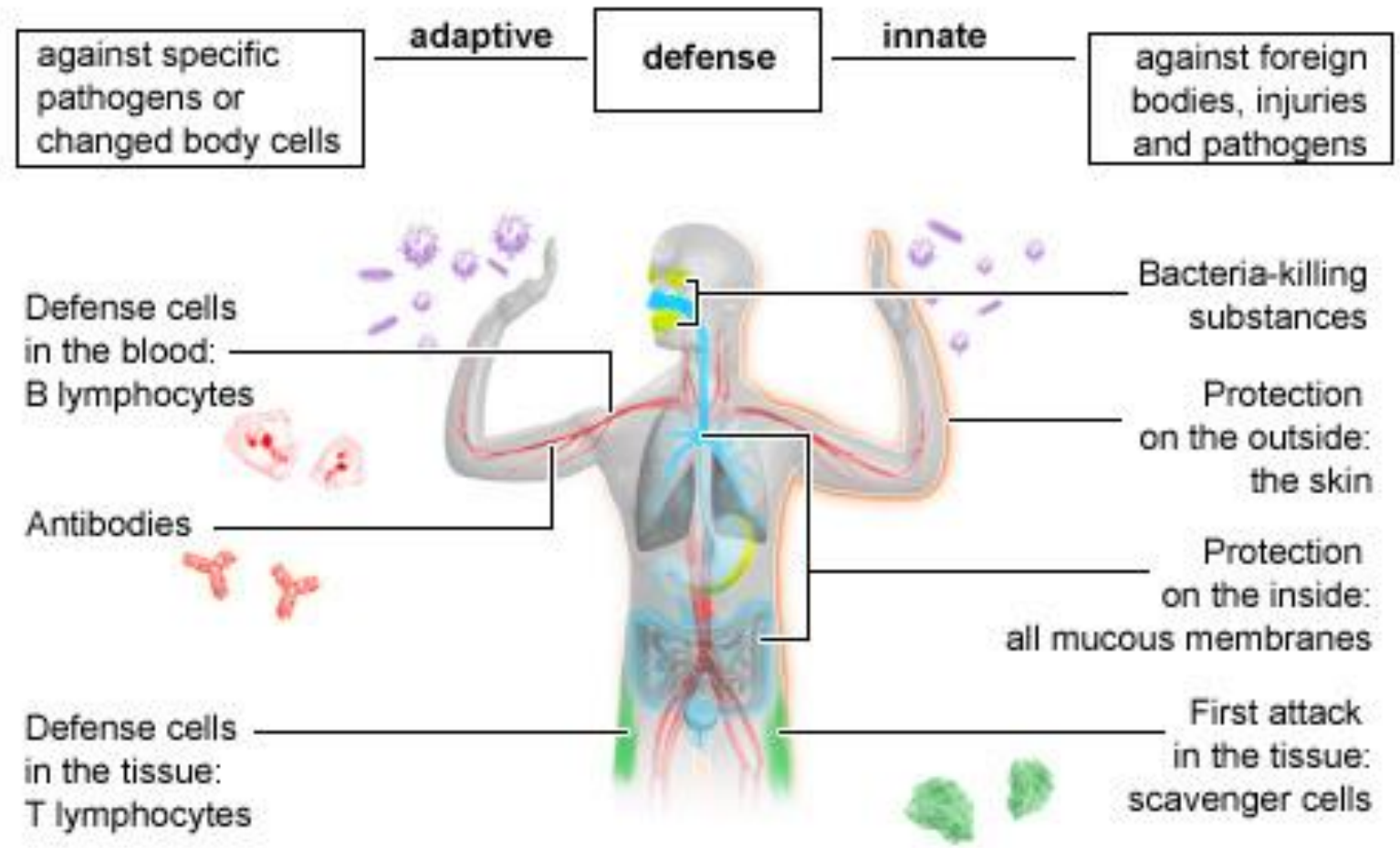
Casual Friday Presents

Autoimmune Mechanisms Pt 2 (key actions)

A BIOGENETIX CLINICAL PRESENTATION

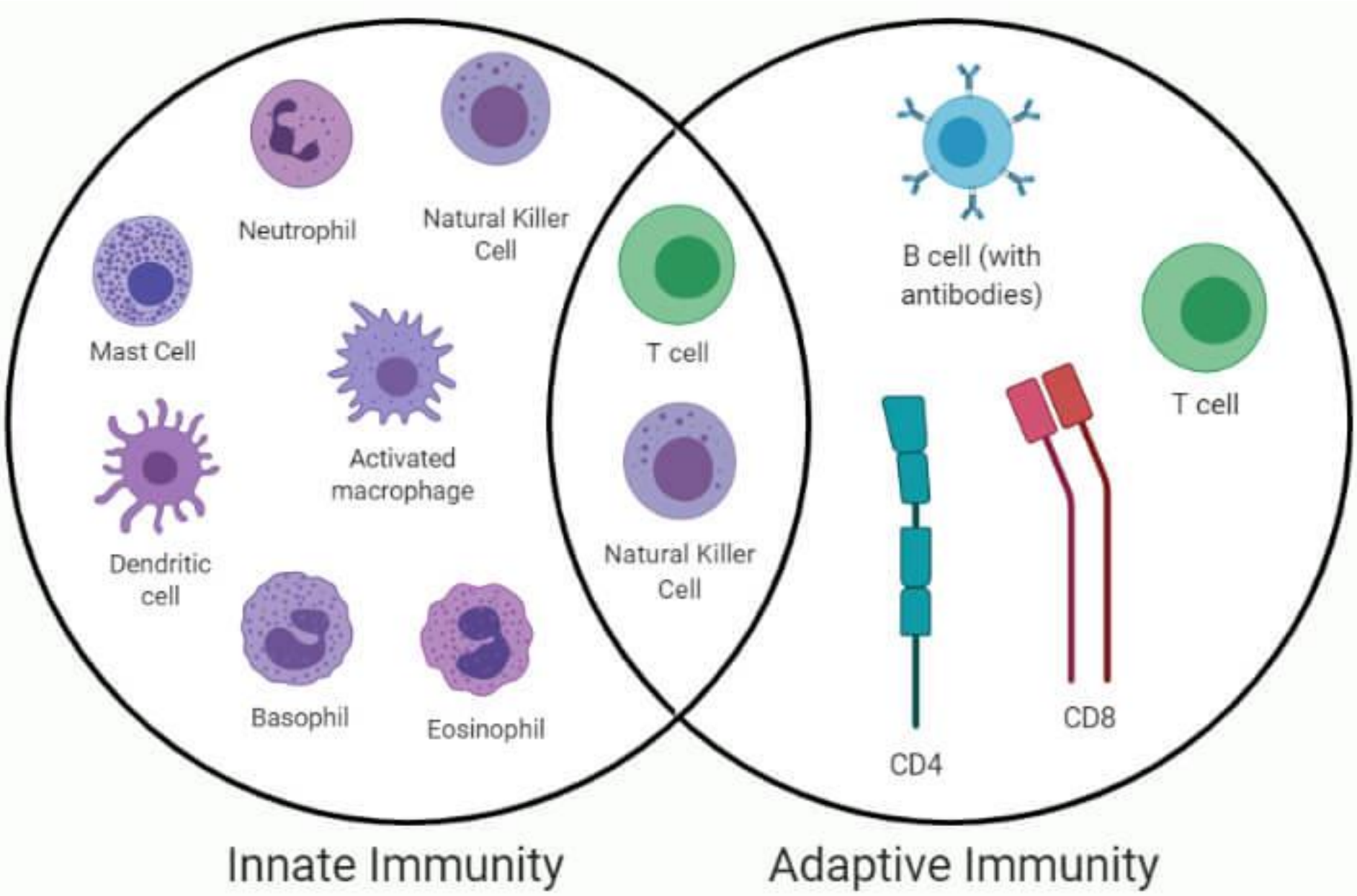
biogenetix.com

Biogenetix

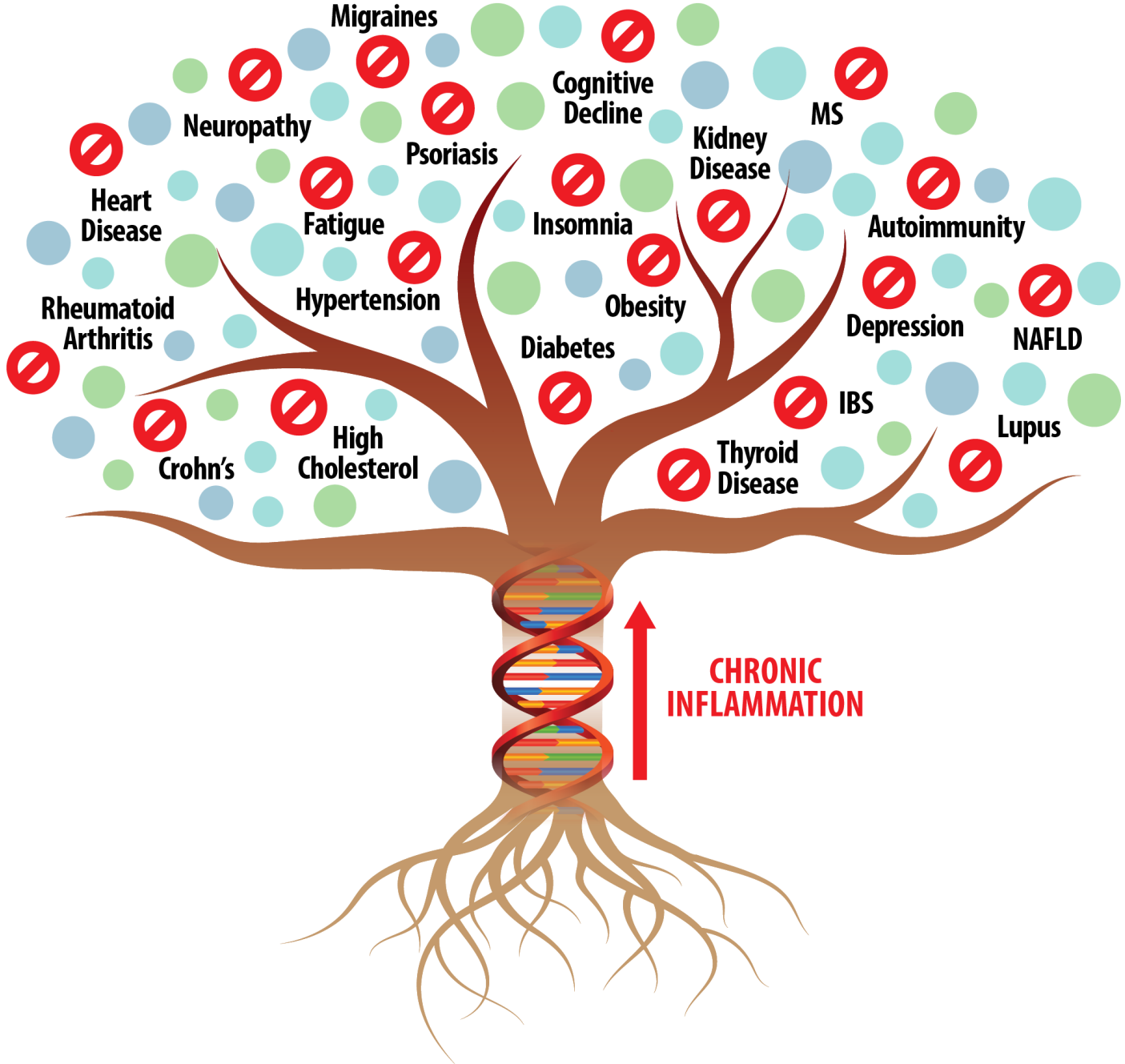


https://www.ncbi.nlm.nih.gov/books/NBK279396/

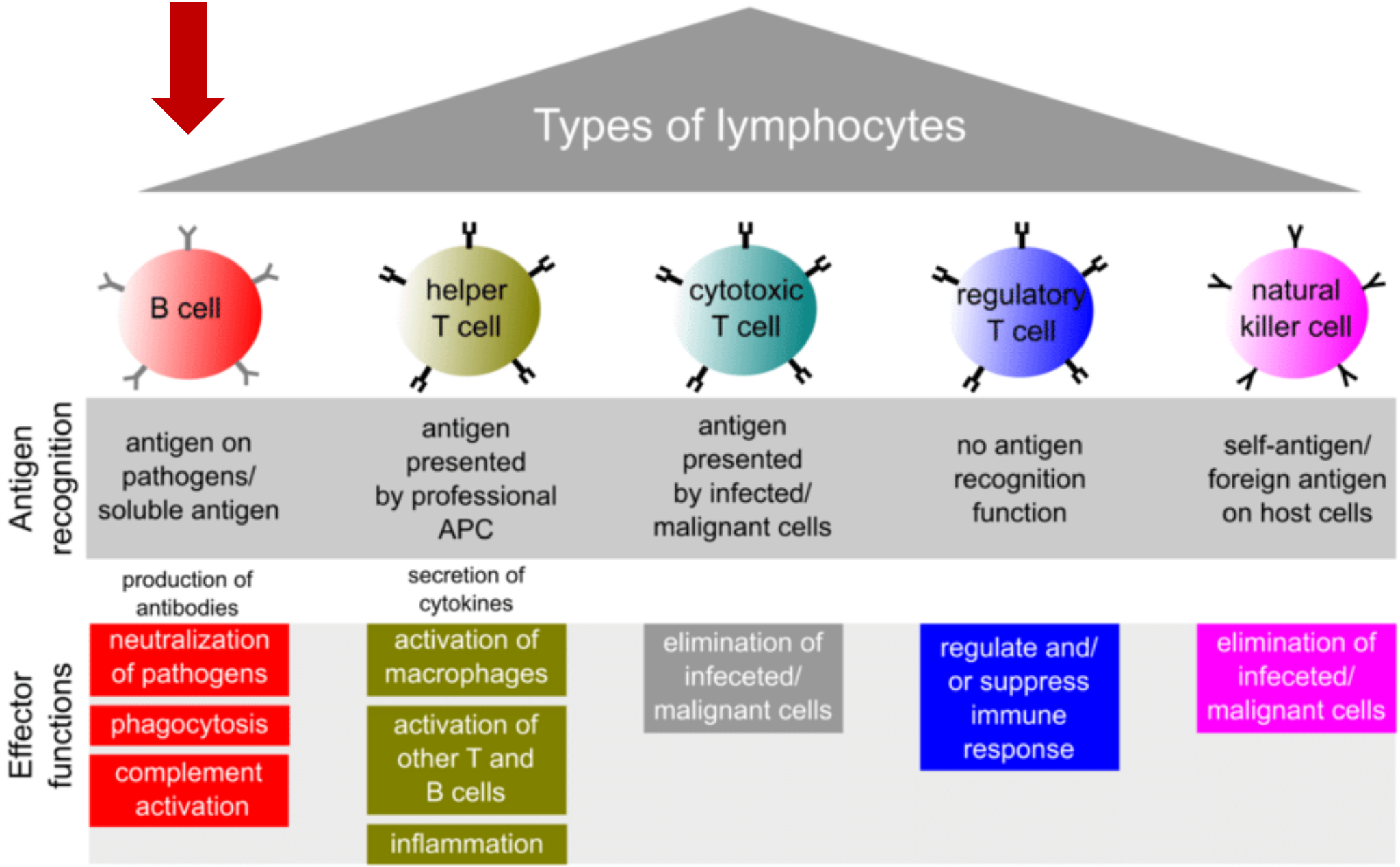
Biogenetix


Neutrophil
Natural Killer Cell
Mast Cell
Activated macrophage
Dendritic cell
Basophil
Eosinophil
T cell
Natural Killer Cell
B cell (with antibodies)
T cell
CD4
CD8
Innate Immunity
Adaptive Immunity

Biogenetix


Migraines
Neuropathy
Psoriasis
Cognitive Decline
MS
Kidney Disease
Heart Disease
Fatigue
Insomnia
Autoimmunity
Hypertension
Obesity
Depression
NAFLD
Rheumatoid Arthritis
Diabetes
IBS
Crohn's
High Cholesterol
Lupus
Thyroid Disease
CHRONIC INFLAMMATION

Biogenetix



https://www.researchgate.net/publication/280663544/figure/fig2/AS:792466320019456@1565950102293/Types-of-lymphocytes-and-their-effector-functions-The-lymphocyte-family-includes-five.png

Biogenetix

National Library of Medicine
National Center for Biotechnology Information

Molecular mimicry in autoimmunity and vaccinations

Miri Blank, Eitan Israeli, Smadar Gertel, Howard Amital, and Yehuda Shoenfeld.

The healthy immune system is tolerant to the molecules which are the building bricks of our body. Braking the self tolerance due to clonal escape, DNA rearrangement epigenetic and environmental factors, all in concert with genetic predisposition, may lead to an autoimmunity termed “The mosaic of autoimmunity” (2). This kaleidoscope of autoimmunity may lead to a variety of autoimmune diseases or to autoimmune (autoinflammatory) syndrome induced by adjuvant (ASIA) (3). One of the mechanisms involved in induction of an autoimmune response is molecular mimicry.

During the last few decades, molecular mimicry was demonstrated between self and non-self molecules that lead to an autoimmune response (4-26). As a prelude, a shared sequence/structure between a non-self microbial/viral infection or a drug and host antigen entails a particular inflammatory state in order to induce an autoimmune state. The severity of the inflammation is influenced by the strength of the infection or perturbation of the immune system. Studies in animal models support the view that a specified infection determines the inflammatory state. To establish the autoimmune nature of the inflammation, it is important to show that it persists in the absence of the inciting microbe. Although the microbe may have been cleared long before disease manifestations appeared, a common infecting agent, may provoke a disease only in combination with genetic or environmental elements, or it may just prime/stimulate the immune system, being a second virus or a nonspecific adjuvant as a second “hit.“ Viruses, microbes, and parasites may brake peripheral self-tolerance and induce and maintain autoimmunity via several overlapping mechanisms such as epitope spreading, bystander activation, viral persistence, or post-translational modifications of self and altered proteins (3-10). The shared epitopes between the pathogens and autoantigen may induce or trigger chronic inflammation, which is mandatory for establishing all the above listed mechanisms that contribute to an autoimmune response by unveiling “hidden” self-epitopes, cross-reactive peptide presentation, determinant spreading, upregulation of Major Histocompatability Complex (MHC), adhesion, co-stimulatory molecules on antigen presenting cells, upregulation of cellular and extracellular processing, apoptosis, infection of professional Antigen Presenting Cells (APCs), autoantibody production subversion of T cell responses and the immunological homunculus networks (1-11). Excluding shared epitopes between a pathogen and self molecules, structural mimicry can be exemplified also between drugs and self molecules. Molecular mimicry can be an inducer of an autoimmune response or a protector of an autoimmune scenario.

Biogenetix

Table 1 Molecular mimicry between pathogens and self antigens in autoimmune diseases.

AUTOIMMUNE DISEASE	SELF ANTIGEN	PATHOGEN MIMETIC
Rheumatic fever	Cardiac myosin, tropomyosin laminin, vimentin, actin, keratin, *N*-acetyl-glucosamine	*Streptoccocus pyogenes* M protein and N-acetyl-glucosamine
Guillain-Barre'	Gangliosides	lipo-oligosaccharide of *Campylobacter jejuni*
Multiple sclerosis	Myelin basic protein (MBP)	Corona, measles, mumps, EBV, human herpes Semliki Forest Virus (SFV) E2 peptide 115–129 Acanthamoeba castellanii (ACA)
Experimental autoimmune encephalomyelitis	Myelin oligodendrocyte glycoprotein (MOG) 18–32	
	Myelin proteolipid protein (PLP)peptide 139–151; MBP89-101	
Myasthenia gravis	Acetylcholine receptor, neurofilaments	Herpes virus, *Hemophilus influenzae*
Chagas' cardiomyopathy	Human beta 1-adrenergic receptor; Cardiac myosin, Cha antigen Common glycolipid antigenson nervous tissue	*Trypanosoma cruzi*-Ribosomal P0; B13 protein; -shed acute-phase antigen (SAPA) ; 160-kDa flagellum; -trypomastigote stage-specific glycoprotein
Systemic lupus erythematosus	Ro 60 kD, Sm, NMDA, dsDNA	EBV,HERV, pneumococcal polysaccharide
Antiphospholipid syndrome	β2-glycoprotein-I	*Hemophilus influenza*, *Neisseria gonorea*, Tetanus toxin, CMV
Ankylosing spondylitis	HLA-B27, type I, II, IV collagen	*Klebsiella pneumoniae*, chlamydia
Lyme arthritis	*DRB1*0401* or *HLA-DRB1*0101* alleles. Human leukocyte function–associated antigen1α (hLFA-1)	*Borrelia burgdorferi* (outer surface protein A - OspA)

National Library of Medicine
National Center for Biotechnology Information

Molecular mimicry in autoimmunity and vaccinations

Miri Blank, Eitan Israeli, Smadar Gertel, Howard Amital, and Yehuda Shoenfeld.

A mimicry scenario was proposed by Pender (19) for **Epstein-Barr virus (EBV)** mediated latent infection of B cells. Human chronic autoimmune diseases, including lupus, multiple sclerosis, Sjogren's syndrome, rheumatoid arthritis, autoimmune thyroiditis, autoimmune hepatitis, and cryptogenic fibrosing alveolitis, are based on infection of auto reactive B-lymphocytes by EBV. Latent EBV infected auto reactive memory B cells may lodge in organs where their target antigen is expressed and act as antigen presenting cells. When CD4+ T cells that recognize antigens within the target organ are activated in lymphoid organs by mimicry with infectious agents, they migrate to the target organ but fail to undergo activation induced apoptosis because they receive a co-stimulatory survival signal from the infected B cells. The auto reactive T cells proliferate and produce cytokines, which recruit other inflammatory cells with resultant target organ damage and chronic autoimmune disease.

https://www.ncbi.nlm.nih.gov/books/NBK459460/

Biogenetix

Microorganisms associated to thyroid autoimmunity

Yunam Cuan-Baltazar, Elena Soto-Vega

Autoimmune thyroid diseases are a group of diseases characterized by a dysfunction of the immune system concerning the thyroid gland, associated with hypothyroidism or hyperthyroidism. The thyroid gland autoimmunity has been recognized as multifactorial. It has been reported that microorganisms may play a role on the pathogenesis of Hashimoto's thyroiditis and Graves´ disease. These could explain the high incidence of the autoimmune thyroid diseases.

Helicobacter Pylori (*H. pylori*) and Hepatitis C virus (HCV) are the microorganisms in which the association with autoimmune thyroid diseases is clearer. The pathophysiologic mechanisms are still not well defined. For *H. pylori*, molecular mimicry has been the most accepted mechanism. It has been proposed Hepatitis C virus as the trigger of the thyroid autoimmunity by exacerbating the production of thyroid auto-antibodies, while some mention that the real factor that triggers the thyroid autoimmunity is the treatment with Interferon alpha (IFN-alpha) by upregulating MHC class I and inducing ligation of CD40+ cells to thyrocytes. Other microorganisms such as Toxoplasma gondii, Human Immunodeficiency virus, Herpes virus and others have reported information about their association with thyroid autoimmune diseases There are no proposals on how these last microorganisms induce thyroid autoimmunity.

Microorganisms associated to thyroid autoimmunity

Yunam Cuan-Baltazar, Elena Soto-Vega

Show more

Less clear literature:

- Yersinia enterocolitica
- Borrelia
- Toxoplasma
- Parvovirus
- Enterovirus (like coxsackie)
- Candida Albicans.

Biogenetix

Review

Interaction between food antigens and the immune system: Association with autoimmune disorders

Aristo Vojdani [a b], Lydia R. Gushgari [c], Elroy Vojdani [d]

Show more

+ Add to Mendeley Share Cite

https://doi.org/10.1016/j.autrev.2020.102459 Get rights and content

Highlights

- Dietary components and their effects on the gut microbiome are major players in autoimmune disease but are often overlooked
- Failure of the oral tolerance mechanism can cause the immune system to react to the very food the body needs for sustenance
- Many foods share sequence homology with human tissues; this molecular mimicry can induce or exacerbate autoimmune diseases
- Factors that contribute to post-translational protein modification may play a role in the induction of autoimmune disease

Biogenetix

Review

Interaction between food antigens and the imm aut

Aristo

It has been shown that environmental factors such as infections, chemicals, and diet play a major role in autoimmune diseases; however, relatively little attention has been given to food components as the most prevalent modifiers of these afflictions. This review summarizes the current body of knowledge related to different mechanisms and associations between food proteins/peptides and autoimmune disorders. The primary factor controlling food-related immune reactions is the oral tolerance mechanism. The failure of oral tolerance triggers immune reactivity against dietary antigens, which may initiate or exacerbate autoimmune disease when the food antigen shares homology with human tissue antigens. Because the conformational fit between food antigens and a host's self-determinants has been determined for only a few food proteins, we examined evidence related to the reaction of affinity-purified disease-specific antibody with different food antigens. We also studied the reaction of monoclonal or polyclonal tissue-specific antibodies with various food antigens and the reaction of food-specific antibodies with human tissue antigens. Examining the assembled information, we postulated that chemical modification of food proteins by different toxicants in food may result in immune reaction against modified food proteins that cross-react with tissue antigens, resulting in autoimmune reactivity. Because we are what our microbiome eats, food can change the gut commensals, and toxins can breach the gut barrier, penetrating into different organs where they can initiate autoimmune response. Conversely, there are also foods and supplements that help maintain oral tolerance and microbiome homeostasis. Understanding the potential link between specific food consumption and autoimmunity in humans may lay the foundation for further research about the proper diet in the prevention of autoimmune diseases.

Biogenetix

Review

Interaction between food antigens and the imm auto

Aristo Vo

In comparison with infections, the role of diet in autoimmunity has been relatively overlooked, although a great many instances linking food and autoimmunity have been reported. Patients with rheumatoid arthritis (RA) report not only an association between food intake and the severity of their symptoms, but also elevated serum IgG, IgA and IgM antibodies against food proteins such as milk, wheat, eggs, fish, pork, lectins and agglutinins [[11], [12], [13], [14], [15]]. Studies indicate that lifestyle choices such as adopting the Mediterranean diet appear to have beneficial effects for RA sufferers [16,17]. Interestingly, across 27 countries the incidence of MS correlated strongly (r^2=0.795) with the consumption of cow's milk [18]. Polyradiculoneuropathy, a normally slow-developing autoimmune neurologic disease, was thought to have been induced after only 4 weeks of exposure in abattoir workers by the aerosolized neural antigens coming from the pig brains they processed, thereby indicating that environmental exposure to food antigens via aerosol can induce similar autoimmune reactions as ingestion of food antigens [19]. A very recent systemic analysis of commonly consumed foods implicated in autoimmunity, such as meats, fish, soybean and grains, found hundreds of peptide epitopes that share homology with human tissue antigen [20]. Using a systematic data-driven approach, this study found that among the 14 different categories of foods that were tested, pig contained disproportionately more shared sequences with almost 70 unique human MS epitopes in different tissues from blood to kidney, thyroid and central nervous system [20]. One possible explanation is that the exposure of the immune system to exogenous molecules with a sufficiently similar structure either breaks tolerance to self-antigens or activates pre-existing but inactive immune system cells. These findings indicate that the interaction between diet and autoimmune disorders is much more extensive than earlier thought and lays the foundation for future studies to find the still undiscovered food peptide epitopes that are also implicated in the pathogenesis and progression of autoimmune diseases.

Review

Interaction between food antigens and the immun autoim

Aristo Vojdani

2. Oral tolerance failure

In the event of a breakdown in the oral tolerance mechanism, autoimmune diseases can be initiated or exacerbated by dietary proteins and peptides, especially those such as pig and others that share homology with human tissue antigens [20–23]. Oral tolerance is established a few months after birth upon the interaction of orally administered food antigens with the immune system in the gut, leading to the generation of food antigen-specific regulatory $CD4^+CD25^+$ cells. Oral tolerance established by Tregs is crucial to the body's health and immune system because it prevents inflammatory reactions towards necessary foods and elements while permitting the immune system to target and destroy pathogens and unwanted antigens.

Immunity and oral tolerance both start developing in the womb, but important tolerance development events can continue to occur throughout a person's life. Modern food production exposes consumers to chemicals and environmental toxins that assault the immune system, causing a failure in the oral tolerance mechanism, opening the barriers, and causing intestinal permeability to food antigens. This inflammation and gut permeability allows undigested food proteins and commensal bacteria or their toxins to enter the blood stream and be presented to the immune system. In this situation, Tregs may become dysregulated, thereby disrupting immune homeostasis and exacerbating inflammation, resulting in the loss of oral tolerance. These events and many other factors can affect a pregnant mother's health and immune system, can also affect the child in the womb (Fig. 1), and can affect adults throughout their lifetime. Therefore, the loss of oral tolerance against food peptide epitopes that share homology with human tissue proteins can result in food immune reactivity and autoimmunity [24–27].

Biogenetix

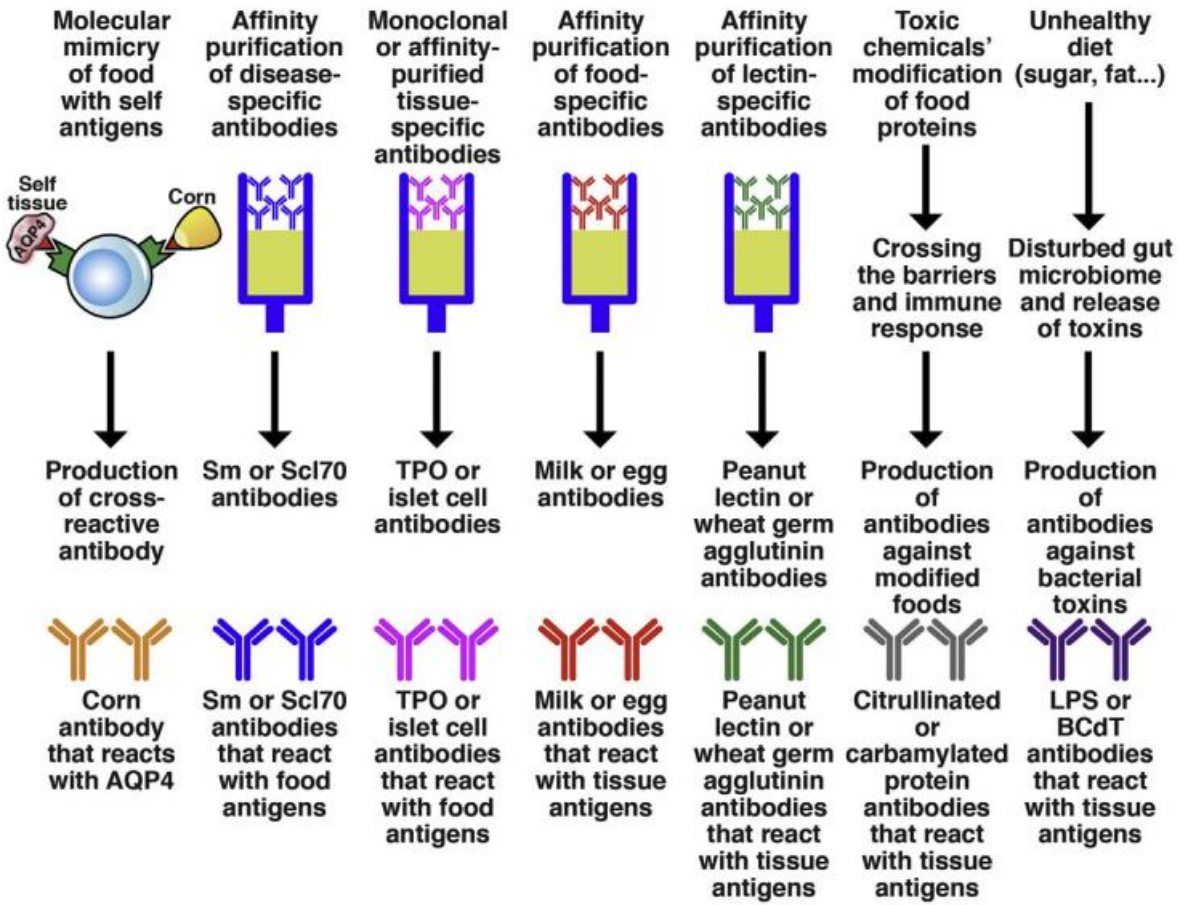


Fig. 2. Possible involvement of food antigens in different autoimmune diseases by the induction of cross-reactive antibody production and their reaction with different tissue antigens.

Review

Interaction between food antigens and the immune system: Association with autoimmune disorders

Ar

3.2. Molecular mimicry and gluten

Gluten has been linked to celiac disease (CD) and non-celiac gluten sensitivity (NCGS). Patients with CD have an immune system that may react to a wide range of peptides. Patients with NCGS and Crohn's disease react to a repertoire of wheat antigens, producing IgG and IgA antibodies against them [34]. Continued and untreated exposure to wheat brings about a worsening of NCGS and CD, and can lead to autoimmunity. In another of our previous studies [46], we examined the possible mechanisms behind autoimmune reaction to nervous system antigens in children with autism. We tested 50 autism patients and 50 controls and found that there was peptide sequence similarity between the wheat protein gliadin antibody (EQVPLVQQ) and cerebellar neural tissue antibody (EDVPLLED). We concluded that in a subgroup of autism patients, antibodies may be produced against both Purkinje cells and gliadin peptides, and that this may be responsible for some of the neurological symptoms of autism.

Biogenetix

Review

Interaction between food antigens and the immune system: Association with aut

Aristo V

3.3. Molecular mimicry and milk

Despite the widespread acceptance of cow's milk as an essential part of child and adult nutrition, cow's milk is actually one of the most common foods that causes immune reactivity, affecting infants, children and adults. From an immunological perspective, it is critical to consider that cow's milk is a mucosal secretion from another species. The principal antigenic components of cow's milk are α-casein, β-casein, κ-casein, butyrophilin and β-lactoglobulin. The strong antigenicity of cow's milk means that drinking it early in life may compound the risks for developing autoimmune disorders such as Behçet's disease, celiac disease, Crohn's disease, MS, systemic lupus erythematosus (SLE), T1D, and uveitis in susceptible patients [29–31,33]. In almost all of these disorders, significantly higher levels of IgG and IgA antibodies against milk proteins are detected in disease sufferers compared to controls [47].

Molecular mimicry between cow's milk proteins and the islets of Langerhans cell proteins has been studied as one possible mechanism for the development of type 1 diabetes from the consumption of cow's milk [46]. Molecular mimicry between the milk protein αS2-casein and retinal S-antigen has also been identified as the cause of uveitis [36].

Biogenetix

Review

Interaction between food antigens and the immune system: Association with aut

Aristo V

8.2. Glyphosate

Glyphosate is the active ingredient of the herbicide Roundup and many other products used for weed control. A 2017 study based in Germany involving 399 urine samples from adults not involved in agricultural work revealed glyphosate residues above the detection limit in the urine of 32% of the subjects [115]. This is despite the fact that a significant amount of the glyphosate binds to albumin and other tissue proteins, not only causing alterations in the proteins' secondary structure, but, as we've mentioned before, supposedly alleviating the detectable levels of glyphosate [101–103,116]. In addition, a remarkable correlation has been shown between the rising rate of glyphosate usage on corn and soy crops in the USA and an alarming rise in a number of different chronic diseases, including autoimmune disorders [117]. This is because glyphosate acts as a non-coding amino acid analogue of glycine, and thus could erroneously be incorporated into proteins in place of glycine, producing neo-antigens that could lead to autoimmune disease [118]. This study found support for this assertion when pigs and cattle were given glyphosate-contaminated feed; a significant amount of glyphosate was detected in the animals' collagen, the principle component of gelatin that contains very high levels of glycine [118].

Biogenetix

Alzheimer's LINX™ - Alzheimer's-Associated Immune Reactivity
BiomeBurden™ Complete – Myco, Micro & Immune Evaluation
Micro-BiomeBurden™ – Candida Virulence Plus
Myco-BiomeBurden™ – Candida Virulence
Array 2 - Intestinal Antigenic Permeability Screen
Array 3X - Wheat/Gluten Proteome Reactivity & Autoimmunity
Array 4 - Gluten-Associated Cross-Reactive Foods and Foods Sensitivity
Array 5 - Multiple Autoimmune Reactivity Screen
Array 7X - Neurological Autoimmune Reactivity Screen - Expanded
Array 10 - Multiple Food Immune Reactivity Screen
Array 10-90 - Multiple Food Immune Reactivity Screen
Array 11 - Chemical Immune Reactivity Screen
Array 12 - Pathogen-Associated Immune Reactivity Screen
Array 14 - Mucosal Immune Reactivity Screen
Array 20 - Blood Brain Barrier Permeability
Array 22 - Irritable Bowel/SIBO Screen
Total Serum IgG/IgA/IgM
The Lymphocyte MAP™ - Comprehensive Lymphocyte Immunophenotyping

Biogenetix™