

# When IT All Goes Wrong and Your Immune System Attacks Its Own Body

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# Overview

- What is autoimmunity?
- Who gets autoimmunity?
- What causes autoimmunity?
- Types of autoimmune disease

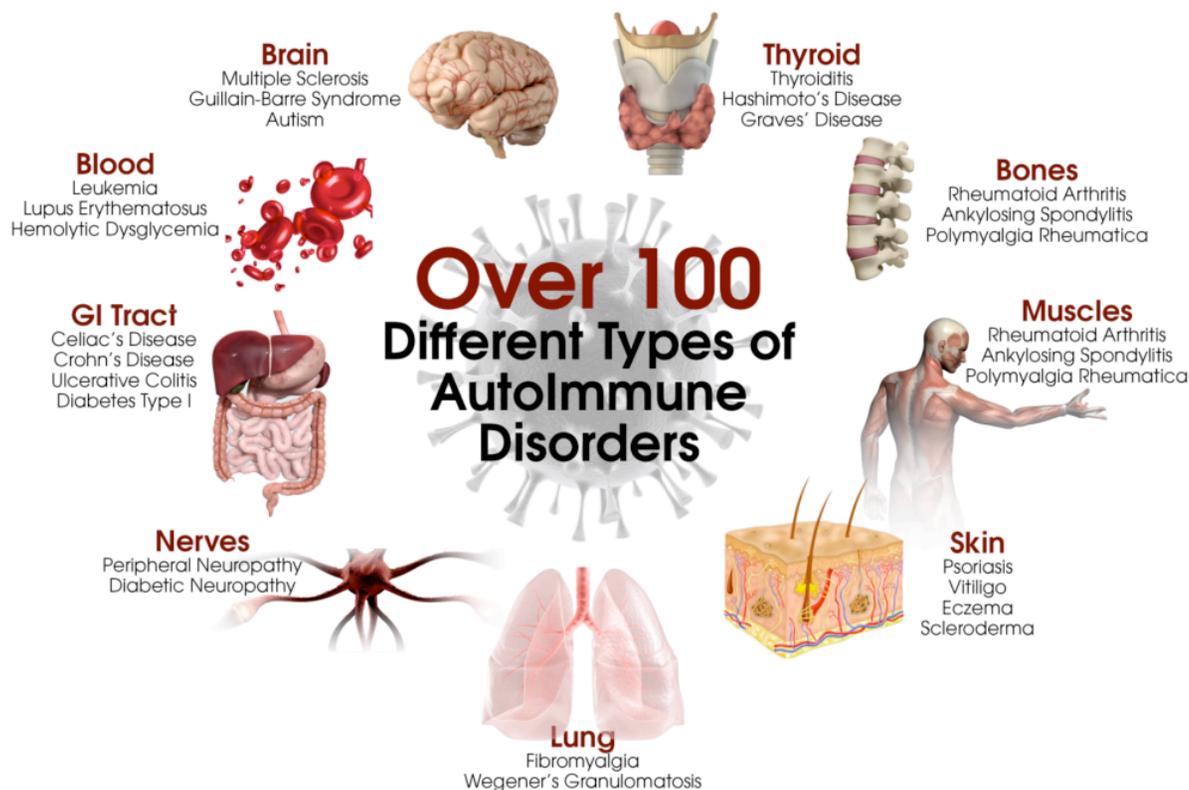


# What is Autoimmunity?

- A misdirected immune response against ones own body
- Present to some extent in everyone and is usually harmless
- A broad range of human illnesses, known as *autoimmune* diseases

# Autoimmune Diseases

Any organ/organ system in the body can be affected



# Who Knows Someone With Autoimmunity?

- ~50 million Americans or 1 in 5 people suffer from an autoimmune disease.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2951969/>
- Autoimmune diseases are usually chronic and can be life-threatening.

# What is it Like to Have Autoimmunity?

- Autoimmunity is devastating and takes a toll on both the patient and their family.
- Singer and song writer Rob Thomas and lead vocalist of Matchbox Twenty wrote “Her Diamonds” for his wife who suffers from a rare autoimmune-like disease similar to lupus.





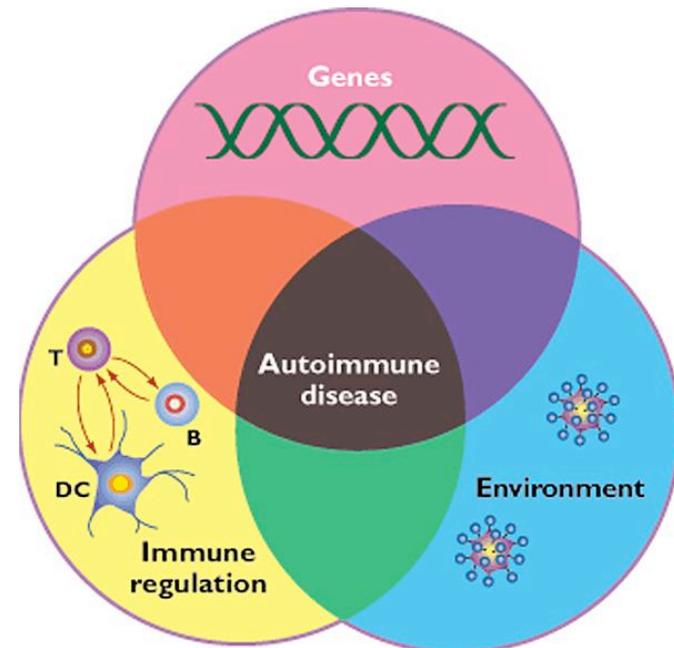
By the light of the moon  
She rubs her eyes  
Says it's funny how the night  
Can make you blind  
I can just imagine  
And I don't know what I'm supposed to do  
But if she feels bad then I do too  
So I let her be

And she says ooh  
I can't take no more  
Her tears like diamonds on the  
floor  
And her diamonds bring me  
down  
Cuz I can't help her now  
She's down in it  
She tried her best and now she  
can't win it's  
Hard to see them on the ground  
Her diamonds falling down



# What Causes Autoimmunity?

- **Genetics:** gender, inheritance
- **Environment:** environmental agents, sunlight, infection
- **Immune Dysregulation**



# Gender

- Women more highly affected (75%) than men.
- Autoimmune diseases are the 6<sup>th</sup> or 7<sup>th</sup> cause of death among females under the age of 75.
- During pregnancy autoimmune disease activity can decrease.
- A flare often follows in the post-partum period.
- Sex hormones play a role.



Psoriasis



Lupus



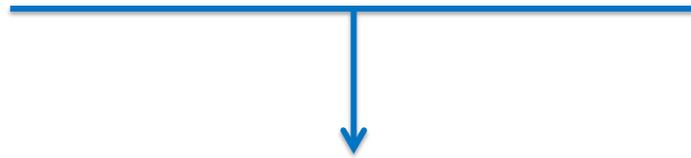
Multiple sclerosis

# Genetics

- Autoimmunity can run in families, i.e., you inherited it from your parents.



Dad  
Black hair



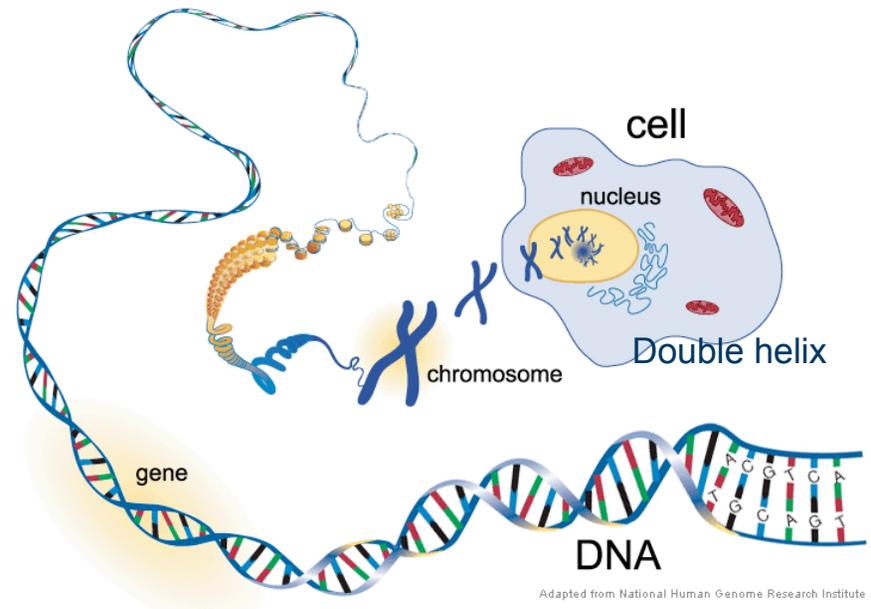
Child  
Brown curly hair



Mom  
Blonde curly hair

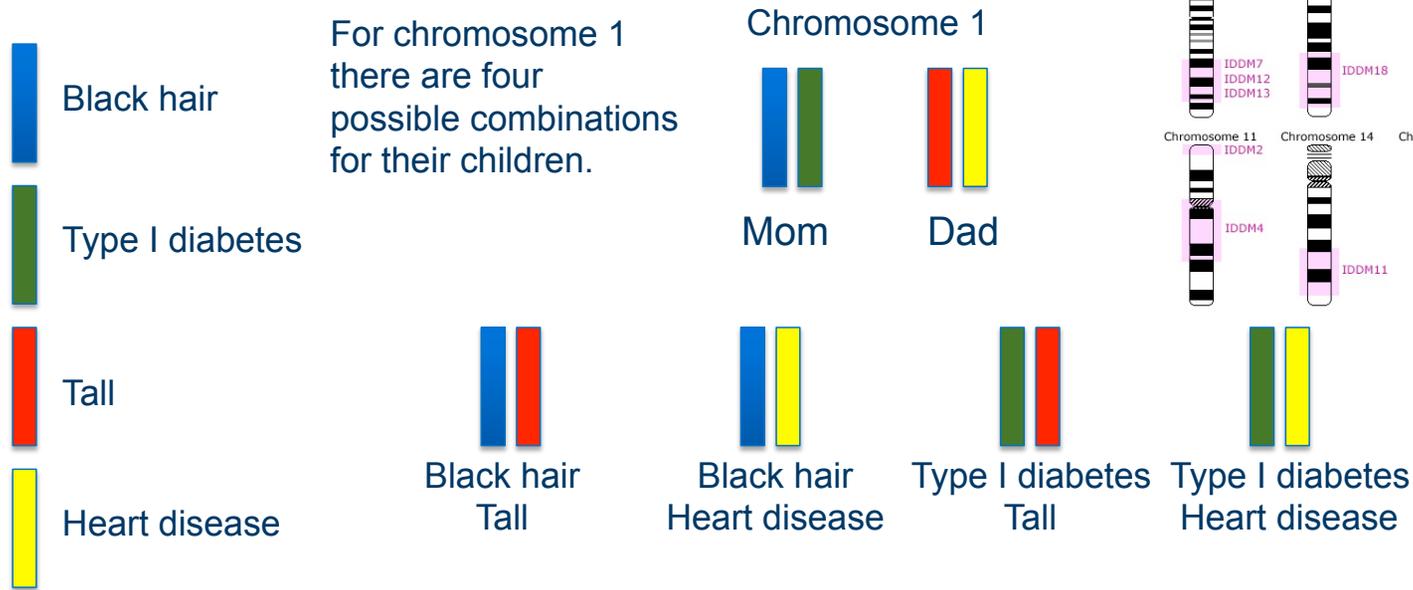
# Genetics of Inheritance

- Genetic material is encoded in your DNA (deoxyribonucleic acid)
  - Main constituent of chromosomes
  - Carrier of genetic information
  - Humans have 23 pairs of chromosomes, for a total of 46
  - You inherit one of each of the 23 from each parent



# Genes

A unit of heredity that is transferred from a parent to offspring that determines some characteristic of the offspring.



Most autoimmune diseases are complex, multigenic traits, i.e., more than one gene involved.

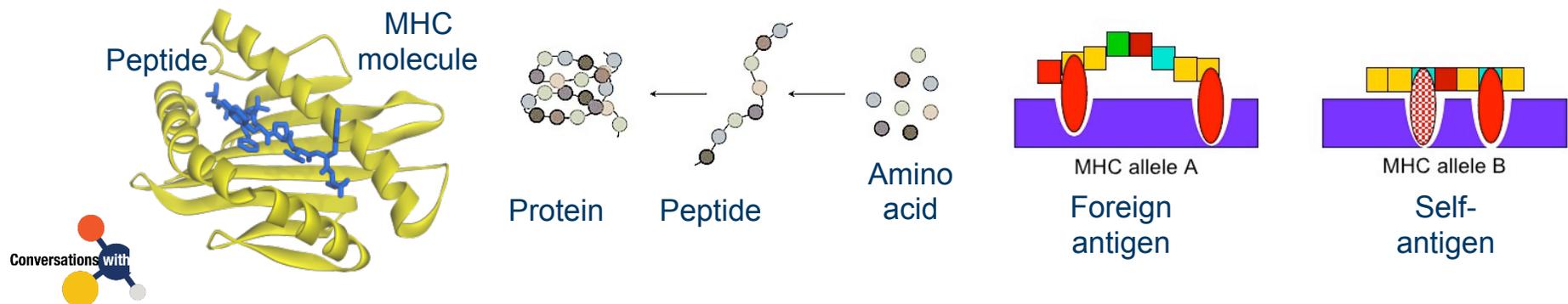
# Major Histocompatibility (MHC) complex

- MHC genes are the strongest genetic risk factor for autoimmunity.
- T cells recognize antigens as a peptide bound to a MHC molecule- called antigen presentation.
- Peptide- small fragment of a protein
- MHC molecules are highly polymorphic, meaning they are similar, but not exactly the same. This affects peptide antigen binding.

Relation between autoimmune diseases with MHC

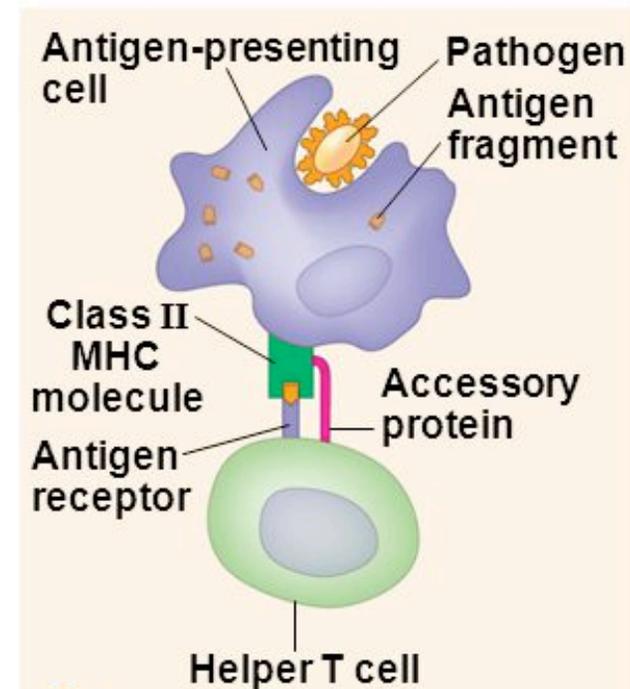
diseases	genotype of HLA	relative risk
ankylosing spondylitis	<b>B27</b>	87.4
Acute anterior uveitis	<b>B27</b>	10.04
Goodpasture's syndrome	<b>DR2</b>	15.9
<b>MS</b>	<b>DR2</b>	4.8
<b>Graves' disease</b>	<b>DR3</b>	3.7
<b>MG</b>	<b>DR3</b>	2.5
<b>SLE</b>	<b>DR3</b>	5.8
<b>IDDM</b>	<b>DR3/DR4</b>	3.2
rheumatoid arthritis	<b>DR4</b>	4.2

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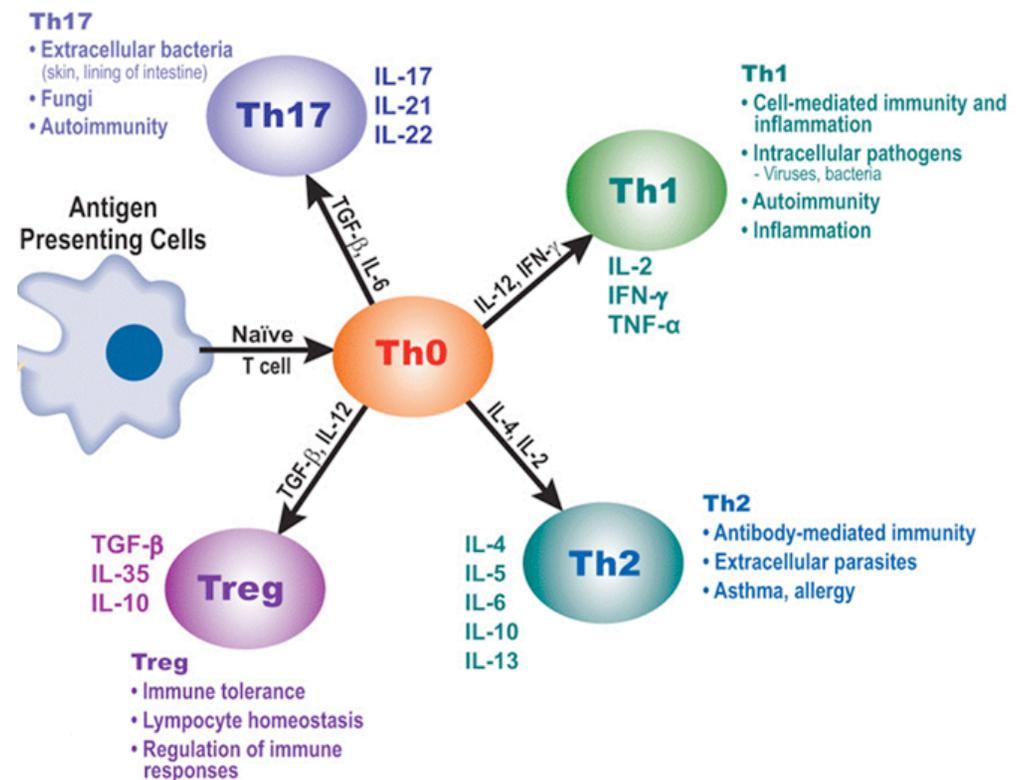
# Antigen Presentation

- Antigen is taken up by an antigen presenting cell (APC)
- Antigen is processed
- Antigen binds MHC molecule
- T cell binds to the antigen:MHC complex
- Cross-talk between the APC and T cell leads to T cell activation



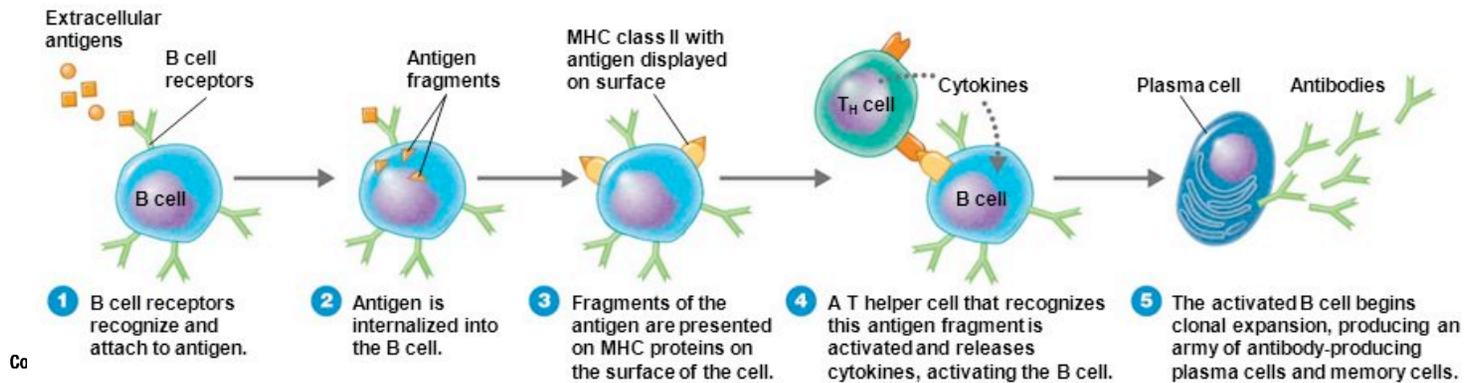
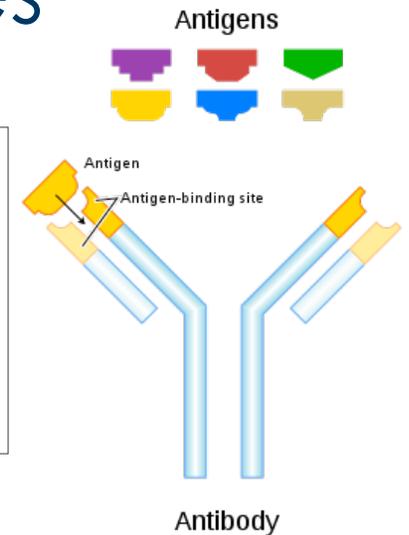
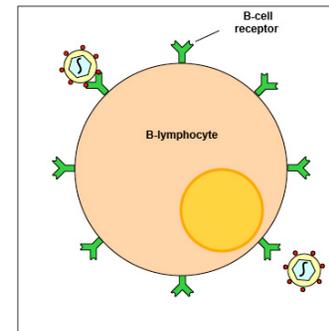
# T Cell Fates

- Following activation T cells differentiate into one of several subsets.
- T cell subsets exhibit unique functions.
- Th17 and Th1 are associated with autoimmunity.
- Treg protect against autoimmunity.
- T cells orchestrate inflammation that damages tissues.



# B Cell Antibody Responses

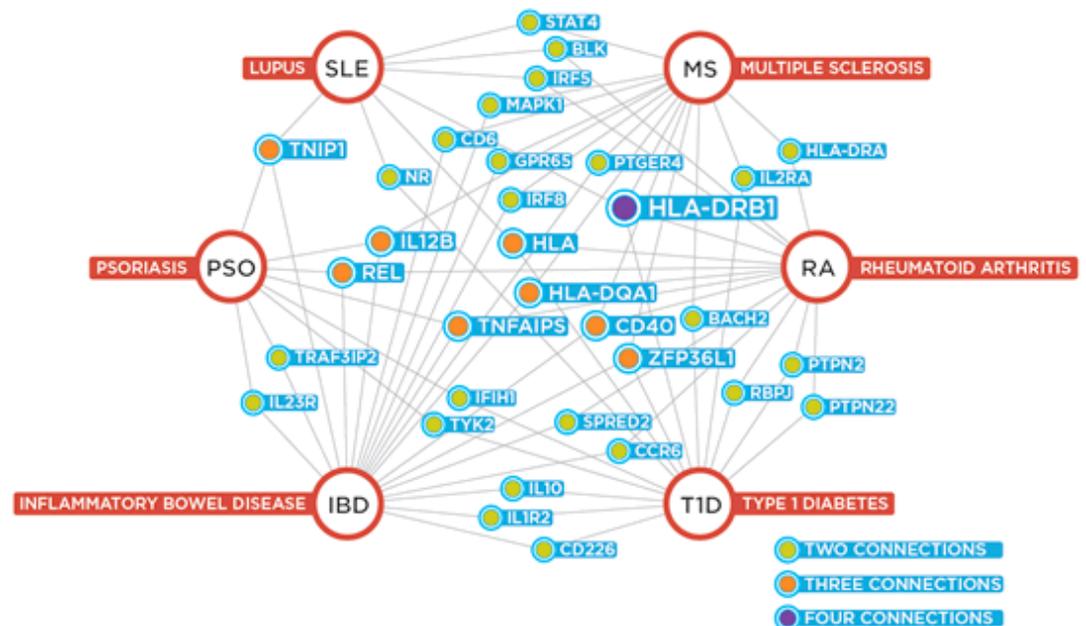
- B Cells recognize antigens as whole proteins.
- B cells internalize antigens and present them to T cells.
- Cross-talk between B and T cells leads to B cell antibody production.
- Antibodies can drive damage to self-tissues.
- Can't bind all proteins



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# Immune Dysregulation

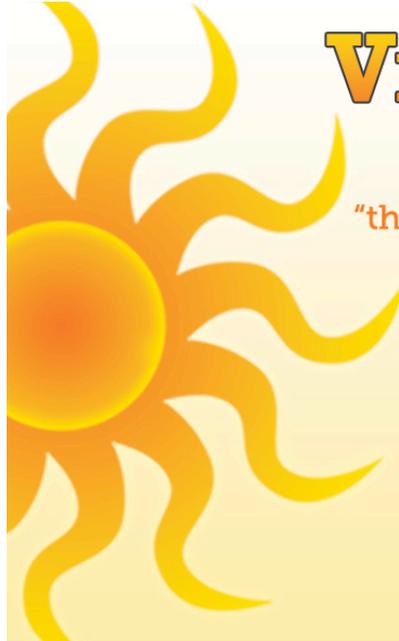
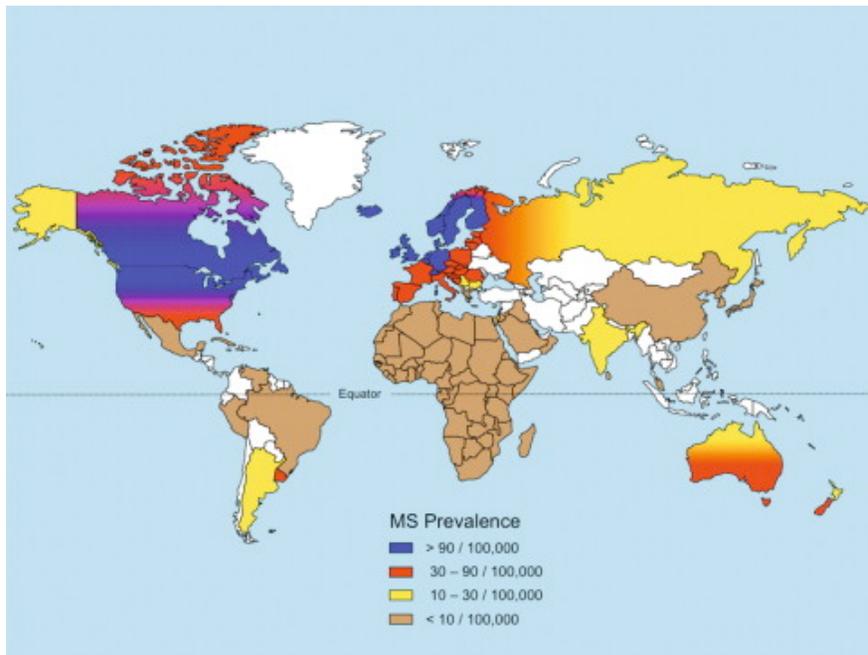
- The immune response is balanced.
- Too little immunity and you can't fight off an infection or you get cancer.
- Too much immunity can lead to attack against self-tissues.
- Many genes associated with autoimmunity regulate the extent of the immune response.



# Environment: Toxins/Chemicals

- There are numerous substances associated with autoimmunity in humans.
  - Asbestos, iodine, heavy metals, pesticides, dioxin
- The most famous case is a musculoskeletal disease that occurred in 1981 in Spain due to contaminated colza oil: **Toxic oil syndrome.**

# Environment: Sunlight



## VITAMIN D

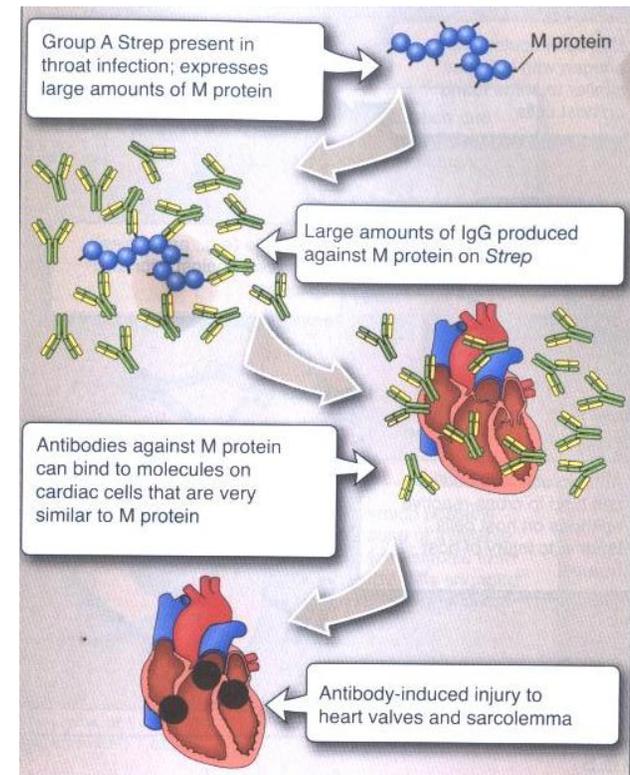
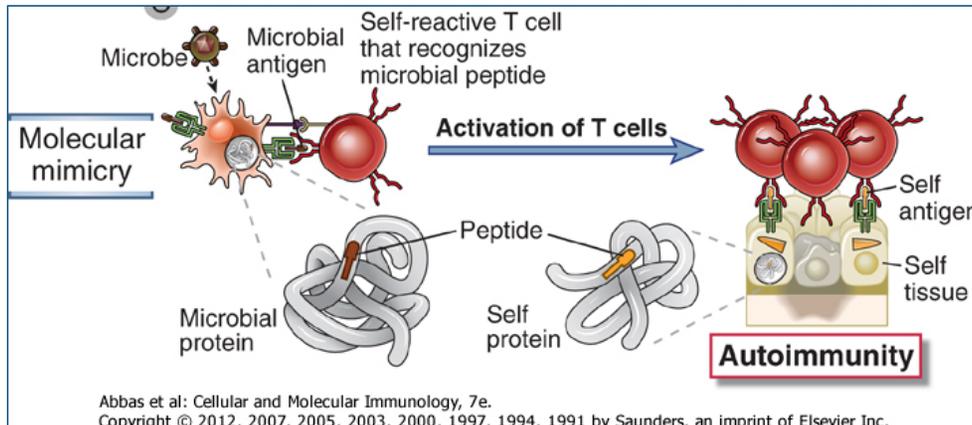
What makes  
"the sunshine vitamin"  
so special?

- Essential for strong, healthy bones
- Promotes absorption of calcium
- Valuable immune-supporting nutrient

Multiple sclerosis incidence increases with distance from the equator.

# Infection: Molecular Mimicry

- Autoimmune diseases can be associated with or preceded by infections.
- Infections do not directly cause the disease.
- Pathogenic antigens resembles a self-antigen
- Rheumatic fever- Occurs after a streptococcus infection (strep throat).



# Autoimmunity Classification

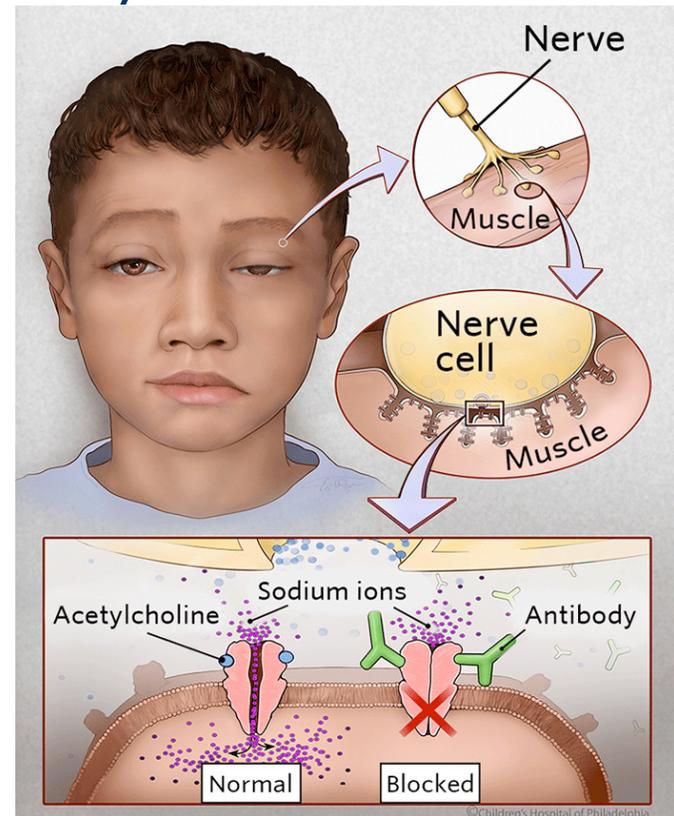
- **Organ specific-** autoimmune response is directed against a single organ.
- **Systemic-** autoimmune response is to an autoantigen expressed in many tissues.

# Two Types of Autoimmunity

- 2 etiologies considered hypersensitivities
- Type III: Immune complex disease (antibody-mediated)
  - Myasthenia gravis, systemic lupus erythematosus
- Type IV: T cell-mediated disease
  - Type I diabetes

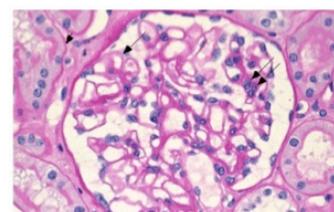
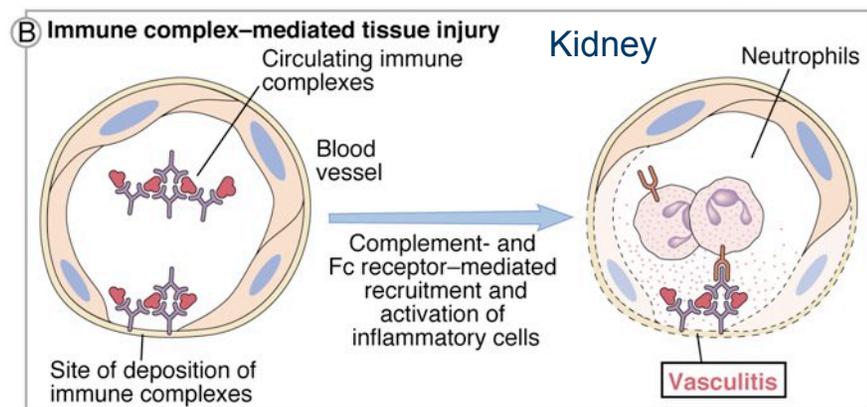
# Antibody-Mediated Organ-Specific Autoimmunity

- **Myasthenia gravis-** neuromuscular autoimmune disease
  - Autoantibodies form against the acetylcholine receptor and block neuromuscular junction transmissions
  - Symptoms: drooping eyelids, mouth weakness and arm or leg weakness

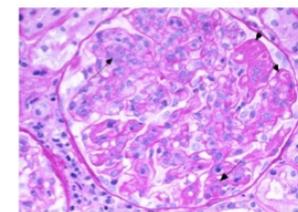


# Antibody-Mediated Systemic Autoimmunity

- **Systemic lupus erythematosus (SLE)**
  - Anti-nuclear autoantibodies
  - Symptoms: rash, painful and swollen joints, fever, hair loss, fatigue
  - Self-reactive antibodies lead to tissue damage



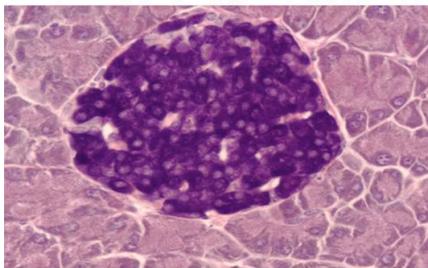
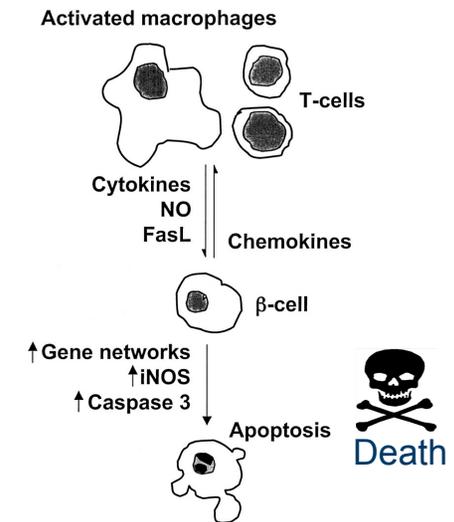
Normal kidney



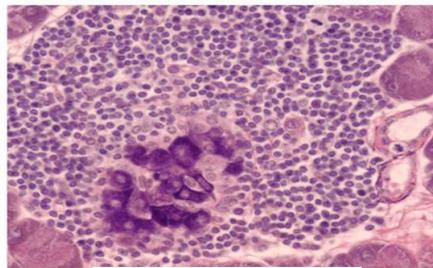
Lupus kidney

# T Cell-Mediated Organ-Specific Autoimmunity

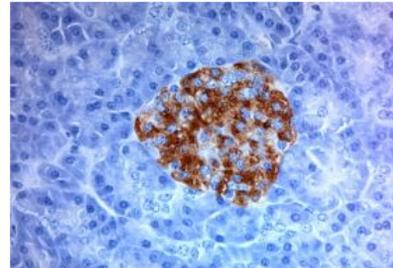
- Type I diabetes
  - T cell response against pancreatic beta cells
  - Beta cells produce insulin, which regulates the amount of glucose (sugar) in the blood.
  - Too much or too little sugar can be deadly.
  - Symptoms: heavy thirst, nausea, vomiting, dry mouth, fatigue, blurred vision



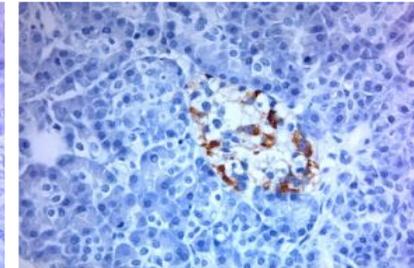
Healthy



Diabetes



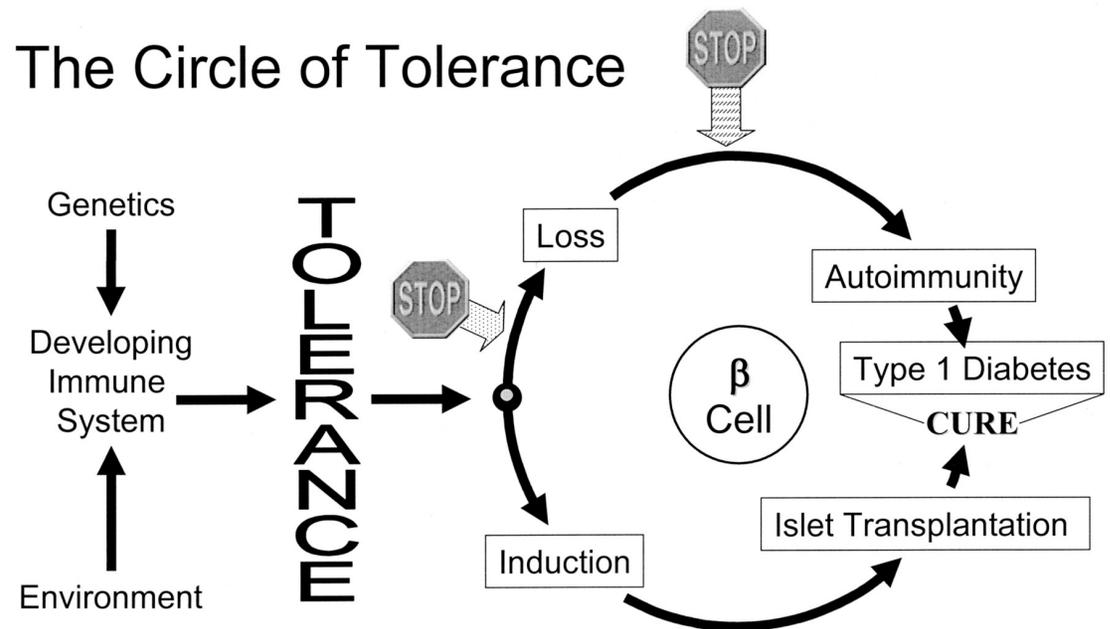
Healthy insulin



Diabetic insulin

# Summary: Autoimmunity Results From a Loss of Immunological Tolerance

- Immune tolerance is the failure to mount an immune response to an antigen.
- When immune cells develop they become educated or “tolerized” to not respond to self-antigens.
- Factors including genetics, the environment and exposure to pathogens can break immune tolerance leading to autoimmunity.



# Things to Know About Autoimmunity

- Difficult to diagnose
- Long list of symptoms: fatigue, chronic pain, rash, fevers...
- Unpredictable cycling of disease from feeling great to horrible
- Takes a mental toll
- Miss out on a lot of life
- Chronic with no cures
- Difficult to treat