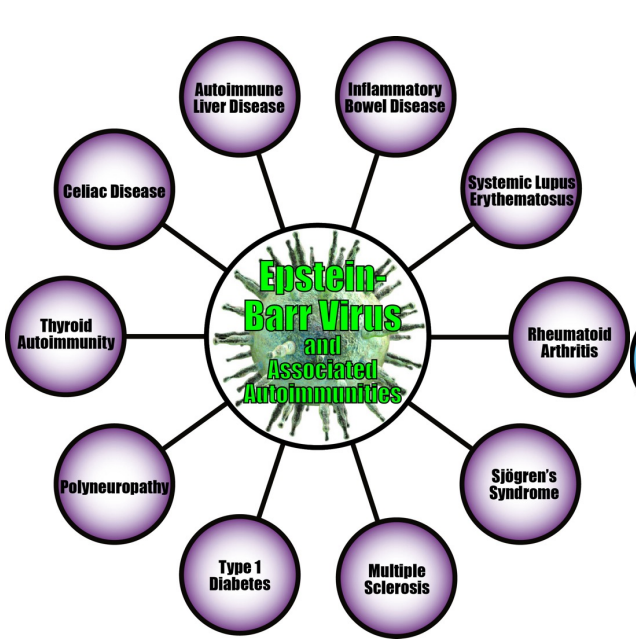
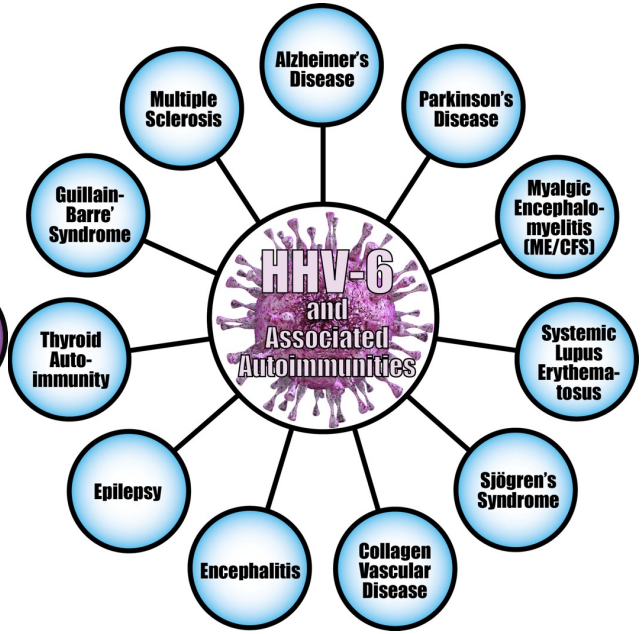
Infection & Autoimmunity





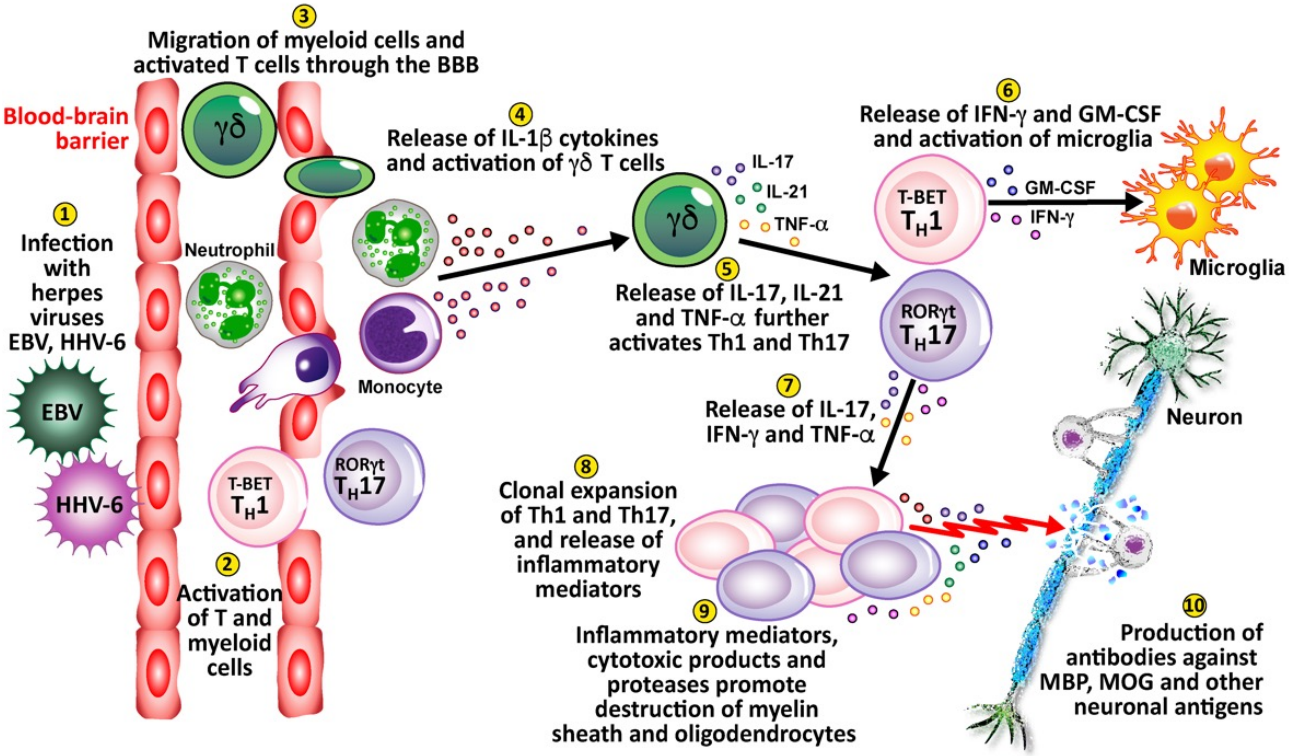
The Autoimmune Viral Trio

Epstein-Barr virus may be leading cause of multiple sclerosis

For immediate release: January 13, 2022

Boston, MA – Multiple sclerosis (MS), a progressive disease that affects 2.8 million people worldwide and for which there is no definitive cure, is likely caused by infection with the Epstein-Barr virus (EBV), according to a study led by Harvard T.H. Chan School of Public Health researchers.

Their findings were published online in Science on January 13, 2022.



10 key pathological processes induced by the herpes family of viruses that results in the destruction of neurons and the production of antibodies against MBP, MOG and other neuronal antigens

Journal of Translational Autoimmunity 5 (2022) 100147

Contents lists available at ScienceDirect

Journal of Translational Autoimmunity

journal homepage: www.sciencedirect.com/journal/journal-of-translational-autoimmunity

A master autoantigen-ome links alternative splicing, female predilection, and COVID-19 to autoimmune diseases

Julia Y. Wang [a,**,1], Michael W. Roehrl [a,1], Victor B. Roehrl [a], Michael H. Roehrl [b,c,d,*]

ABSTRACT

Chronic and debilitating autoimmune sequelae pose a grave concern for the post-COVID-19 pandemic era. Based on our discovery that the glycosaminoglycan dermatan sulfate (DS) displays peculiar affinity to apoptotic cells and autoantigens (autoAgs) and that DS-autoAg complexes cooperatively stimulate autoreactive B1 cell responses, we compiled a database of 751 candidate autoAgs from six human cell types.

processing, and vesicle transport. Interestingly, the coding genes of autoAgs predominantly contain multiple

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A B S T R A C T

At least 657 of these have been found to be affected by SARS-CoV-2 infection based on currently available multi-omic COVID data, and at least 400 are confirmed targets of autoantibodies in a wide array of autoimmune diseases and cancer.

least 400 are confirmed targets of autoantibodies in a wide array of autoimmune diseases and cancer. The autoantigen-ome is significantly associated with various processes in viral infections, such as translation, protein processing, and vesicle transport. Interestingly, the coding genes of autoAgs predominantly contain multiple

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ABSTRACT

The autoantigen-ome is significantly associated with various processes in viral infections, such as translation, protein processing, and vesicle transport. Interestingly, the coding genes of autoAgs predominantly contain multiple exons with many possible alternative splicing variants, short transcripts, and short UTR lengths.

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ABSTRACT

Altered expression in viral infections suggests that viruses exploit alternative splicing to reprogram host cell machinery to ensure viral replication and survival. While each cell type gives rise to a unique pool of autoAgs, 39 common autoAgs associated with cell stress and apoptosis were identified from all six cell types, with several being known markers of systemic autoimmune diseases.

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A B S T R A C T

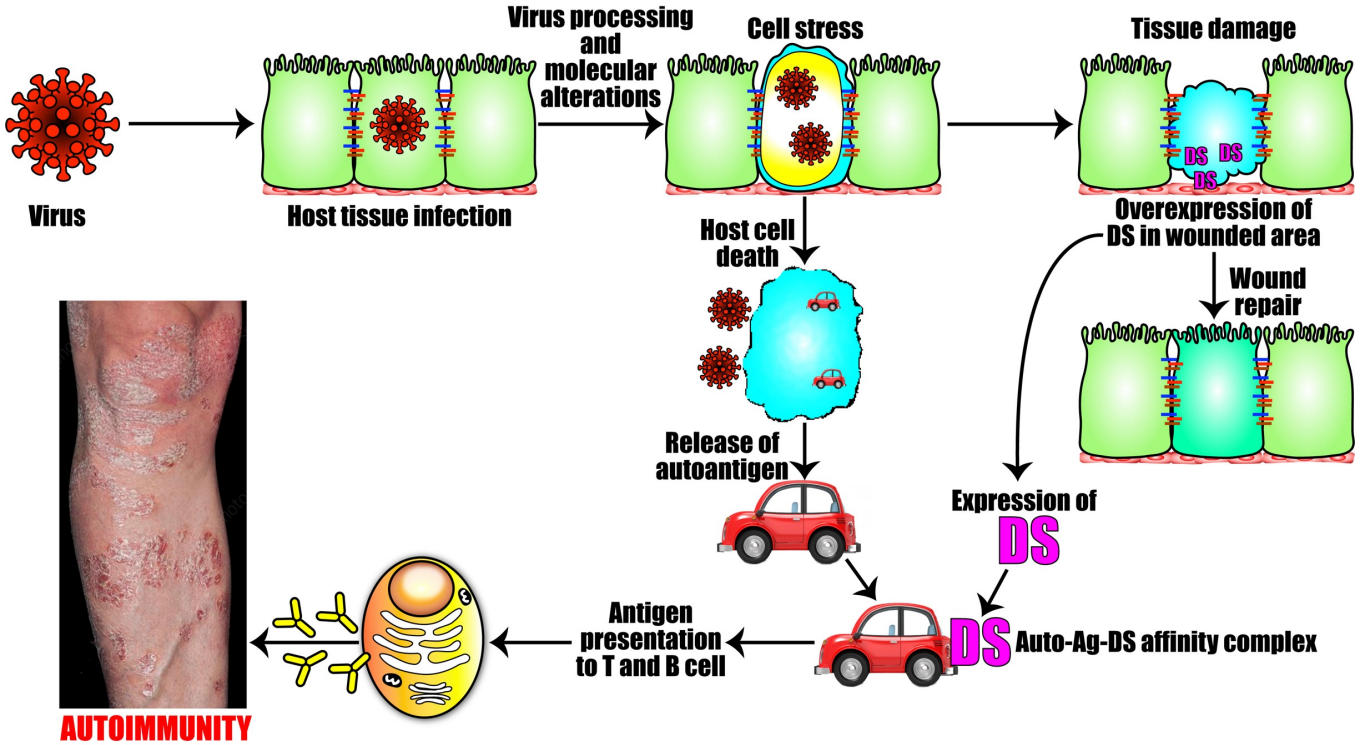
Overall, this master autoantigen-ome provides a molecular guide for investigating the myriad of autoimmune sequalae to COVID-19 and clues to the rare adverse effects of the currently available mRNA and viral vector-based COVID vaccines.

least 400 are confirmed targets of autoantibodies in a wide array of autoimmune diseases and cancer. The autoantigen-ome is significantly associated with various processes in viral infections, such as translation, protein processing, and vesicle transport. Interestingly, the coding genes of autoAgs predominantly contain multiple

Common autoantigens with affinity for DS that have been altered by SARS-CoV-2 infection.

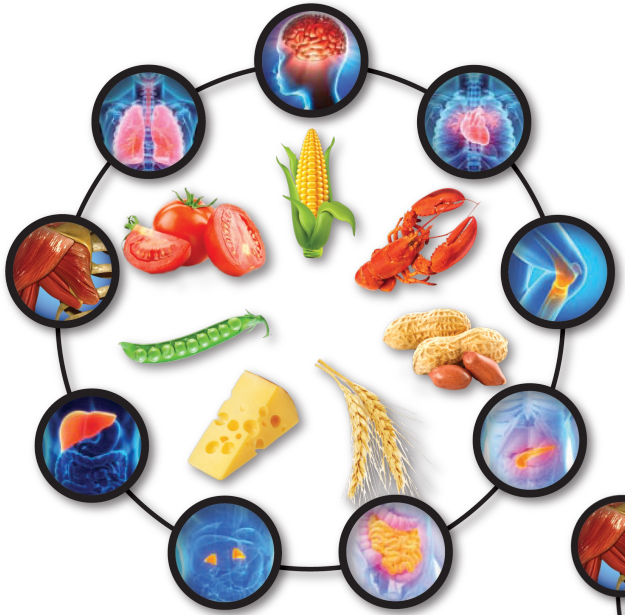
• Actin	• Nuclear RNA	• Protein disulfide isomerase
• Albumin	• Alpha enolase	• Mitochondrial antigens
• Brain acid soluble protein	• Fibulin 1	• Cytochrome P-450 reductase
• Complement C1q binding protein	• Histones	• Serpin
• F-actin subunit α	• hnRNP	• Lupus La protein (La/SSB)
• Cytoskeleton-associated protein	• U1, U2 snRNP	• Tallin 1, 2
• Collagen types 1-12	• Heat shock proteins	• Tropomyosin
• Cartilage-associated protein	• Sm-like protein (U6)	• α, β tubulin
• DNA damage-binding protein	• Myosin	• Vinculin

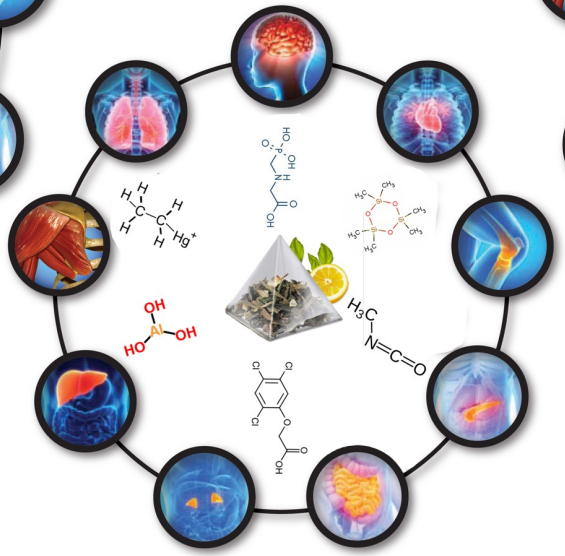
Journal of Translational Autoimmunity 5 (2022) 100147

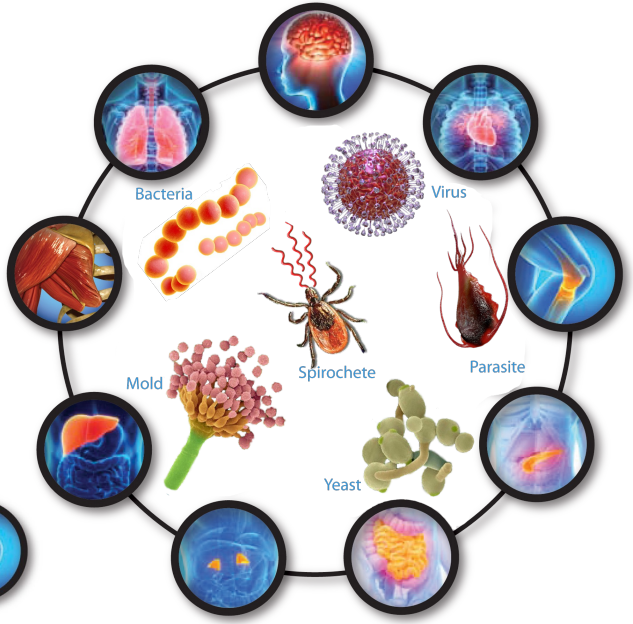


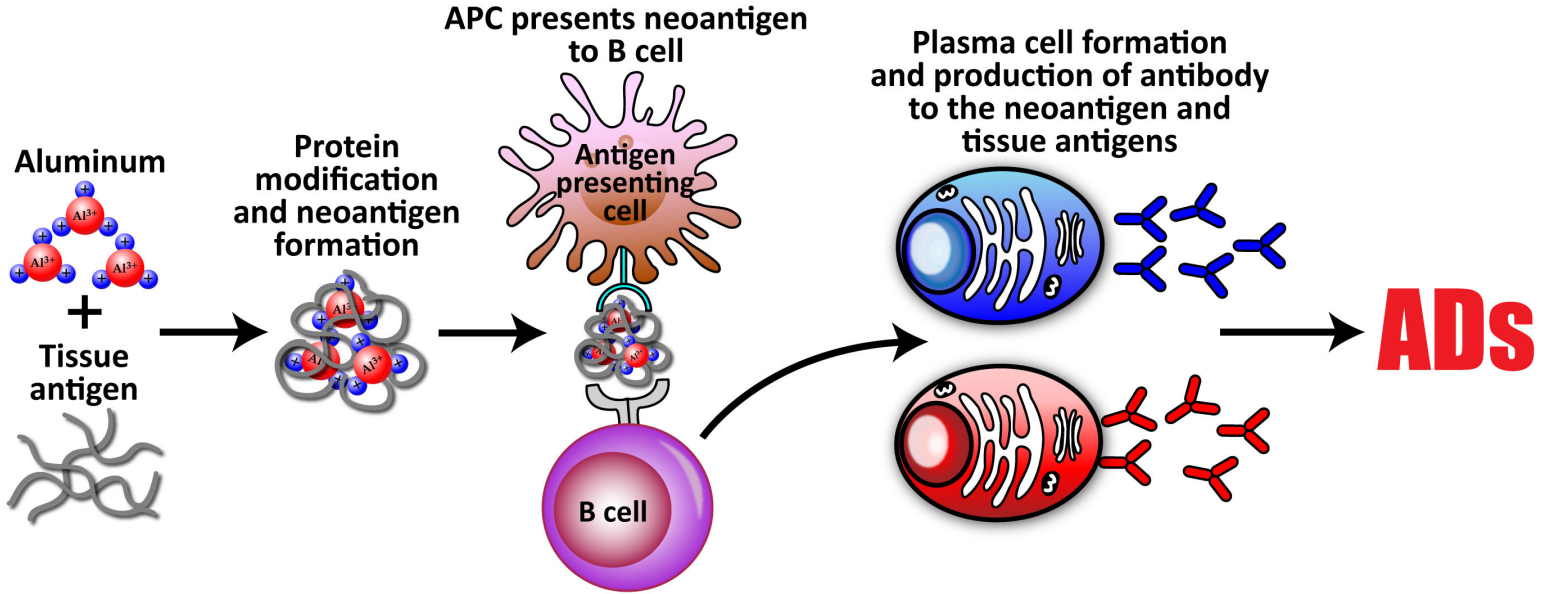
How viral infections lead to autoimmune disease by induction of tissue damage. Viral infections induce significant molecular changes in the host cell that result in cell death and tissue damage. Autoantigens shed from apoptotic cells form affinity complexes with dermatan sulfate (DS) that is overexpressed in the wounded area. Antigen presentation and activation of B_1 cell results in autoantibody secretion and autoimmune disease.

Triggers of Autoimmunity



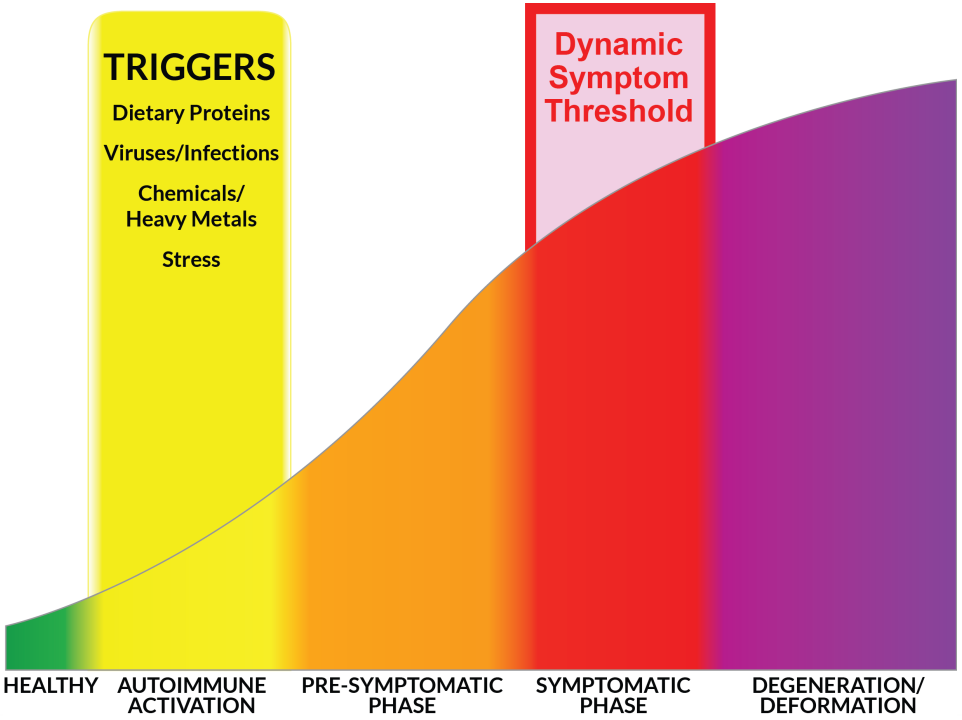






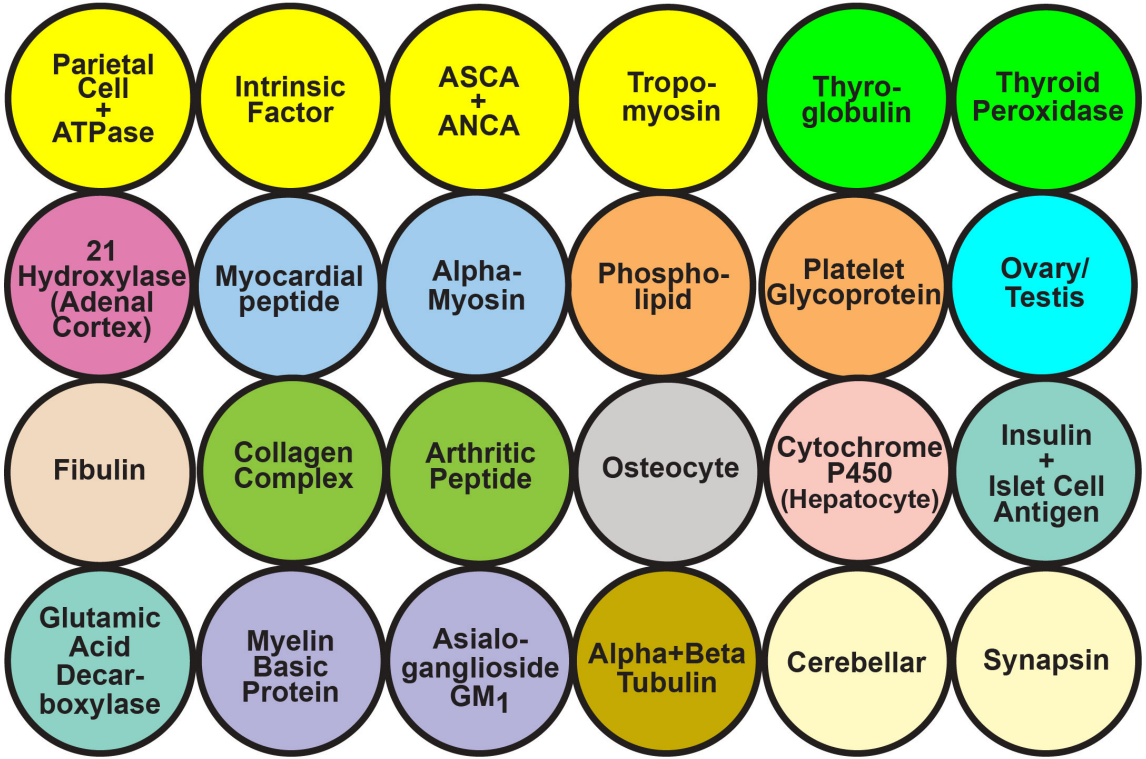
Schematic presentation linking aluminum to the development of autoimmune disease. Aluminum binds to host tissue antigens such as albumin or hemoglobin, forming neoantigens. Antigen-presenting cells present these neoantigens to B cells, resulting in their differentiation into antibody-secreting plasma cells. Production of autoantibodies by plasma cells against both the aluminum and the host tissue antigens may lead to tissue damage in autoimmune diseases (ADs).

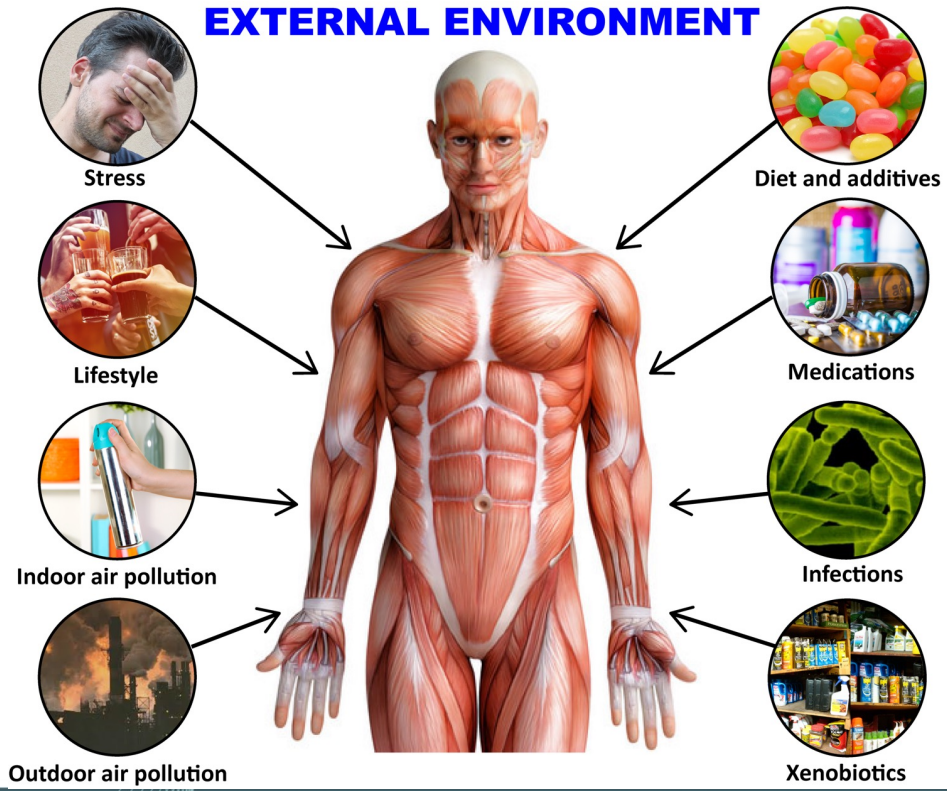
Identify the state of disease

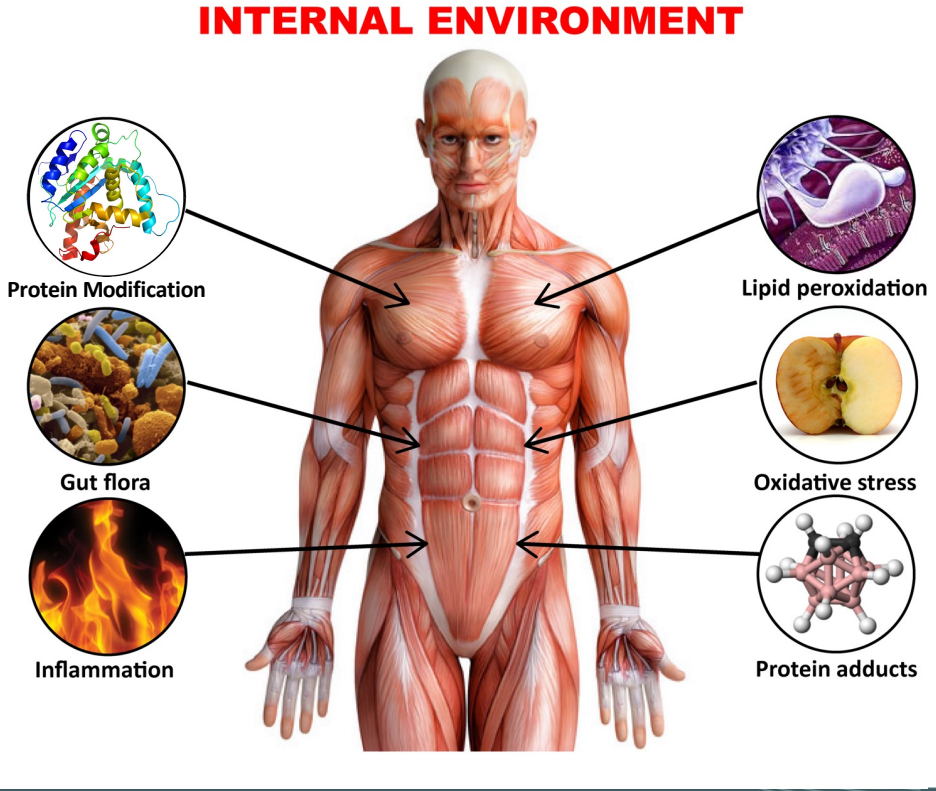


Array 5

Multiple Autoimmune Reactivity Screen




EXTERNAL ENVIRONMENT
Stress
Lifestyle
Indoor air pollution
Outdoor air pollution
Diet and additives
Medications
Infections
Xenobiotics


INTERNAL ENVIRONMENT
Protein Modification
Gut flora
Inflammation
Lipid peroxidation
Oxidative stress
Protein adducts

Brief Reviews

The Journal of Immunology
2021, Vol. 207(7): 1725-1733

Small Molecule Metabolites at the Host–Microbiota Interface

Jason D. Bishai* and Noah W. Palm†

The trillions of bacteria that constitutively colonize the

specific microbial metabolite-mediated impacts on immunity.

The trillions of bacteria that constitutively colonize the human gut collectively generate thousands of unique small molecules. These microbial metabolites can accumulate both locally and systemically and potentially influence nearly all aspects of mammalian biology, including immunity, metabolism, and even mood and behavior.

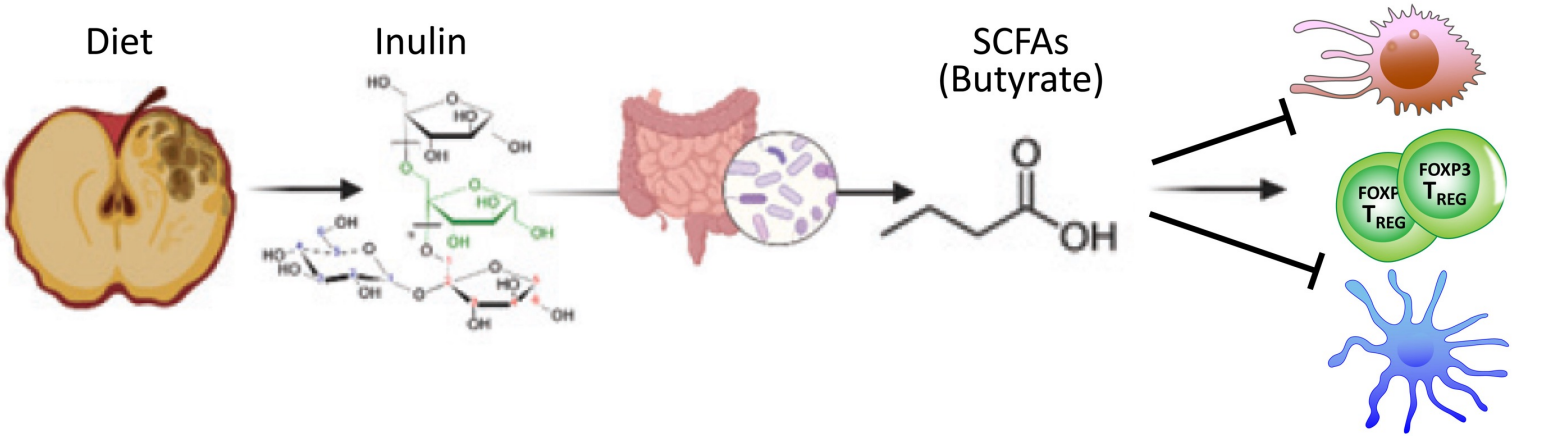
exhaustive list of all known bioactive microbial small molecules, we select a few examples from each key class of metabolites to illustrate the diverse impacts of

metabolites.

Biotransformations of exogenously consumed compounds

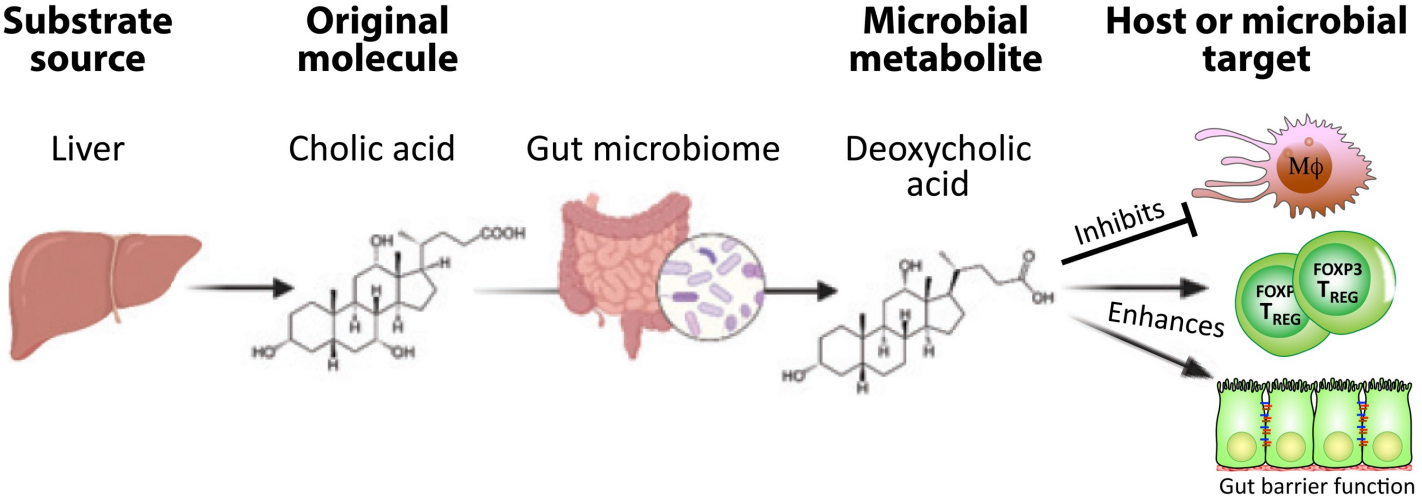
Brief Reviews

Modified from The Journal of Immunology
2021, Vol. 207(7): 1725-1733



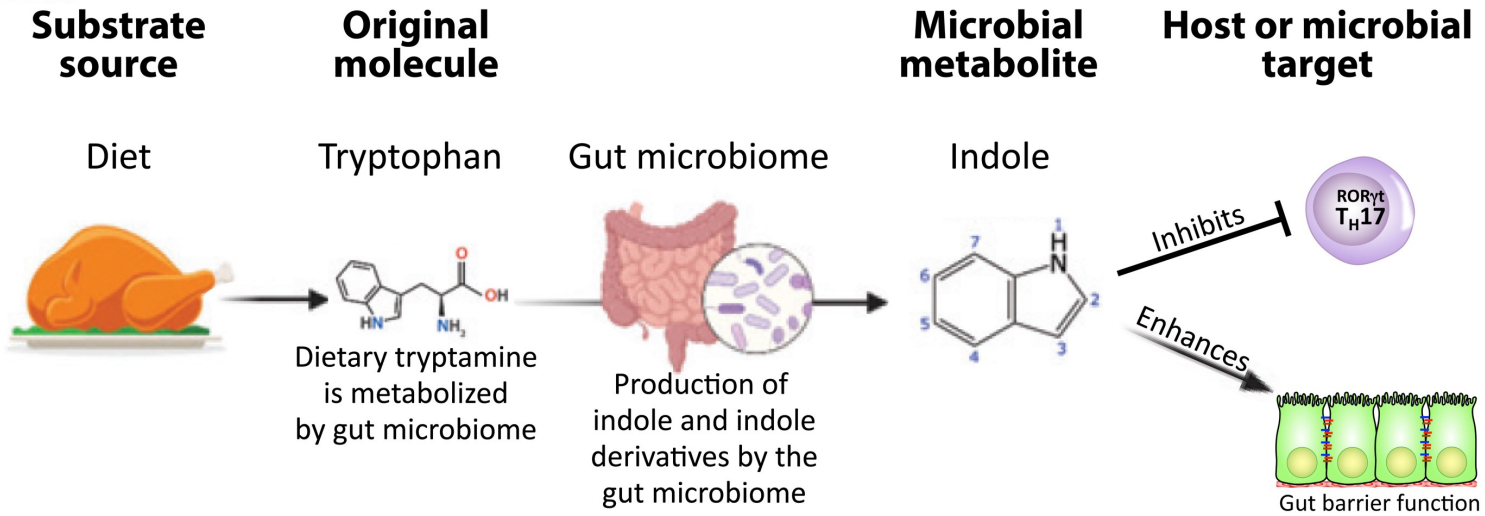
Energy Balance

Modified from The Journal of Immunology
2021, Vol. 207(7): 1725-1733



Detoxification

Modified from The Journal of Immunology
2021, Vol. 207(7): 1725-1733



Signalling

frontiers in Immunology

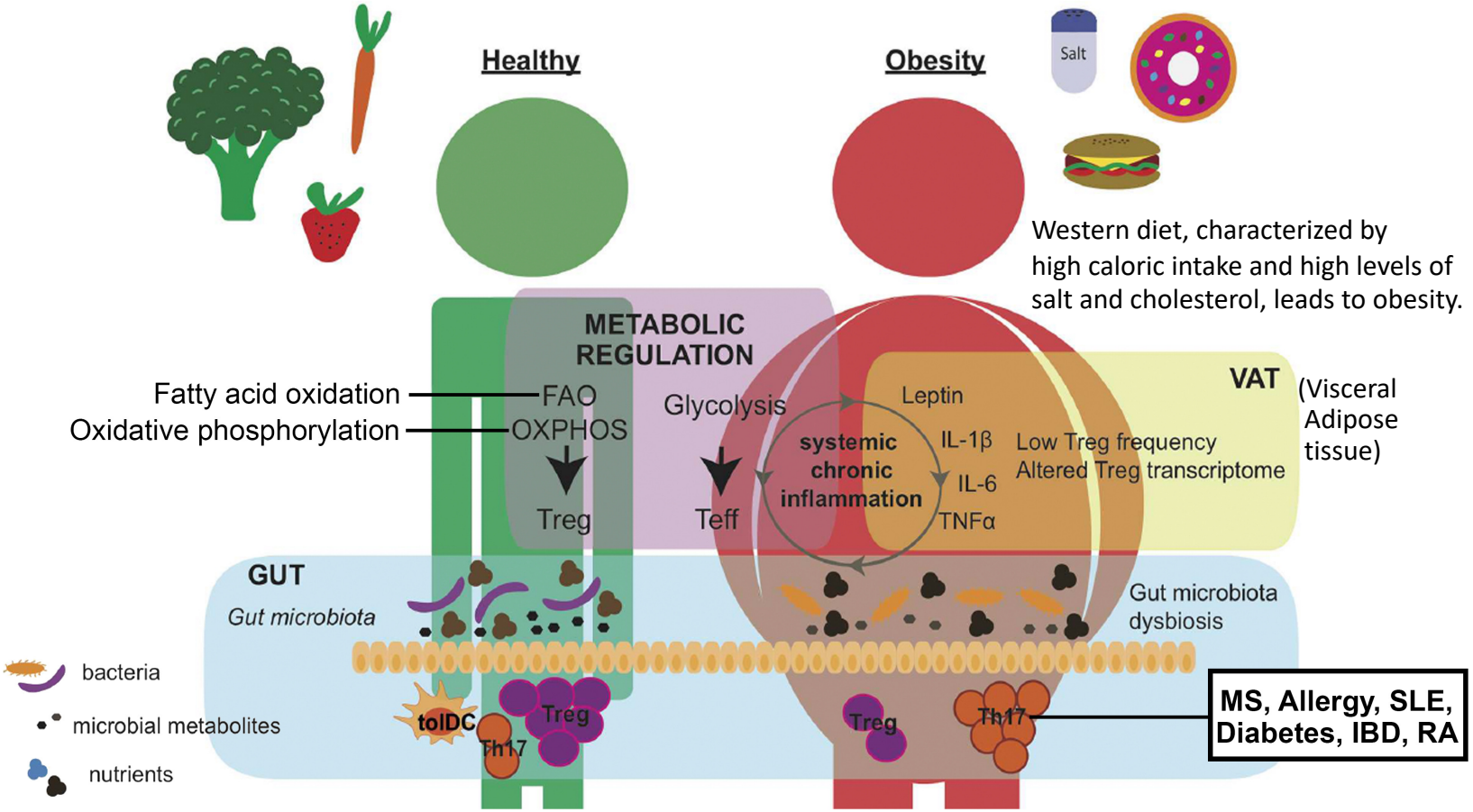
2020, Vol. 11, Article 253

MINI REVIEW
published: 21 February 2020
doi: 10.3389/fimmu.2020.00253

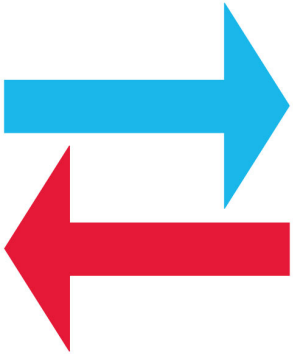
The Impact of Dietary Components on Regulatory T Cells and Disease

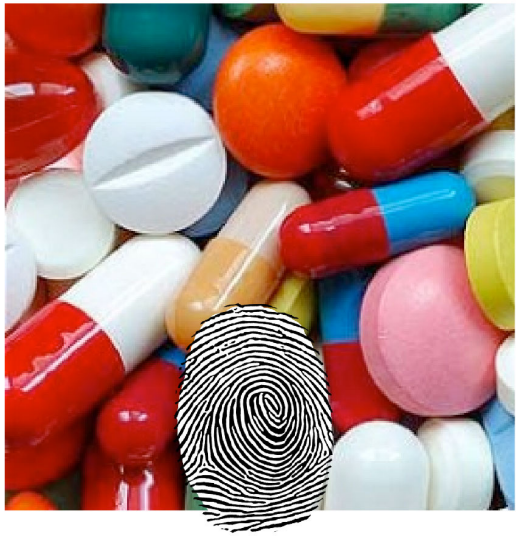
*Rebeca Arroyo Hornero, Ibrahim Hamad, Beatriz Côrte-Real and Markus Kleinewietfeld**

The rise in the prevalence of autoimmune diseases in developed societies has been associated with a change in lifestyle patterns. Among other factors, increased consumption of certain dietary components, such as table salt and fatty acids and excessive caloric intake has been associated with defective immunological tolerance. Dietary nutrients have shown to modulate the immune response by a direct effect on the function of immune cells or, indirectly, by acting on the microbiome of the gastrointestinal tract. FOXP3^{+} regulatory T cells (Tregs) suppress immune responses and are critical for maintaining peripheral tolerance and immune homeostasis, modulating chronic tissue


Healthy
Obesity
Salt
Western diet, characterized by high caloric intake and high levels of salt and cholesterol, leads to obesity.
METABOLIC REGULATION
Fatty acid oxidation
FAO
Oxidative phosphorylation
OXPHOS
Glycolysis
Treg
Teff
Leptin
IL-1β
IL-6
TNFα
systemic chronic inflammation
VAT
(Visceral Adipose tissue)
Low Treg frequency
Altered Treg transcriptome
GUT
Gut microbiota
Gut microbiota dysbiosis
bacteria
microbial metabolites
nutrients
tolDC
Treg
Th17
Treg
Th17
MS, Allergy, SLE, Diabetes, IBD, RA

Personalized mucosal, humoral and cellular immunity is the core of personalized medicine





Personalized Immunity

Personalized Medicine