

Importance of Awareness and Research for Lupus

Dec 9, 2017

LFA Indiana Chapter Symposium

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Allegheny Health Network

Pittsburgh, Pa

Lupus



Lupus is also a Public Health Issue

Pittsburgh Post-Gazette

One of America's Great Newspapers

your health



What important nutrient is not among those many popular fortified cereals for kids?
STORY, PAGE E-4

SECTION
E
TUESDAY
JUNE 11,
2002

FAMILY MATTERS PAGE E-2 RESEARCH FRONT PAGE E-3 HEALTH FORUM PAGE E-3 CONSUMER UPDATE PAGE E-4 FITNESS FOR ALL PAGE E-6

Learning about lupus



Potomac High School senior Dawn Cline visited UPMC's new Lupus Center of Excellence with classmates.

New UPMC center focuses on finding a cure and draws the interest of a young, would-be researcher



Juliette Hale, who suffers from lupus, talked to students last month about the limitations the disease imposed on her daily life.

Raw pink blotches marred the black skin of one young woman's face. A blue bandana covered a scarred scalp where hair no longer grows. In contrast, the young white woman seated nearby had no obvious skin problems and her blonde hair was fashionably cut. Outwardly it appeared that Juliette Hale, 36, of Monroeville, and April Clark, 29, of Stoneboro in Mercer County have little in common other than their age and gender.

But on the inside, they are very much the same. They have lupus, an unpredictable and incurable autoimmune disease. Their immune systems are attacking and destroying healthy tissue for no apparent reason, with devastating consequences.

Last month, Hale and Clark, along with staff members of the University of Pittsburgh's recently created Lupus Center of Excellence and its co-director Drs. Susan Manzi and Joseph Alarcon, told a handful of middle- and high-school students about the condition that, one way or another, is an important part of their lives.

"This is our mission to try to figure out

what caused this disease and try to come up with a cure," Alarcon told the teen-agers from Marshall Middle School in the North Allegheny School District and from the city's Peabody High School.

"We're hoping some of you may someday join our mission and try to accelerate discovery of a cure for lupus."

The three middle school girls had taken steps by collecting \$370 door-to-door to donate to the lupus center.

And Potomac senior Dawn Cline, 18, put together a lupus awareness project last summer while participating in the Governor's School in health care. Her uncle has the disease and her mother once

worked in Manzi's lab.

"A lot of people know a lot about cancer or AIDS, but you never hear anything about lupus," Dawn later said. "When I realized that, I thought it would be interesting to create a program where people learn about lupus."

As part of her Governor's School project, Dawn wrote a 10-page paper and made a presentation called "Lupus: What's That?" to several biology classes at her high school. She then selected fellow students interested in pursuing a career in science or medicine to attend a lupus awareness day at the center.

There the young people heard more about the disease, not only from doctors and researchers but also from people who have it.

For instance, sometime sometime Hale's skin problems. She uses sun block with a protection factor of 15, far higher than most people need. She wears long sleeves and pants in the summer and is afraid to go outside during the day. Chewing food hurts her face.

Clark's skin isn't scarred, but she's

SEE LUPUS, PAGE E-2



Allegheny
Health Network

LFA: Elevating Lupus on the National Healthcare Agenda

FEDERAL WORKING GROUP ON LUPUS AT NIH

.....> Forum convened by the National Institutes of Health aimed at producing a comprehensive look at lupus in the federal government; ***2016 Action Plan for Lupus Research.***

NATIONAL LUPUS PATIENT REGISTRY PROGRAM AT CDC

.....> Generated **\$43.7 million** in total funding to date; Developed the **National Public Health Agenda for Lupus.**

PEER REVIEWED MEDICAL RESEARCH PROGRAM AT DoD

.....> Total PRMRP lupus project funding to date is **\$17.4 million.**

“COULD I HAVE LUPUS?” CAMPAIGN WITH THE OFFICE ON WOMEN’S HEALTH

.....> **\$2.3 million** appropriated over 3 years to create a national lupus awareness campaign that garnered more than **\$70 million in donated and earned media.**

THE LUPUS INITIATIVE WITH THE OFFICE OF MINORITY HEALTH

.....> Generated **\$10.6 million** in funding to date. Focus on primary care provider education and new focus is clinical trial education.

CONGRESSIONAL LUPUS CAUCUS

.....> **Established in 2012;** Co-chaired by Representatives Rooney (R-FL), Keating (D-MA), Ros-Lehtinen (R-FL) and Johnson (D-TX); 63 Members.

Objectives:

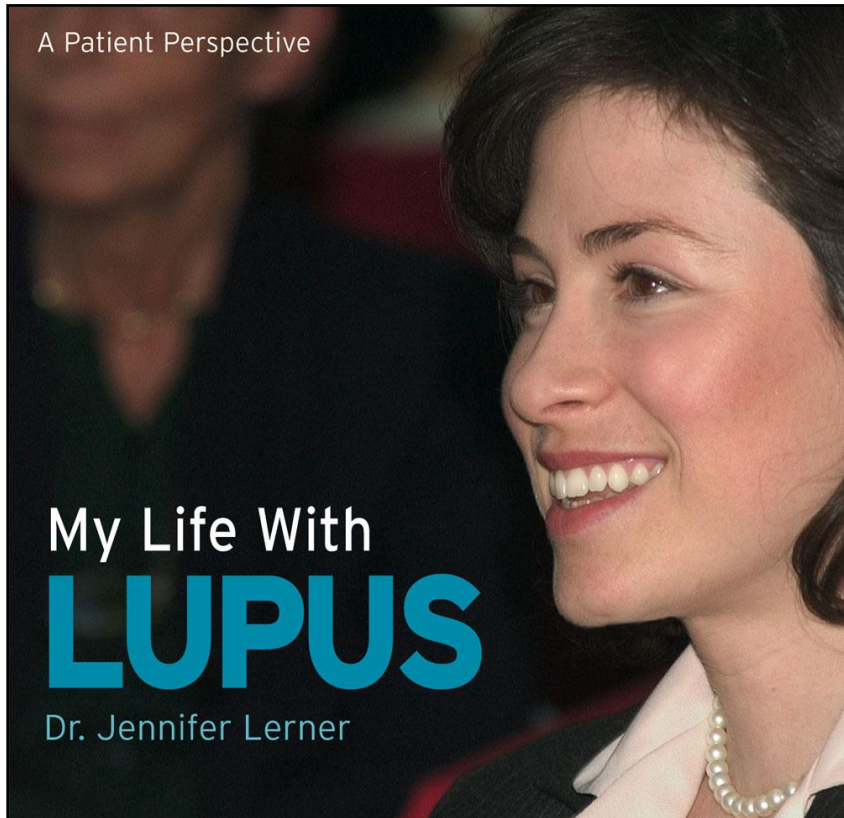
What is lupus?

What causes lupus?

What are important health issues in lupus?

What treatments are on the horizon?

Lupus Facts



- 1.5-2.0 million in US
 - 90% women
 - Peak onset 15-45 yrs age
 - Children, men, and elderly
 - 1/250 Black women
 - 4 x more common
- ↑↑ Hispanic, Asian,
Native American

Lupus, the Chameleon: Many Disguises Difficult to Capture



- No two look exactly alike
- Spectrum of signs and symptoms
- Impacts young people, minorities
- Symptoms can evolve over time
- You have to think of lupus to diagnosis it
- No one blood test that can diagnose lupus

Lupus, the Chameleon: Many Disguises Difficult to Capture

LFA and CDC - call to action

- 6.5 million, 4 states and 3 Indian Health Service regions
- Lupus more common AA, Hispanic, Asian, Native Americans
- Lupus more severe in these populations (kidney)
- Diagnosis 10 yrs younger in AA



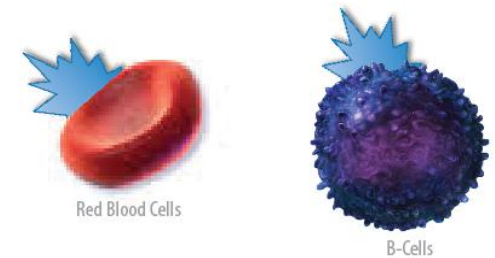
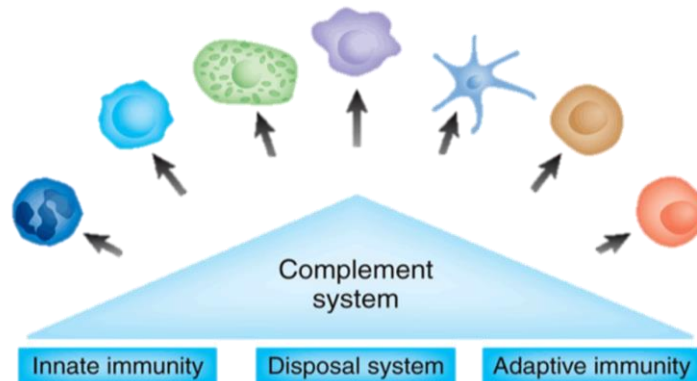
We are NOT identifying everyone with lupus

New Diagnostic Tests for Lupus

Blood levels
Complement
C3, C4

Complement Activation

Cell-Bound Complement
Activation Products
CB-CAPs



Objectives:

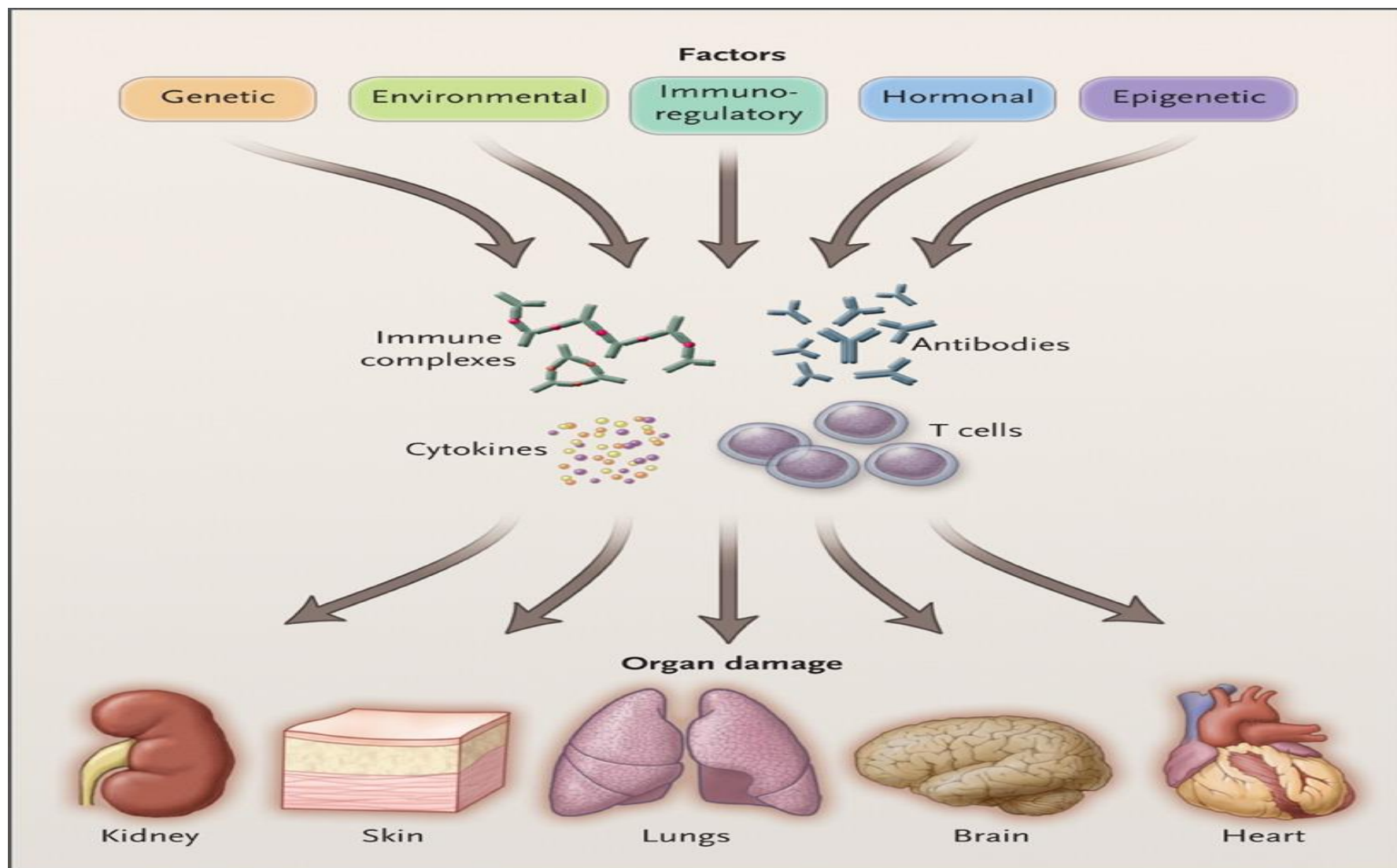
What is lupus?

What causes lupus?

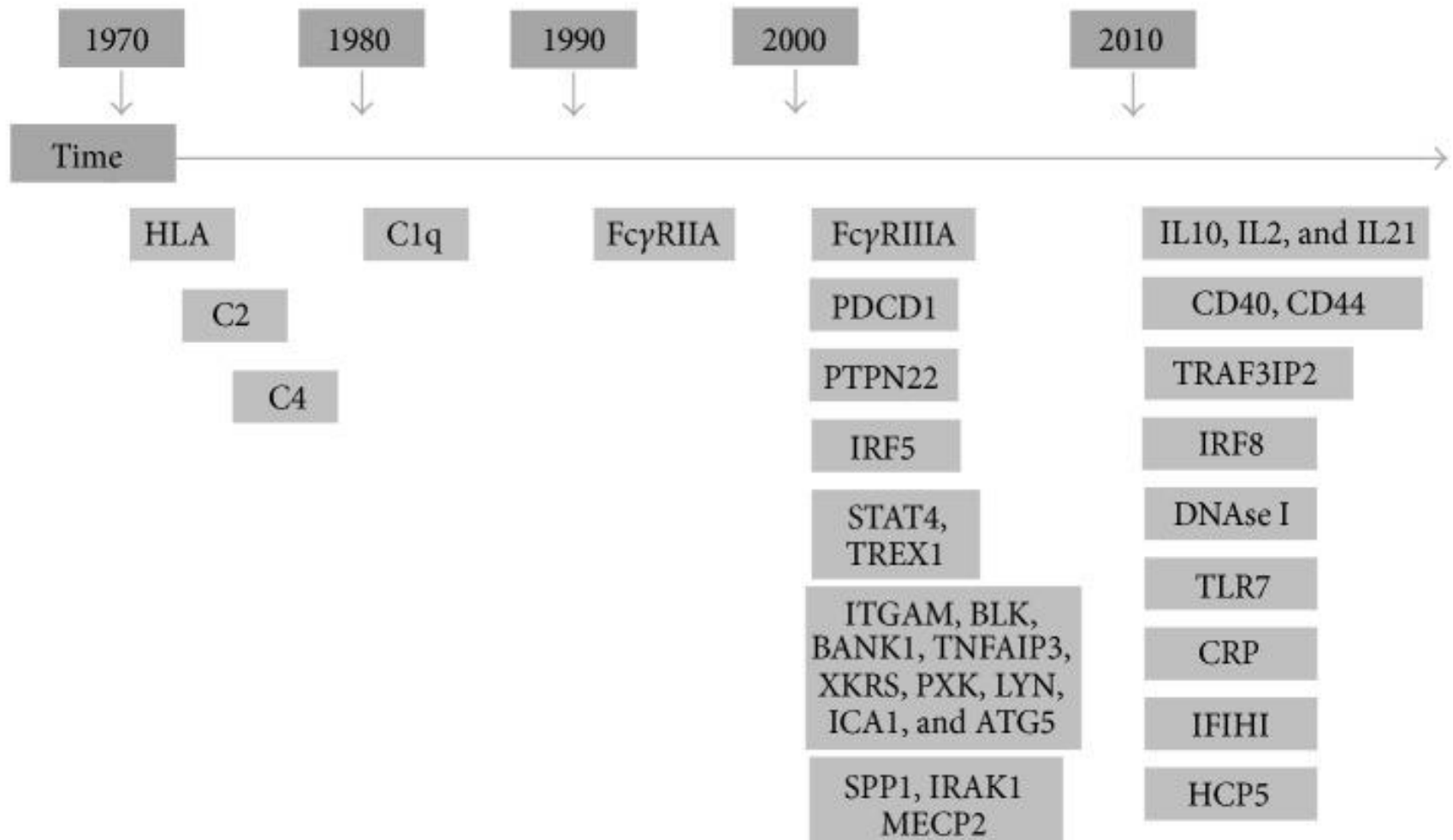
What are important health issues in lupus?

What treatments are on the horizon?

Heterogeneity of Systemic Lupus Erythematosus

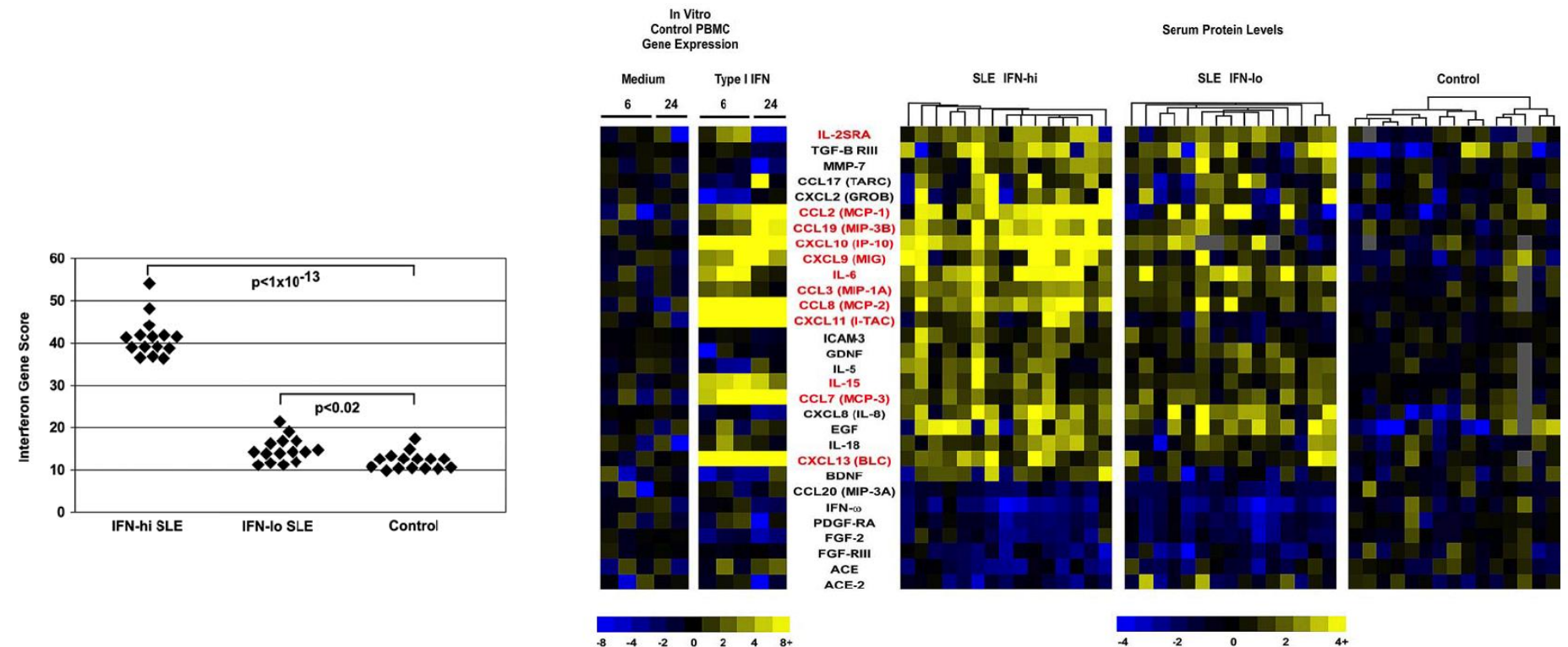


Timeline of lupus gene discoveries



Elevated Serum Levels of Interferon-Regulated Chemokines Are Biomarkers for Active Human Systemic Lupus Erythematosus

Jason W. Bauer¹, Emily C. Baechler¹, Michelle Petri², Franak M. Batliwalla³, Dianna Crawford¹, Ward A. Ortmann¹, Karl J. Espe¹, Wentian Li³, Dhavalkumar D. Patel⁴, Peter K. Gregersen³, Timothy W. Behrens^{1,2,4}



Objectives:

What is lupus?

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What are important health issues in lupus?

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- Mental Health
- Heart Health



Depression and anxiety are common in lupus

232/1827 (13%) lupus patients had a mood disorder within 6 months diagnosis

Depression

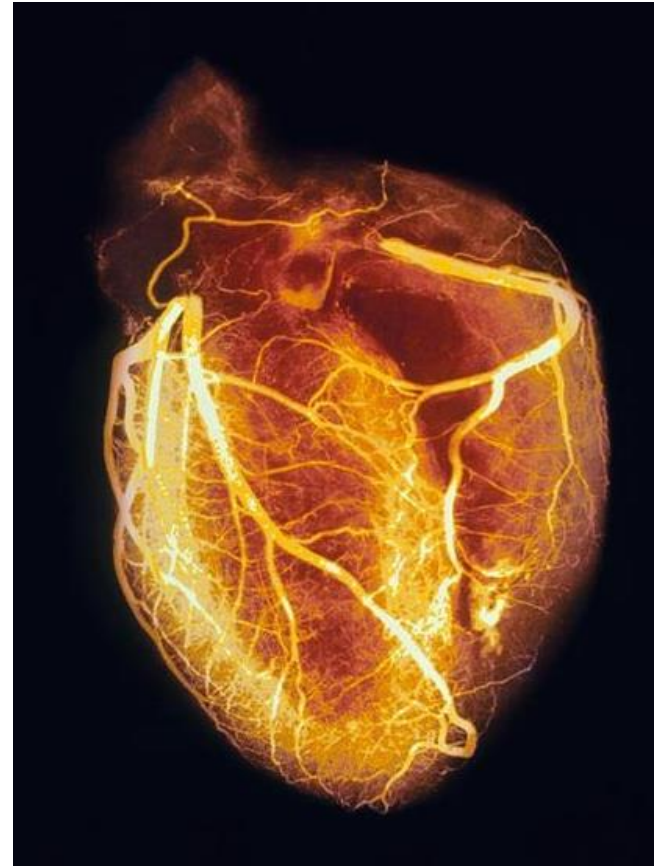
Georgia Lupus Registry

- 519 SLE patient
 - 31% had depression
 - 22% had both anxiety and depression
- Only 59% had been screened

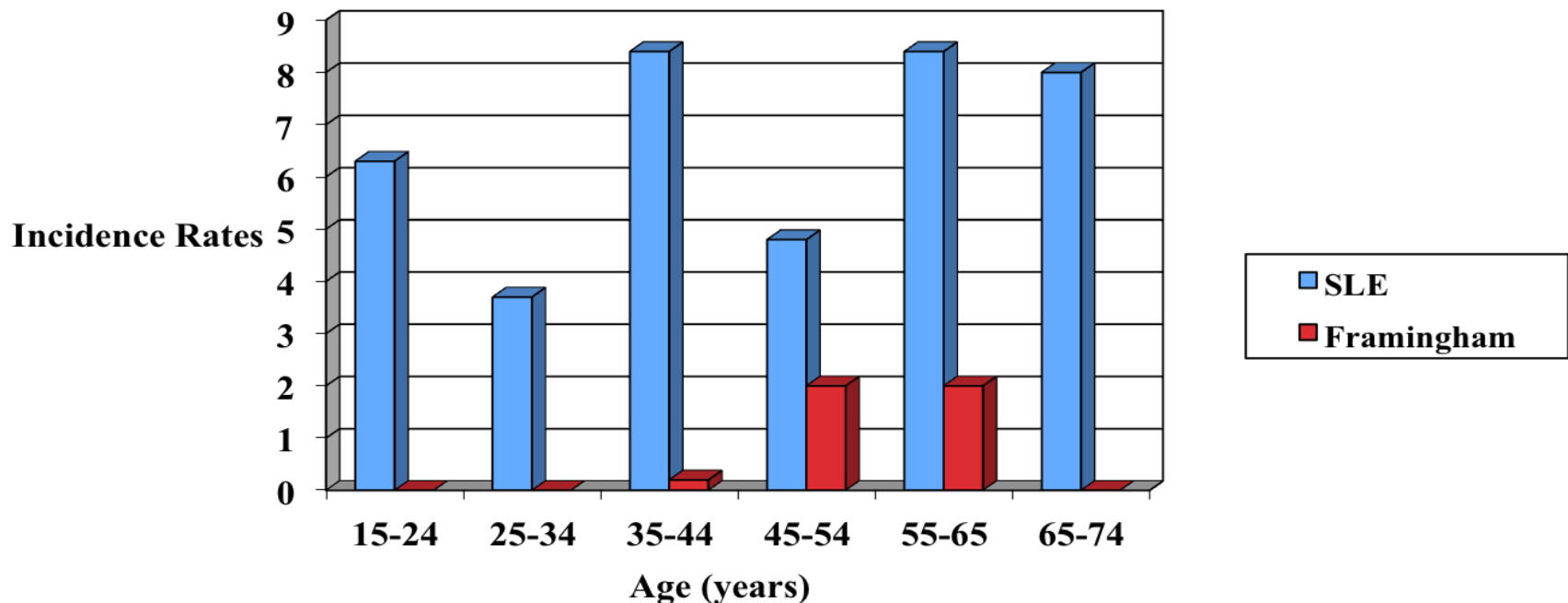
Need to screen for depression and anxiety in patients with lupus

Need to treat depression and anxiety

Heart Health



Incidence Rates Heart Attacks in Lupus compared to those without Lupus



50-fold increased risk in 35-44 yr

AHA Guideline

Effectiveness-Based Guidelines for the Prevention of Cardiovascular Disease in Women—2011 Update A Guideline From the American Heart Association

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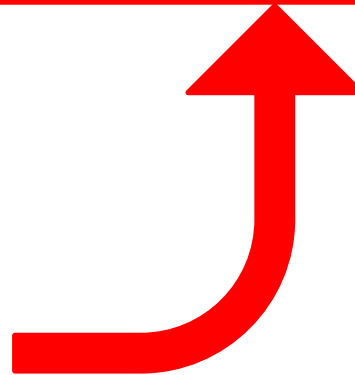
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Table 2. Classification of CVD Risk in Women

Risk Status	Criteria
High risk (≥ 1 high-risk states)	<p>Clinically manifest CHD</p> <p>Clinically manifest cerebrovascular disease</p> <p>Clinically manifest peripheral arterial disease</p> <p>Abdominal aortic aneurysm</p> <p>End-stage or chronic kidney disease</p> <p>Diabetes mellitus</p> <p>10-y Predicted CVD risk $\geq 10\%$</p>
At risk (≥ 1 major risk factor[s])	<p>Cigarette smoking</p> <p>SBP ≥ 120 mm Hg, DBP ≥ 80 mm Hg, or treated hypertension</p> <p>Total cholesterol ≥ 200 mg/dL, HDL-C < 50 mg/dL, or treated for dyslipidemia</p> <p>Obesity, particularly central adiposity</p> <p>Poor diet</p> <p>Physical inactivity</p> <p>Family history of premature CVD occurring in first-degree relatives in men < 55 y of age or in women < 65 y of age</p> <p>Metabolic syndrome</p> <p>Evidence of advanced subclinical atherosclerosis (eg, coronary calcification, carotid plaque, or thickened IMT)</p> <p>Poor exercise capacity on treadmill test and/or abnormal heart rate recovery after stopping exercise</p> <p>Systemic autoimmune collagen-vascular disease (eg, lupus or rheumatoid arthritis)</p> <p>History of preeclampsia, gestational diabetes, or pregnancy-induced hypertension</p>

Systemic autoimmune collagen-vascular disease
(eg, lupus or rheumatoid arthritis)



Objectives:

What is lupus?

What causes lupus?

What are important health issues in lupus?

New treatments on the horizon?

FDA Approved Drugs for SLE

Corticosteroids

Hydroxychloroquine

ASA

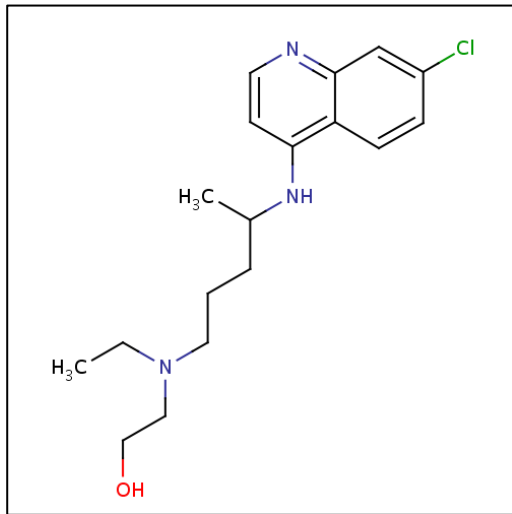
50-year drought

Belimumab approved 2011

Hydroxychloroquine:

Beyond Disease Activity

Multiethnic Longitudinal Cohort (n=635)

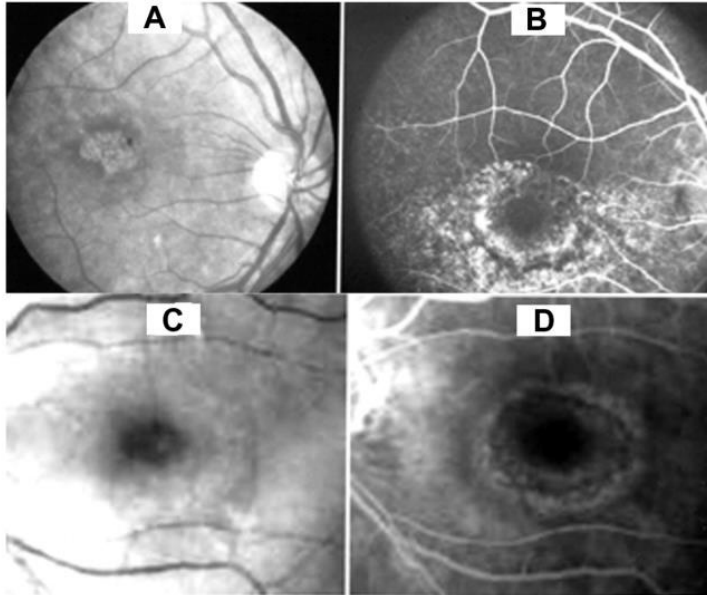


- **Improved survival**
- **Decrease in flares**
- **Decrease in kidney damage**
- **Decrease in skin-damage**
- **Decrease in vascular events**

Safe during pregnancy

Hydroxychloroquine Side Effects

Retina



Skin



Hyperpigmentation

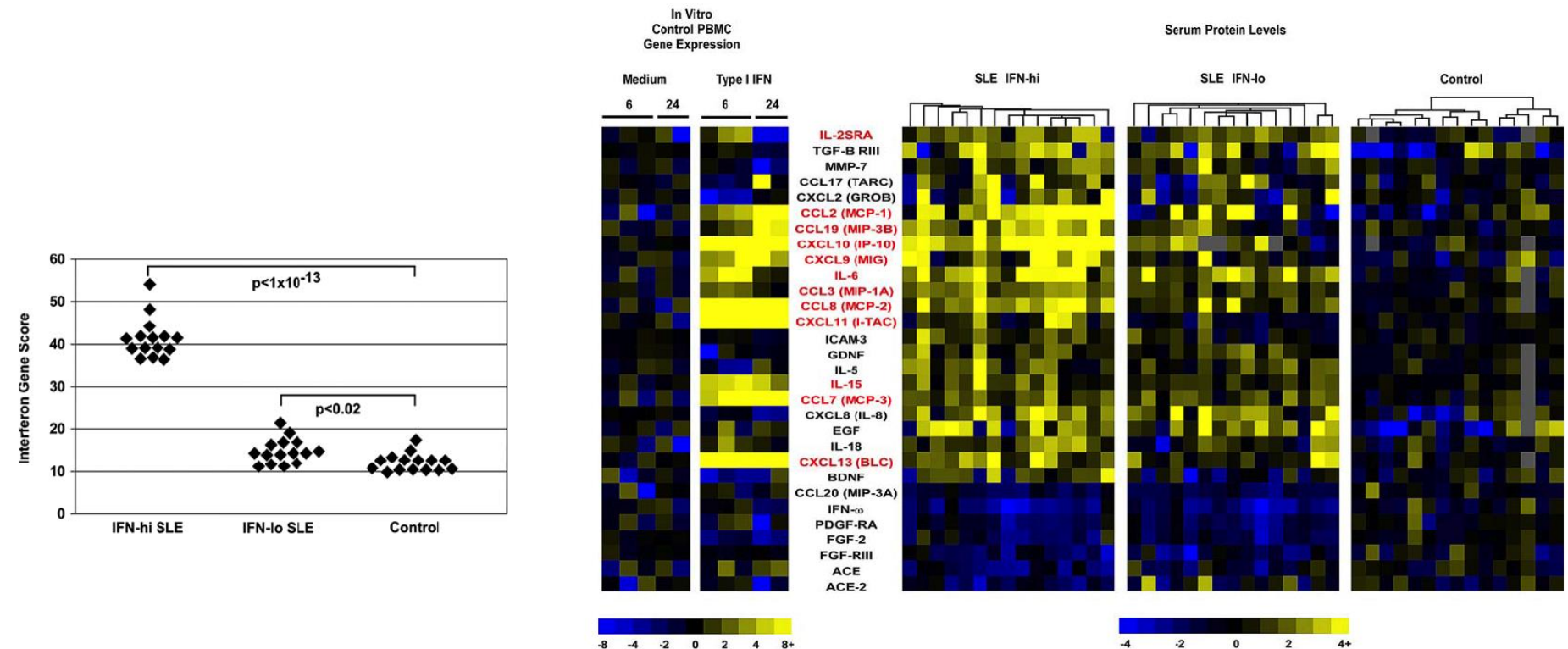
- **Weight based dosing**

Farrell DF. Clin Ophthalmol 2012
Marmor MF. Ophthalmology 2011
Joyce :European Heart Journal 2012
Sumpter et al. Lupus 2012

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Optical coherence tomography (SD-OCT), or fundus autofluorescence (FAF)

Elevated Serum Levels of Interferon-Regulated Chemokines Are Biomarkers for Active Human Systemic Lupus Erythematosus

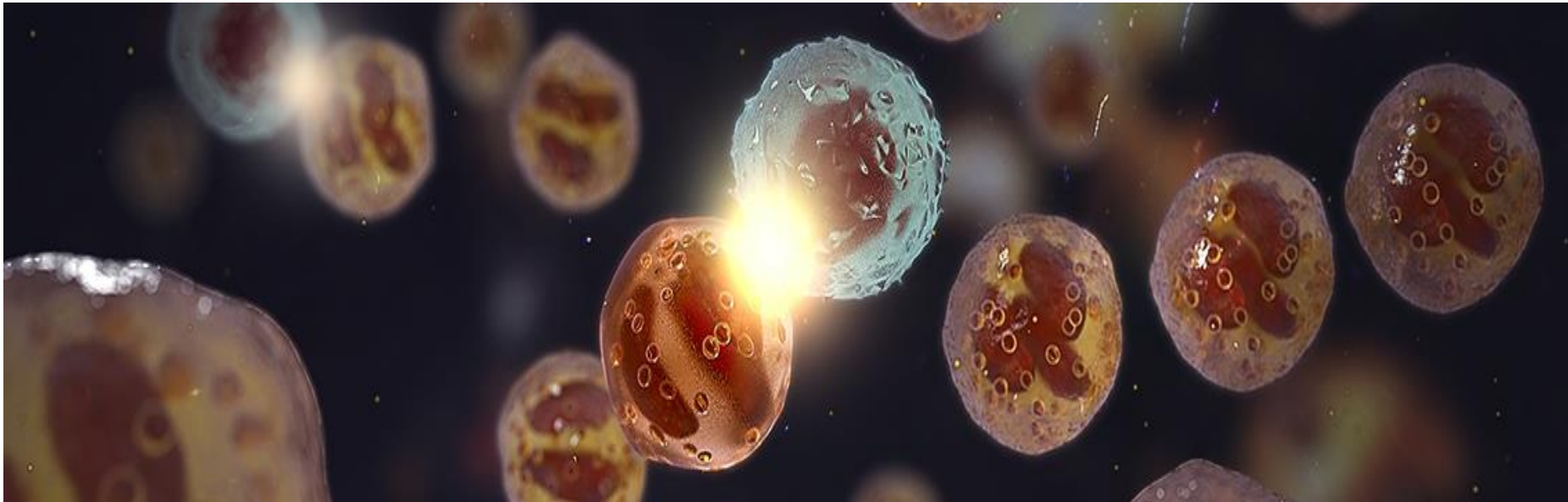
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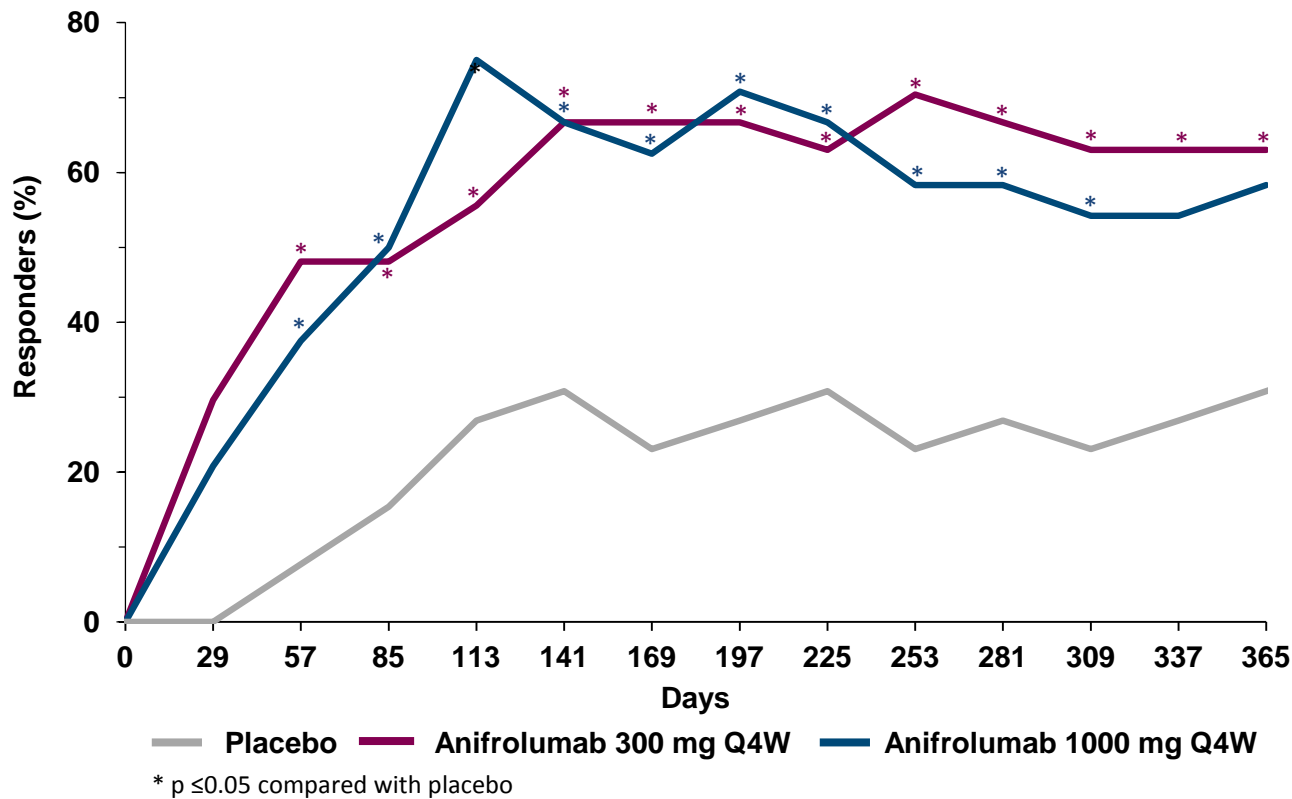
Anifrolumab, an anti-interferon-alpha receptor monoclonal antibody, in moderate to severe systemic lupus erythematosus (SLE)

R Furie¹, JT Merrill², VP Werth^{3,4}, M Khamashta⁵, K Kalunian⁶, P Brohawn⁷, G Illei⁷, J Drappa⁷, L Wang⁷ and S Yoo⁸

¹Division of Rheumatology, Hofstra North Shore –LIJ School of Medicine, North Shore – LIJ Health System; Great Neck, NY, USA; ²Oklahoma Medical Research Foundation, Oklahoma City, OK, USA; ³Philadelphia VA Medical Center; Philadelphia, PA, USA, ⁴University of Pennsylvania, Philadelphia, PA, USA; ⁵Graham Hughes Lupus Research Laboratory, King's College London, The Rayne Institute, St Thomas' Hospital, London, UK, ⁶UCSD School of Medicine, La Jolla, CA, USA; ⁷MedImmune, Gaithersburg, MD, USA; ⁸Regenxbio, Rockville, MD, USA



Significant Improvement in Skin Rashes and Disease Activity



Day 1



Day 281



Patient was receiving 300 mg/day anifrolumab

Pipeline for New Lupus Therapies....to name a few

Late-Breaking ACR 2017

Ustekinumab(IL12/23) in active SLE Phase 2a (Stelara)

Met the primary endpoint!!

Intravenous (IV) 6 mg/kg or placebo (PBO) at week 0, followed by subcutaneous (SC) injections 90 mg or placebo every eight weeks, both in addition to standard of care therapy for 24 weeks.

(**60 percent** vs. **31 percent**, respectively, $P=0.0046$).

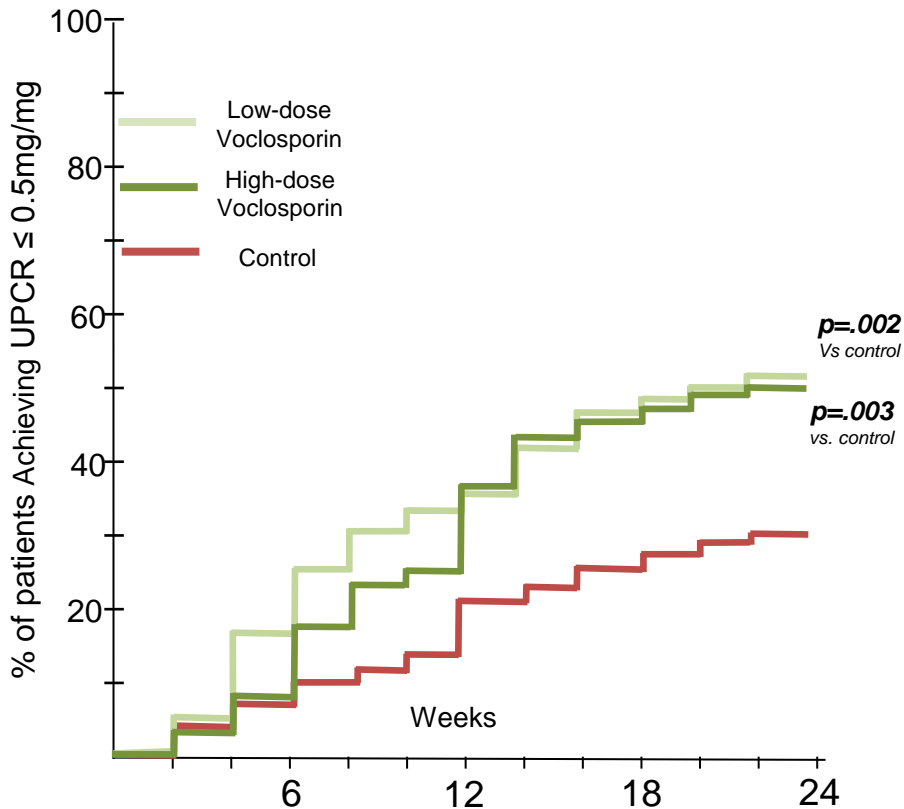
Pipeline for New Lupus Therapies....to name a few

- **Anifrolumab (TULIP 1,2), s.q, long term extension**
- **ACTHAR in active SLE**
- **Baricitinib (LY3009104)** (oral) active arthritis/rash
- **M295** BTK inhibitor (BCR signaling molecule)
- **Dapirolizumab Pegol (DZP)** CD40L (UCB)
- **CC-220** (Celgene)
- **BIIB059** (Biogen)
- **GDC-0853** BTK Inhibitor (Genentech)

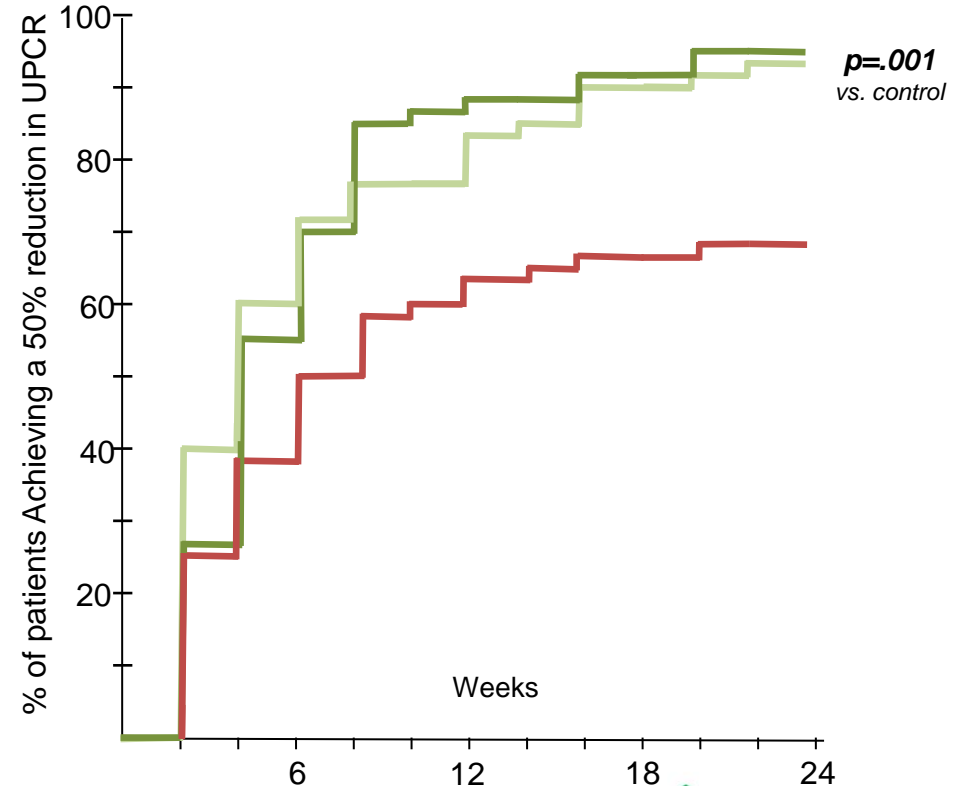
Voclosporin:

Lupus Kidney Disease

Kaplan Meier Plot – **Time to Complete Remission**
(measured by UPCR)



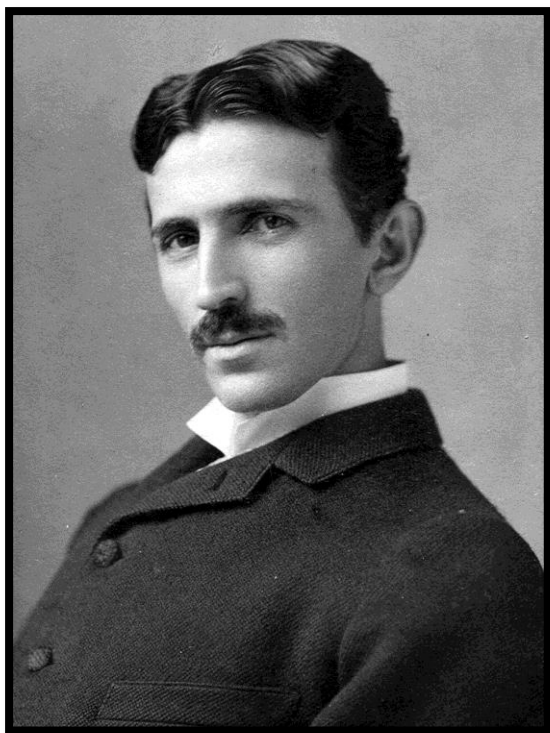
Kaplan Meier Plot – **Time to Partial Remission**
(measured by UPCR)



Pipeline for New Kidney Therapies- to name a few

- **ALLURE** (abatacept vs placebo) add on to steroids and MMF
- **BLISS-LN** (belimumab vs placebo) add on to steroids and cyclophosphamide
- **TULIP-LN1** (anifrolumab) added to steroids/MMF
- **Rituximab Trials:**
 - **RING** (maintenance add on to SOC),
 - **CALIBRATE** (belimumab added after rituximab and cyclophosphamide)
 - **RITUXILUP** (no steroids),
- **Anti-TWEAK** antibody (TNF-like weak inducer of apoptosis)
- Other: anti-MIF antibody (macrophage inhibitory factor); anti-IL-21 antibody; ACTHAR





**“It will soon be possible to
transmit wireless messages
around the world so simply that
any individual can carry and
operate his own apparatus.”**

—Nikola Tesla (1909)

There will be a world without lupus.