

Connecting Lupus with genetics and biochemistry

Effective methods in dealing with
chronic disease

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Auto Immune Disease Statistics

NIH (National Institute of Health)

- 23.5 million Americans suffered from autoimmune disease
- This study only included 24 diseases
- A few are . . .

- Type 1 diabetes
- Rheumatoid arthritis
- Psoriasis
- Multiple sclerosis
- Inflammatory bowel
- Addison's disease

- Graves' disease
- Sjogren's syndrome
- Hashimoto's thyroiditis
- Myasthenia gravis
- Vasculitis
- Celiac Disease

Systemic lupus erythematosus (Lupus)

A chronic and complex autoimmune disease that affects the joints, skin, brain, lung, kidneys, and blood vessels causing widespread inflammation and tissue damage

Lupus Statistics

- ▶ Those with Lupus
 - 1.5 million Americans
 - 5 million people worldwide have a form of lupus
- ▶ Lupus is more common in women
 - 90+ % female
 - Mostly childbearing age
- ▶ Develop this disease between age 15 and 44
- ▶ The CDC estimated 16,000 new cases are discovered each year
- ▶ (SLE) Systemic Lupus Erythematosus is most common

Forms of lupus

- ▶ **Systematic lupus**
 - Accounts for 70% of all cases
 - Half of cases affect a major organ or tissue in the body
- ▶ **Continuous lupus**
 - Accounts for 10% of cases and primarily affects the skin
- ▶ **Drug-induced lupus**
 - Accounts for another 10% of lupus cases
 - Caused by high doses of specific medications
- ▶ **Neonatal lupus**
 - Very rare
 - Mother's antibodies affect the fetus
 - Causing skin rashes, liver problems, and low blood cell count
 - Symptoms often disappear completely after 6 months with no lasting effects

How lupus affects the immune system

- ▶ The immune system is an elaborate network of cells, tissues, and organs
 - Protects the body from invaders– bacteria, viruses, fungal infections, & parasites
- ▶ Usually, the immune system acts upon foreign substances
 - Immune system cells trying to combat cells of the body are weeded out during the development process.
- ▶ However, in Lupus and other autoimmune diseases, the immune system begins to recognize and attack “itself”
 - The cells of the immune system begin to injure the body’s own tissues
- ▶ This phenomenon is similar to “friendly fire” and can cause permanent scarring
- ▶ Ultimately jeopardizes the function of certain organs and body systems
- ▶ Certain cells and processes of the immune system have been identified as playing a role in lupus.

Cells and processes of the immune system in Lupus

- ▶ T-Cells, B-Cells, and Antibodies
- ▶ Neutrophils
- ▶ Cytokines
- ▶ Complement proteins

Effective Methods – Diagnosing autoimmune diseases

- 1) Biochemistry Testing
- 2) Heavy metal toxicity testing
- 3) Food allergy testing
- 4) Genetic testing

The combination of these test results –

- Determine how disease is affecting the body
- Identify the root causes

Effective Methods – Diagnosing autoimmune diseases

- ▶ **Biochemistry**– blood analysis
 - Amino acid profile, immune system function, adrenal function, markers of inflammation, other needed specific labs
- ▶ **Heavy Metal Toxicity Testing**– provoked urine test
 - Shows concentration of 20 different types of heavy metal that may affect proper body functions
- ▶ **Food allergy and sensitivity testing**–blood tests
 - To identify inflammation, sensitivity, other negative responses to certain foods
 - Also identifies responses to inhalants mold and specific spices
- ▶ **Medical Genetic testing** –saliva testing
 - Determine variable genetic factors that influence diseases
- ▶ Additional testing may be needed pending patient symptoms and medical history

Auto Immune Diseases – Triggers

Diet

- Gluten
- Sugar

Lack of exercise/Excessive exercise

- Neglecting to eliminate toxins from the body
- Increase ammonia levels in the body

Hormonal imbalance

- Alterations of 16 hydroxy – estrogen metabolites

Genetics

- Expression of variable genetic SNPS
- Hereditary factors
- HLA antigens

Inflammation

- Non-productive response involving immune cells ,blood vessels ,and molecular mediators

Heavy metals blocking essential chemical functions in the body

- The inhibition of specific chemical pathway production in the body

Environmental exposures

- Inhalation of molds and other toxins

Stress/Oxidative Stress

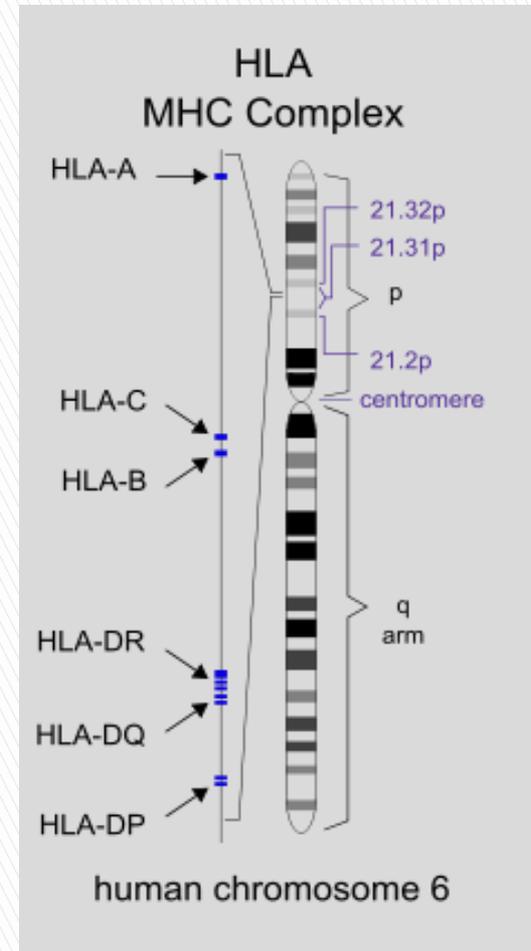
Methylation

Infections

Human Leukocyte Antigen

Human Leukocyte Antigen (HLA)

- System is the major histocompatibility complex (MHC) in humans
- Controlled by genes located on chromosome 6
- Encodes cell surface molecules
- Specialized to present antigenic peptides to the T-cell receptor (TCR)
- T Cells . . . Class II MHC molecules
- Cell-surface proteins are responsible for the regulation of the immune system



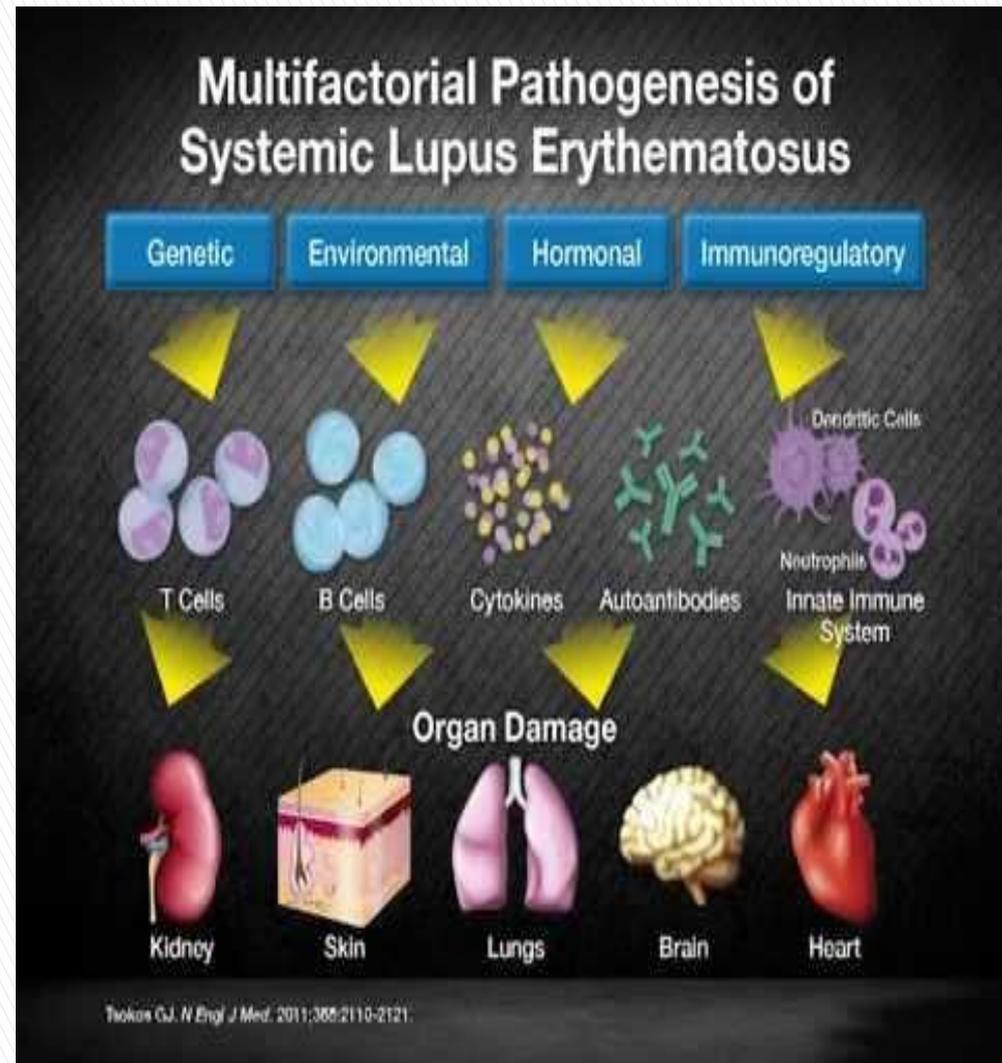
Antinuclear Antibodies

Antibodies

- Have major pathogenic significance in diagnoses and management of patient's with Lupus
- ANA's are directed against several nuclear antigens and can be grouped into four categories
 - 1) Antibodies to DNA
 - 2) Antibodies to histones
 - 3) Antibodies to non-histone proteins bound to RNA
 - 4) Antibodies to nucleolar antigens

Majority of pathology in Lupus – Related to immune complex deposits

- Immune complexes deposit in various organs and trigger inflammation
- Identifying the triggers for Lupus assist with proper treatment and relief of symptoms
- Our approach . . .
 - Identify root causes of disease
 - Implement individualized plan of care



Research in Lupus

Çagla Tükel and Stefania Gallucci,
Temple University School of Medicine

- Biofilm, bacterial communities in the body, may provoke the onset of lupus.
- When these bacterial communities are formed, they are very resistant to treatment. What we found is happening with these biofilms is there is this protein called an amyloid protein. We think there could be a link between biofilm associated diseases and amyloid associated diseases.
- The protein of interest is an amyloid called “Curli”, which is currently being treated with antibodies.
- Biofilm infections are extremely common in humans. Ear infections and urinary tract infections are just two examples of these kinds of infections.
- The flares in Lupus could be associated with the spikes in the Curli antibodies and maybe this could be a biomarker for the disease.
- Symptoms vary from patient to patient because any organ in the body could be attacked, although symptoms are often very flu-like. This makes lupus difficult to diagnose.
- Underlying infections may actually trigger the disease.
- It is important to study ways to better diagnose these underlying infections and treat them.

Research in Lupus

Lahita RG, Bucala R, Bradlow HL, Fishman J.

Determination of 16 alpha-hydroxyestrone by radioimmunoassay in Lupus

- A radioimmunoassay for the feminizing metabolite 16 alpha-hydroxyestrone was applied to a variety of volunteers.
- Increase in this metabolite was detected in patients with active Lupus.
- Increased levels of 16 alpha-hydroxyestrone-modified proteins in pregnancy and in systemic lupus erythematosus.
- The ketolic estrogen 16 alpha-hydroxyestrone (16 alpha OHE) reacts with lysine residues, forming stable covalent adducts with proteins.
- We report that elevated levels of plasma 16 alpha OHE led to increased formation of 16 alpha OHE-protein adducts and that the level of these adducts increases with the half-life of the protein.
- The modification of proteins by 16 alpha OHE may be a link in the relationship between female hormones, pregnancy, and systemic lupus erythematosus.
- It is important to study ways to better diagnose these underlying infections and treat them.

Pharmacy options for Lupus

Treatments

1. Abatacept (Orencia)
2. Anti-interferon-alpha antibody
3. Blisibimod (Benlysta)
4. Leflunomid (Arava)
5. Lupuzor
6. Prograf
7. Rapamycin (Sirolimus, Rapamune)
8. Rituximab (Rituxan)
9. Stem Cell Transplantation
10. TACI-Ig (Atacicept)
11. Tacrolimus (Prograf)

Treatment Action

1. Targets T-Cells with a special protein called CTLA4
2. Targets INF-a a chemical to fight viruses
3. A biologic design to blocks signals that, from a protein called BAFF that stimulates B sales
4. Stops the overproduction of amusing cells that leads to swelling inflammation stiffness and joint pain
5. Developed to change the behavior of a specific type of T cell involved in lupus disease
6. Works by interfering with T-cell function
7. Effects T cell function and inhibits a control point in the MTOR cell
8. Targets specific proteins called CD 20 on the surface of B cells
9. In severe cases is used to rebalance the immune system
10. Blocks signals from BAFF and also blocks signals from another molecule called APRIL
11. Works by interfering with T cell functions

Our approach for Treating autoimmune diseases

- Facilitate a healthy GI tract (diet)
- Remove heavy metal or environmental toxins that negatively affect the methylation cycle
- Identify/treat pathogens and infections
- Strengthen the immune system
- Monitor progress with follow-up labs to make treatment adjustments

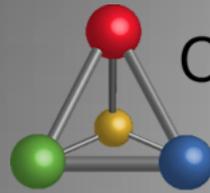
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Questions

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Thank You

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