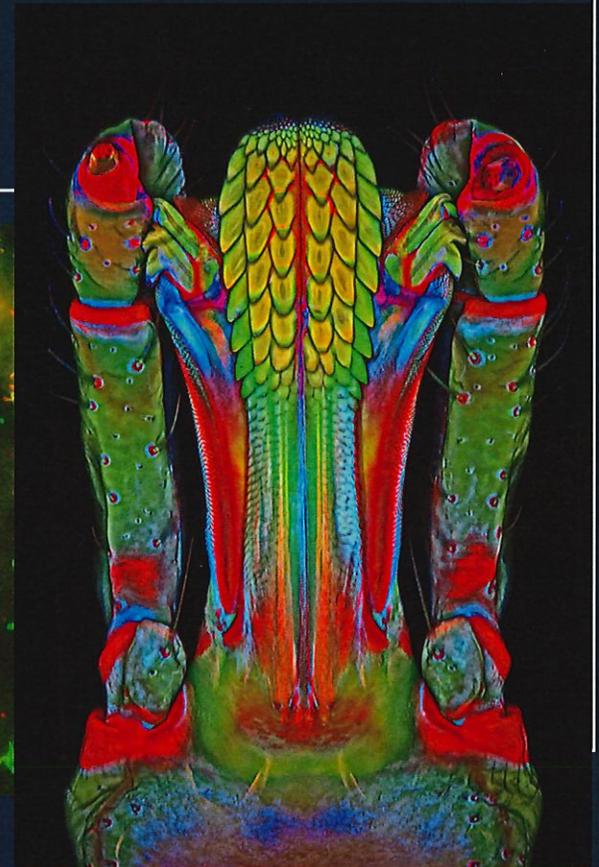
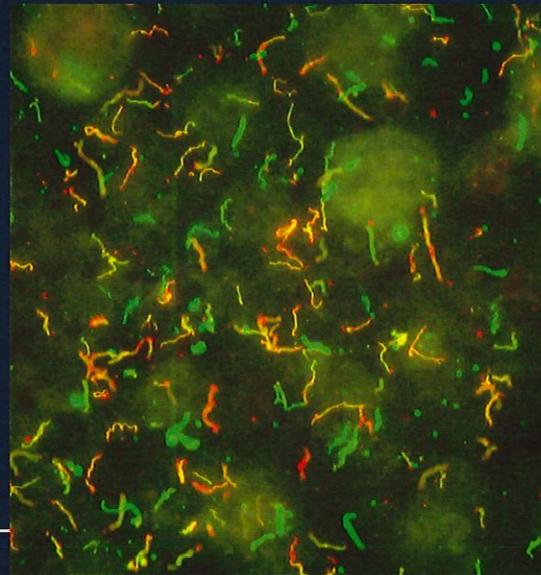


# Conquering Lyme Disease: Science Bridges the Great Divide

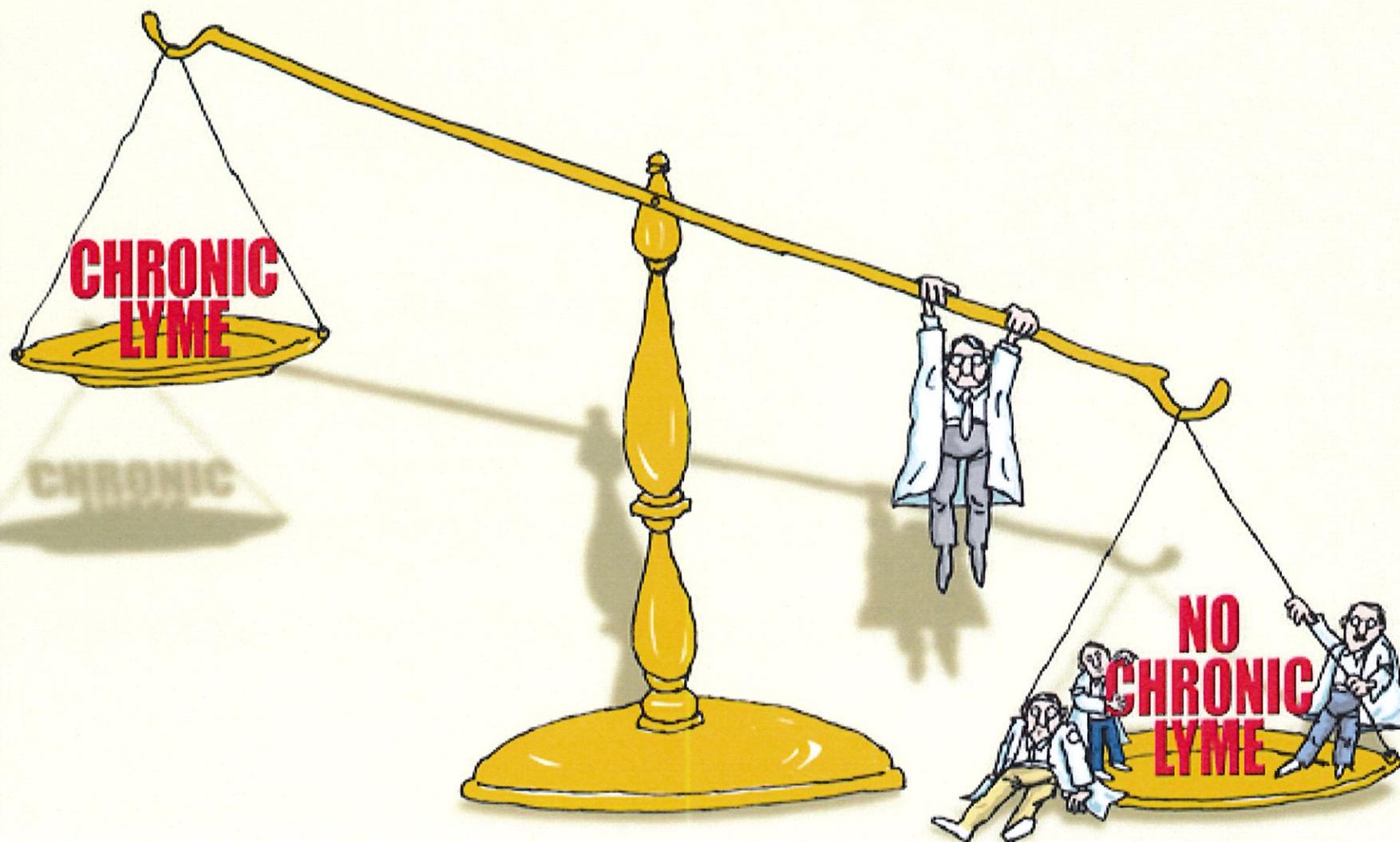


By David Skidmore

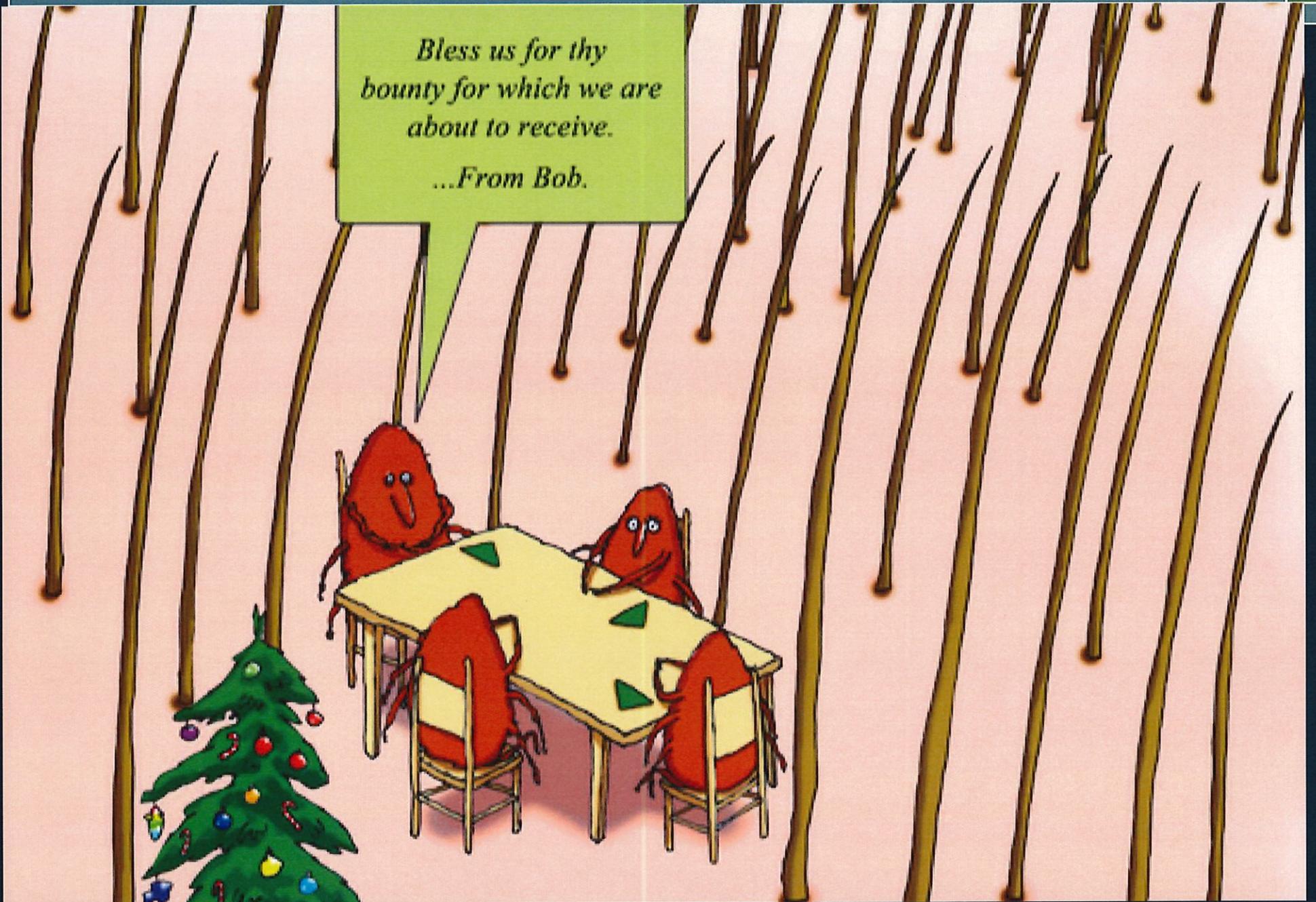
We have  
Lyme Disease  
and we  
need Help!  
...please.



“Throwing Weight Around” by David Skidmore



*Bless us for thy  
bounty for which we are  
about to receive.  
...From Bob.*



Ticks preparing for a human blood meal

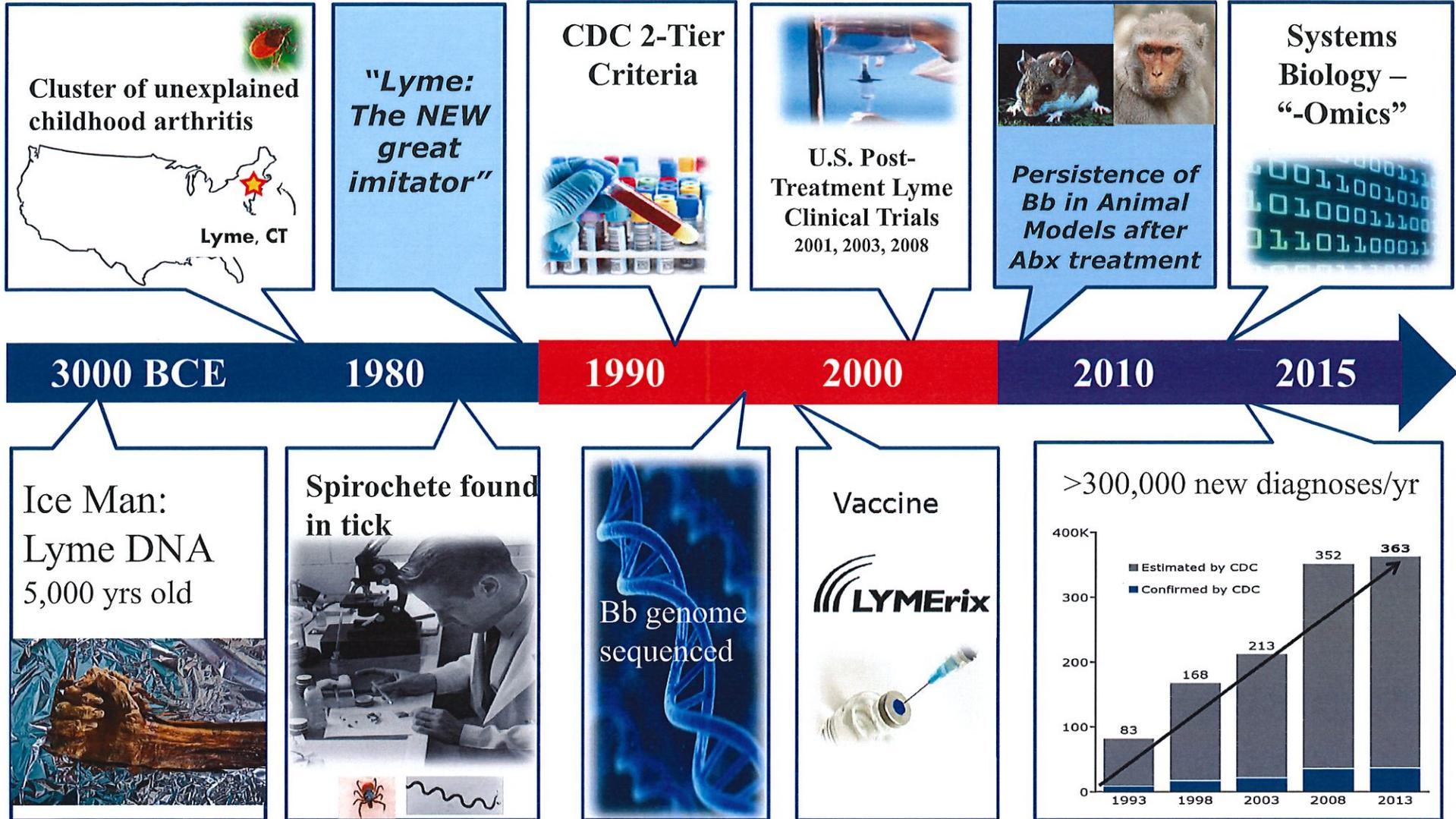
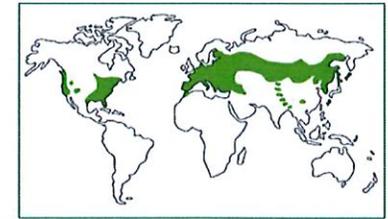
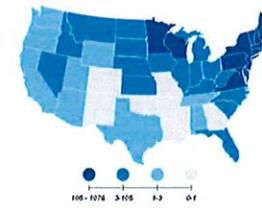
By David Skidmore



## Major Periods in the History of Lyme Disease

- 1976-1990      Discovery & Openness
- 1990- 2008      Narrow Definitions, Conflict & Entrenchment
- 2008-      Renewed discovery & exploration

# A brief history of Lyme disease...



# The efforts of mothers, families, and patients have advanced the research through funding and awareness



Polly Murray



GLOBAL  
LYME  
ALLIANCE



CALDA



Patients & Parents  
Mobilize

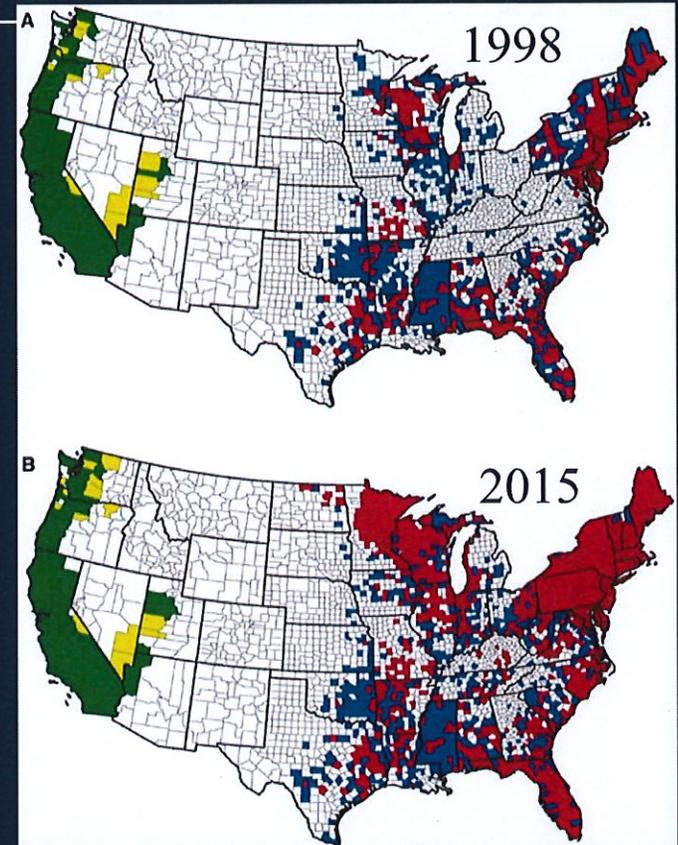
# Paradigm Shifts of last decade

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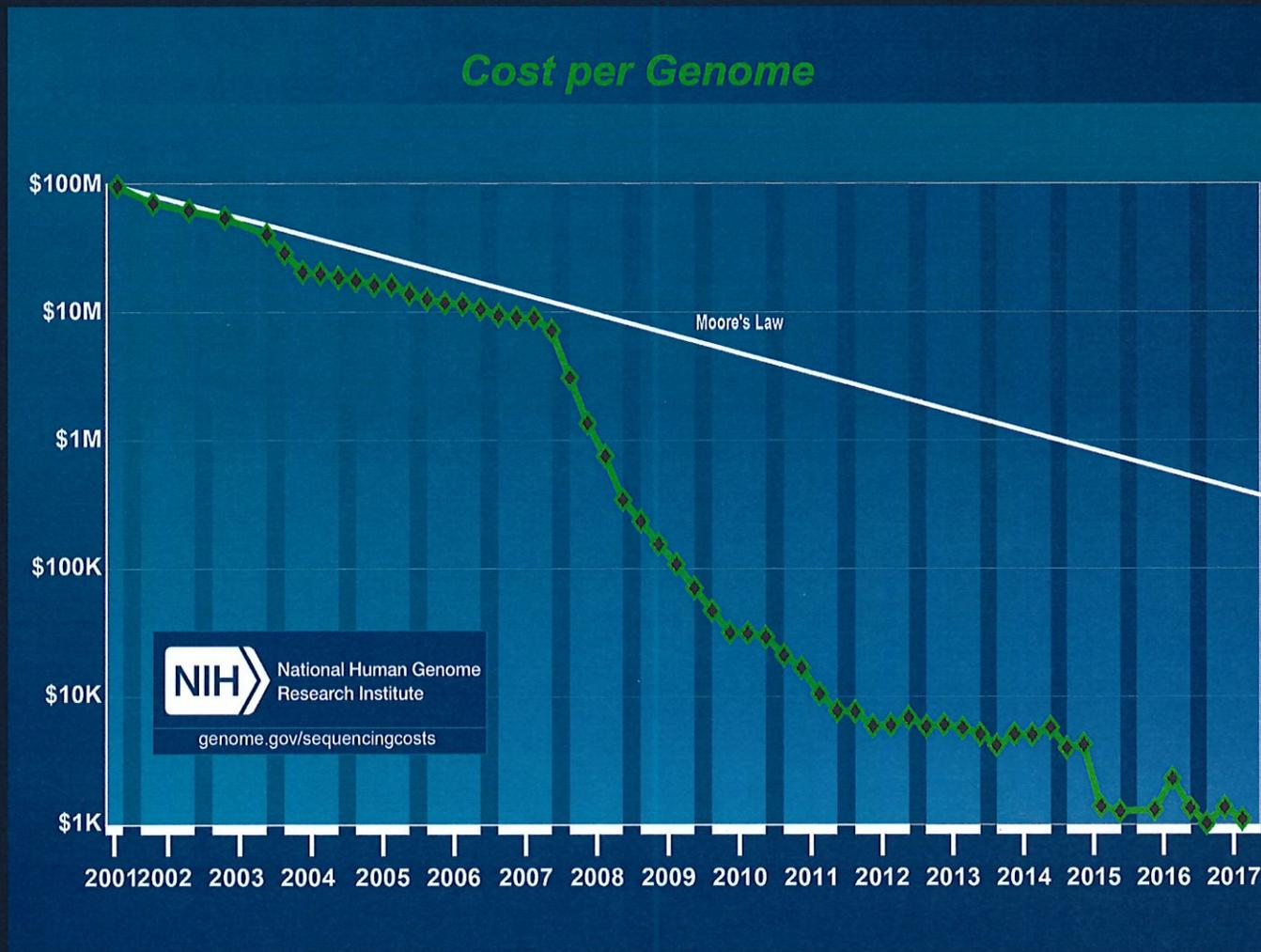
- Recognition that Lyme Disease is not simple
  - Current blood tests are inadequate
    - Only 35-50% sensitive in early Lyme disease
  - Spirochetes can persist – even after standard antibiotic treatment – a new focus of research
  
- Recognition that chronic symptoms have biological correlates (in the brain, spinal fluid, & blood)

# Paradigm Shifts of last decade

- **Recognition: an epidemic**
  - The geographic spread of ticks is expanding
- **Discovery of new microbes in the ticks**
- **Recognition of the brain's involvement in persistent symptoms.**

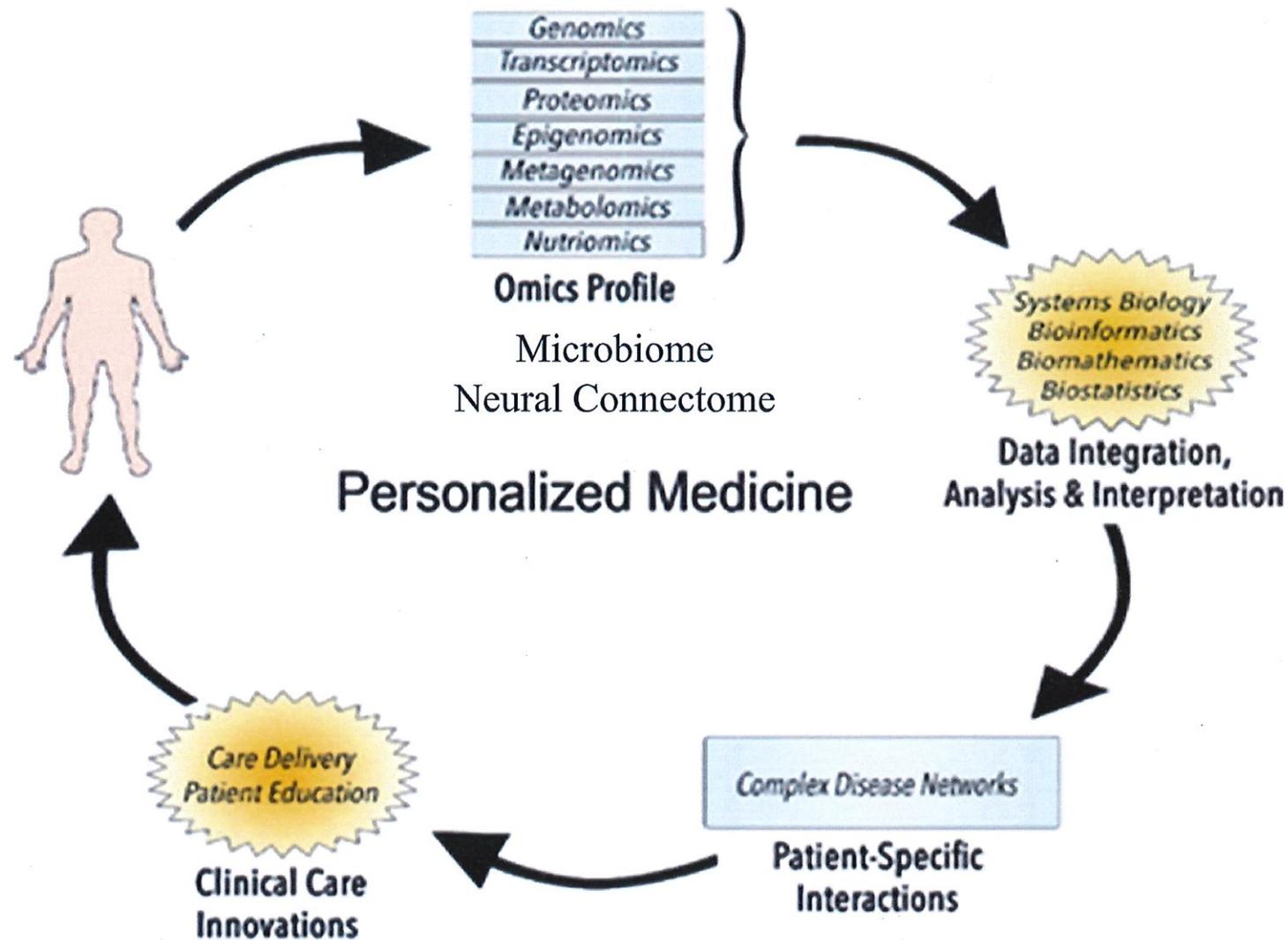


# Technology Advances – Genome sequencing is now fast & inexpensive: cost up to \$1 billion in 1999-2003



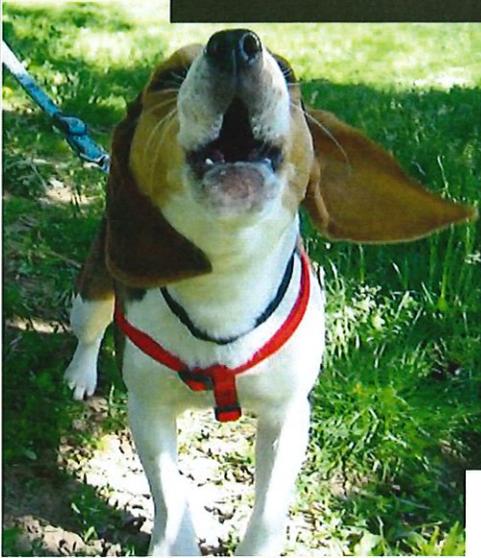
**CURRENT COST: ~\$1,000**

# Technology Advances: new assays & biomarkers - the power of OMICS



# Intriguing Images

Borrelia spirochetes persist despite antibiotics.  
This has been shown in many species.

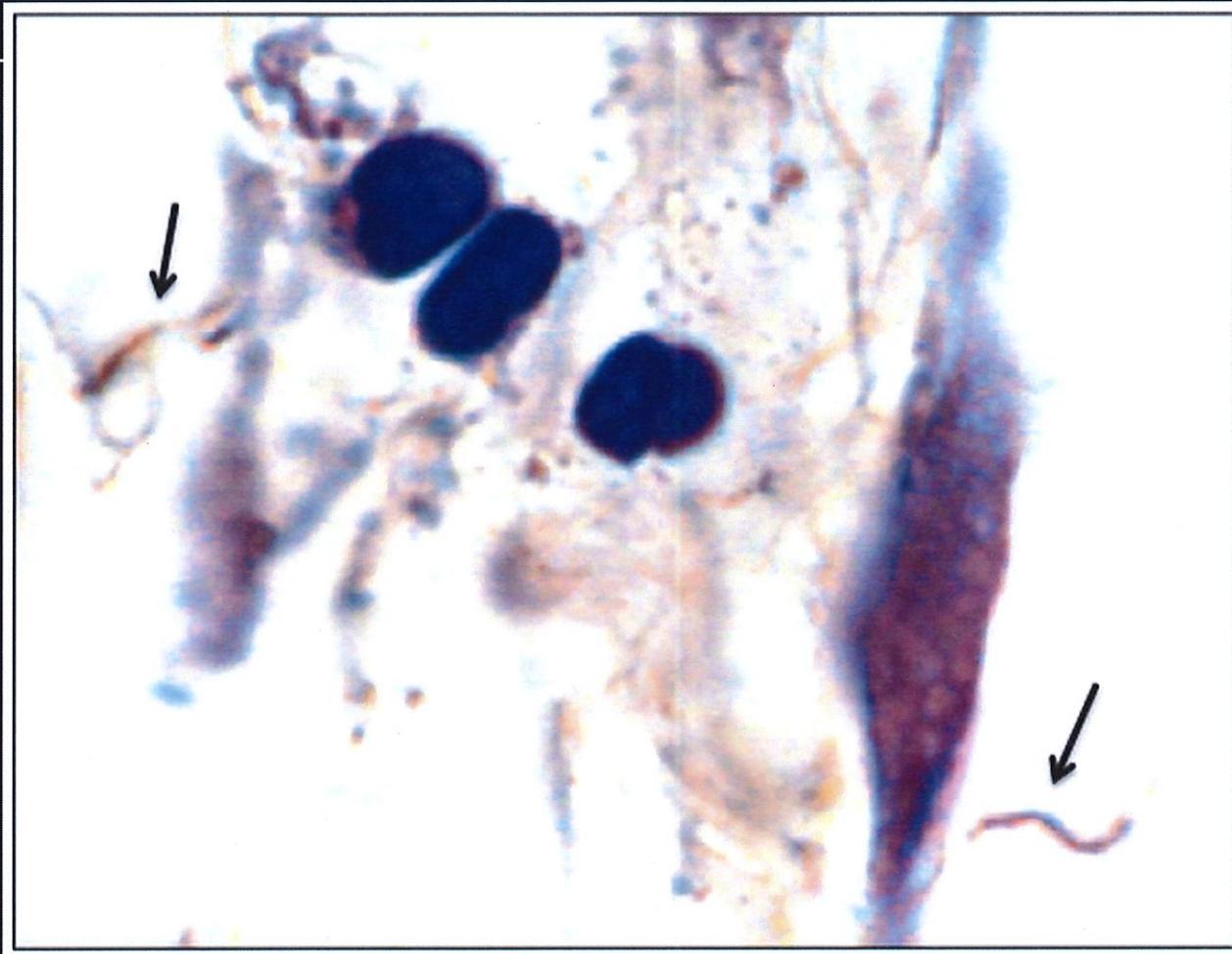


Often with minimal or  
No Disease



Slide courtesy of Stephen Barthold, UC Davis

## Spirochetes can be visualized within tissue of a mouse at 12 months following antibiotic treatment.



Hodzic E, Imai D, Feng S, Barthold SW (2014) Resurgence of Persisting Non-Cultivable *Borrelia burgdorferi* following Antibiotic Treatment in Mice. PLoS ONE 9(1): e86907. doi:10.1371/journal.pone.0086907

<http://www.plosone.org/article/info:doi/10.1371/journal.pone.0086907>



## Persistence of *B burgdorferi* in the Rhesus Macaque

Monica Embers, Tulane University

# The human xenodiagnostic study

(Marques et al, CID, 2014)

- Tick from 1 of 9 persons with previously treated Lyme Disease tested positive by PCR for DNA of the Lyme spirochete.

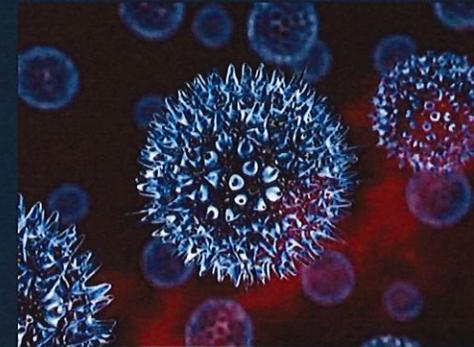


# Advances: Metagenomic Next Generation Sequencing enable rapid detection of All Microbes

**Bacteria**



**Viruses**



**Fungi**



**Parasites**



*Turn around time: hours to days (vs. days – weeks)*

*Allows one to cast a wide net to discover all microbes –  
not just a single fishing pole/guess to catch one microbe*

## Advances: Cell-based assays become negative after treatment – marker of cure?

- Assesses cytokine response to Lyme protein stimulation of human T-cells (or macrophages)



- In early Lyme Disease (EM) (Callister 2016):
  - 69% sensitivity
  - After treatment (2 months later) – 80% negative

# Advances in Diagnosis: Metabolomics-based assay

metabolic biosignature: sugars, peptides, lipids, nucleic acids

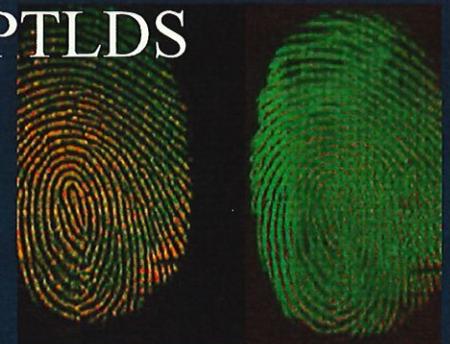


## Early Lyme vs Controls (Molins et al, 2015)

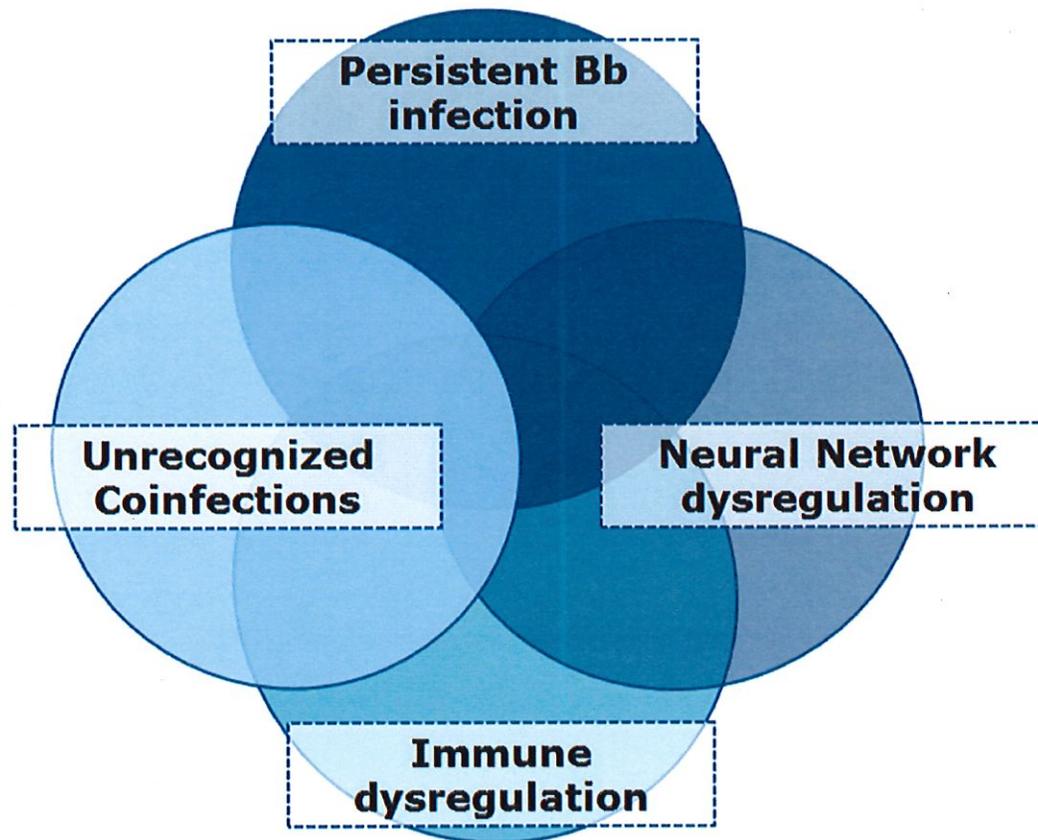
- **88% sensitive in early Lyme** (2x higher than 2-Tier assay)
- Differentiates Lyme from other diseases  
Correct differentiation 93% of Lyme from CFS & Fibromyalgia

Next: study Post-treatment Lyme disease using Metabolomics

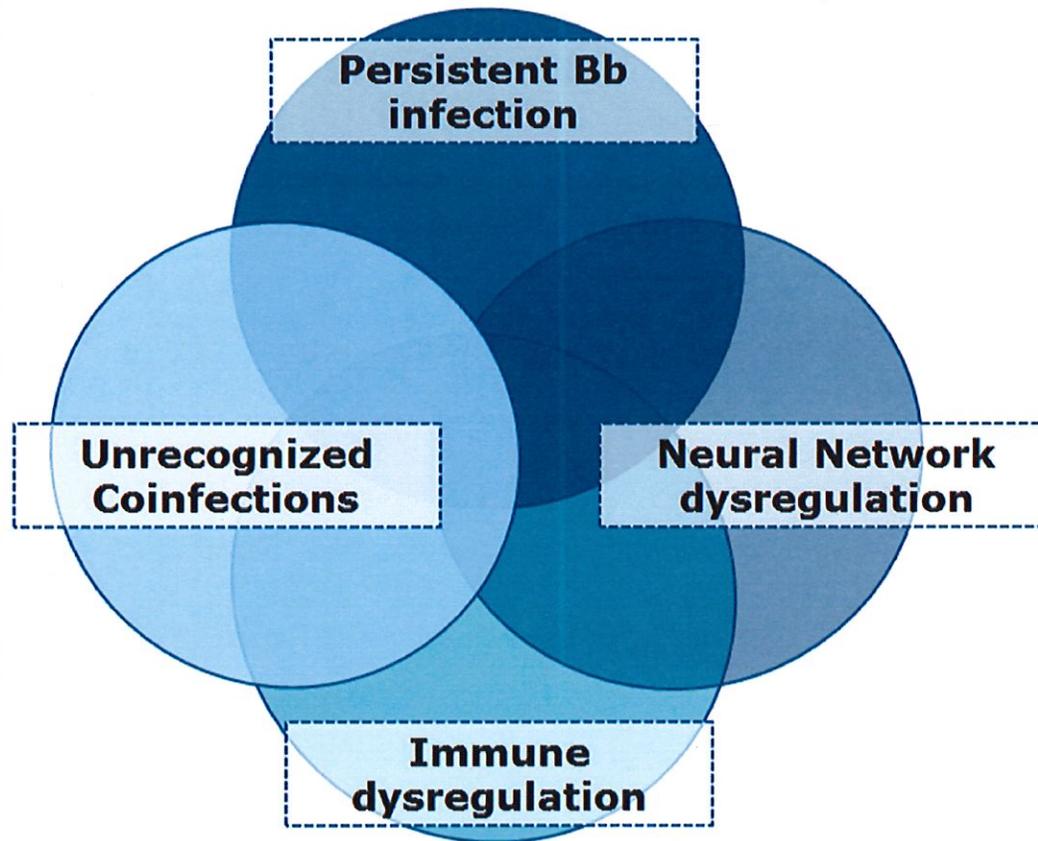
- To identify a biosignature of recovery and of PTLDS
- To suggest new treatments



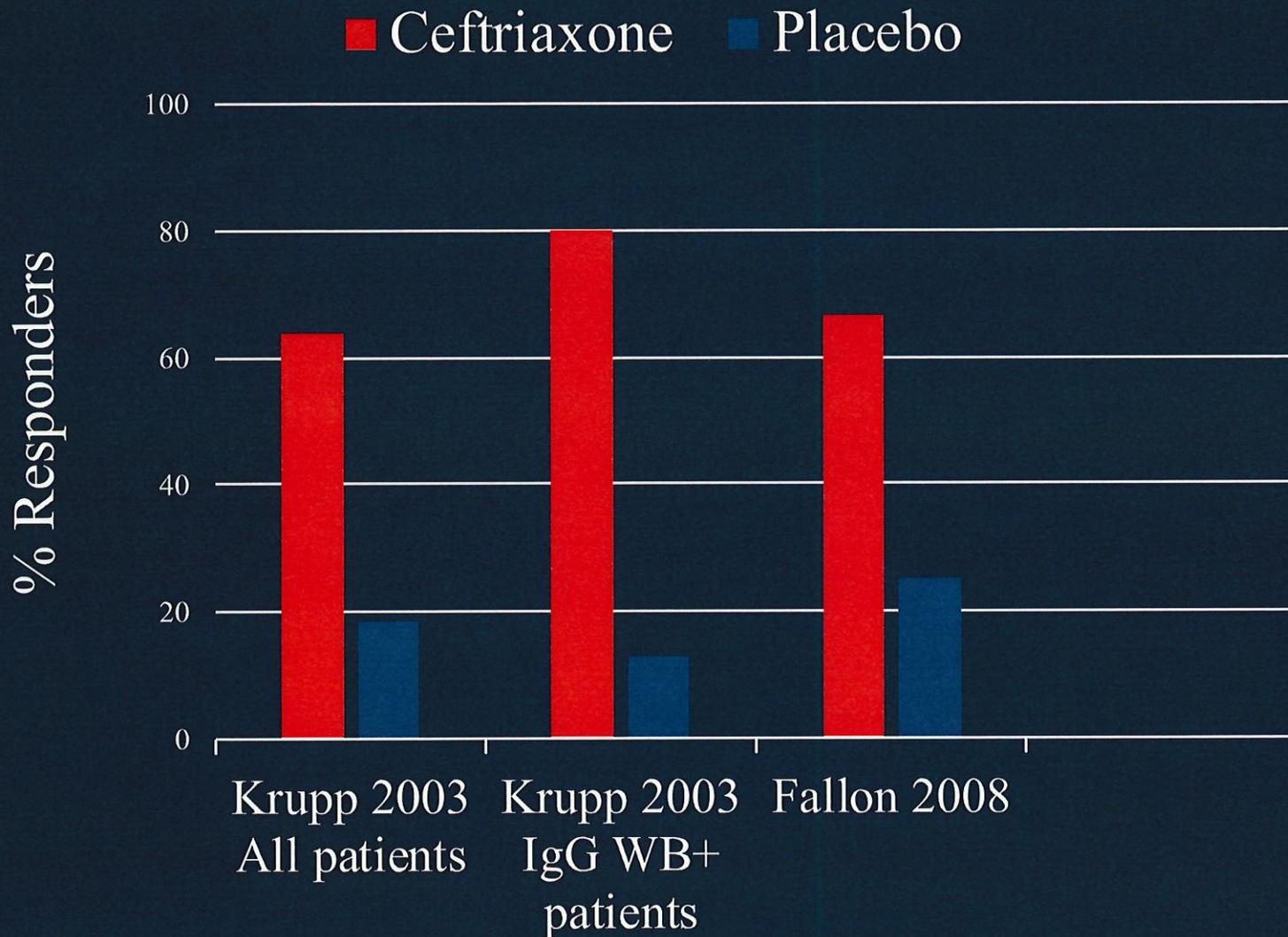
## Causes of Persistent symptoms under investigation



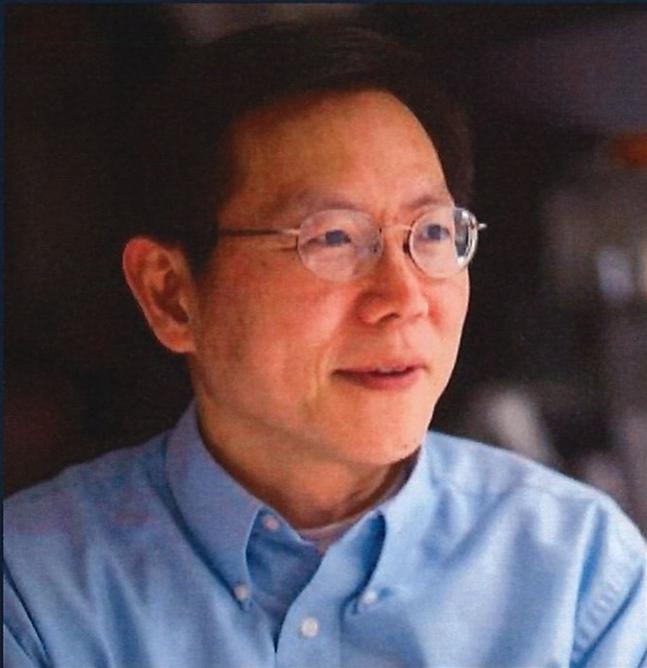
## Causes of Persistent symptoms under investigation



# Advance: repeated antibiotic therapy can help persistent fatigue. Columbia & Stonybrook NIH Studies



# Advance: Persister *Borrelia* require different approaches for eradication



Ying Zhang, MD (Hopkins)



Kim Lewis, PhD (Northeastern)

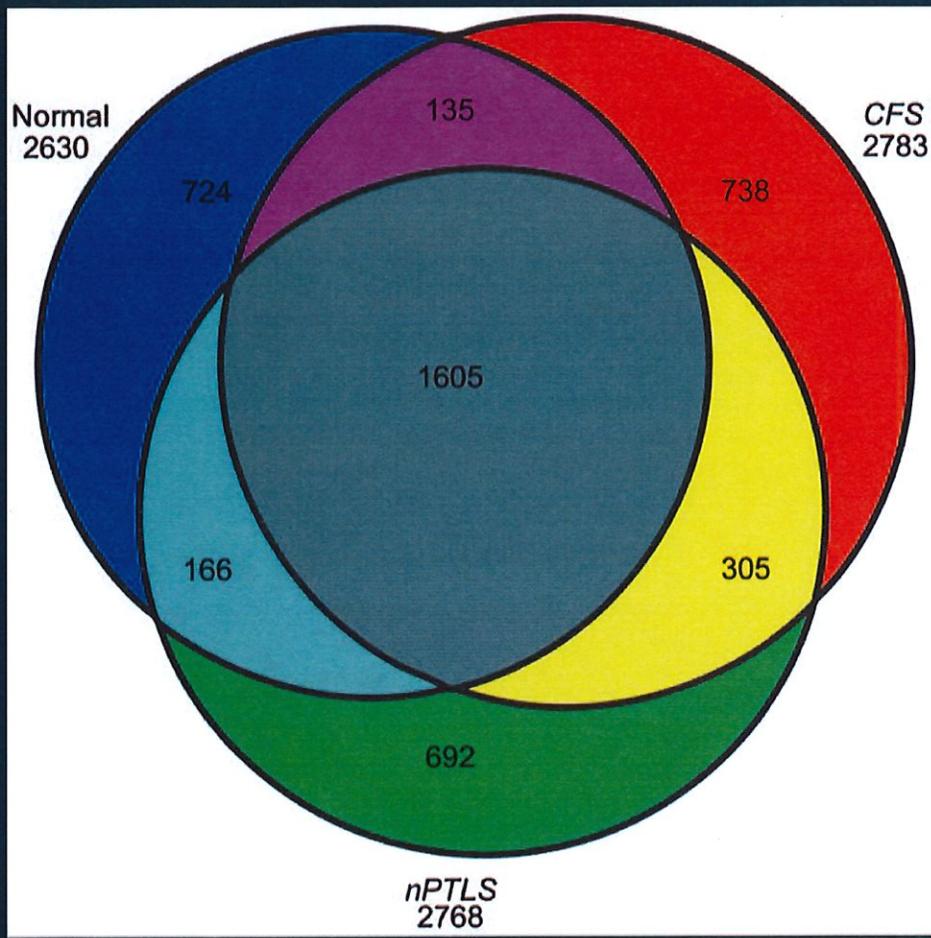
# Advance: ticks carry more than just the agent of Lyme disease

- *Borrelia miyamotoi*
- *Borrelia mayonii*
- *Babesia Microti*
- *Anaplasma phagocytophylum*
- *Ehrlichia*
- Powassan Virus

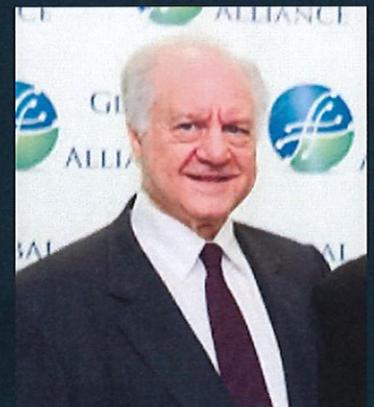


Rafal Tokarz

# Advance: Recognition that Lyme disease leads to an altered Cerebrospinal Fluid protein profile ( 692 unique proteins)

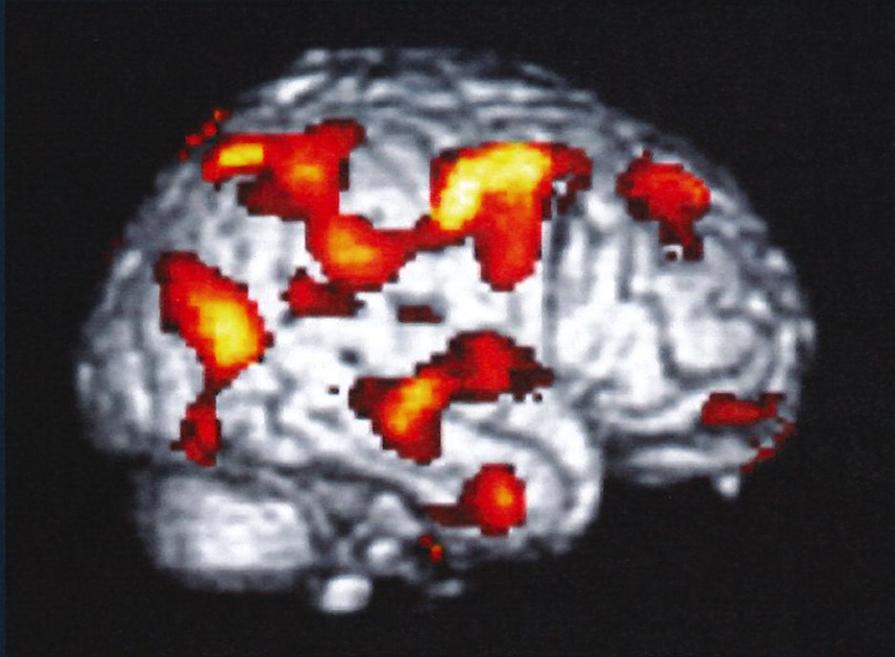


- This proteomic CSF profile differentiated post-treatment Lyme disease from Chronic Fatigue
- **Persistent symptoms are associated with an increase in immune proteins**

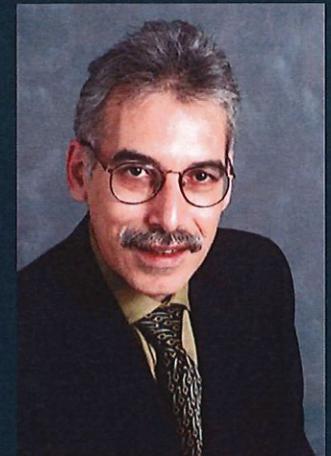
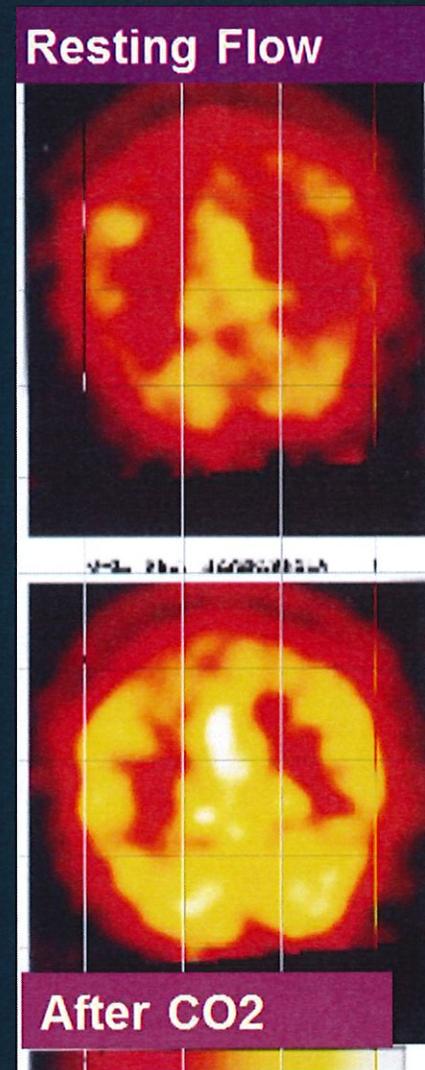


Advance: recognitions that patients with chronic Lyme symptoms have objective brain changes: altered brain metabolism & blood flow. (Columbia Imaging studies)

---



The patient group showed a diminished ability to enhance blood flow compared to controls (8.2% for patients vs 28.1% for controls,  $p < .02$ ) (Fallon et al, JAMA Psychiatry, 2009)



Harold Sackeim

# Current research: Do human post-mortem brains from LD harbor Lyme spirochetes?

## □ Columbia

- Andrew Dwork
- Gorazd Rosoklija
- Jim Goldman
- Brian Fallon



## □ Tulane:

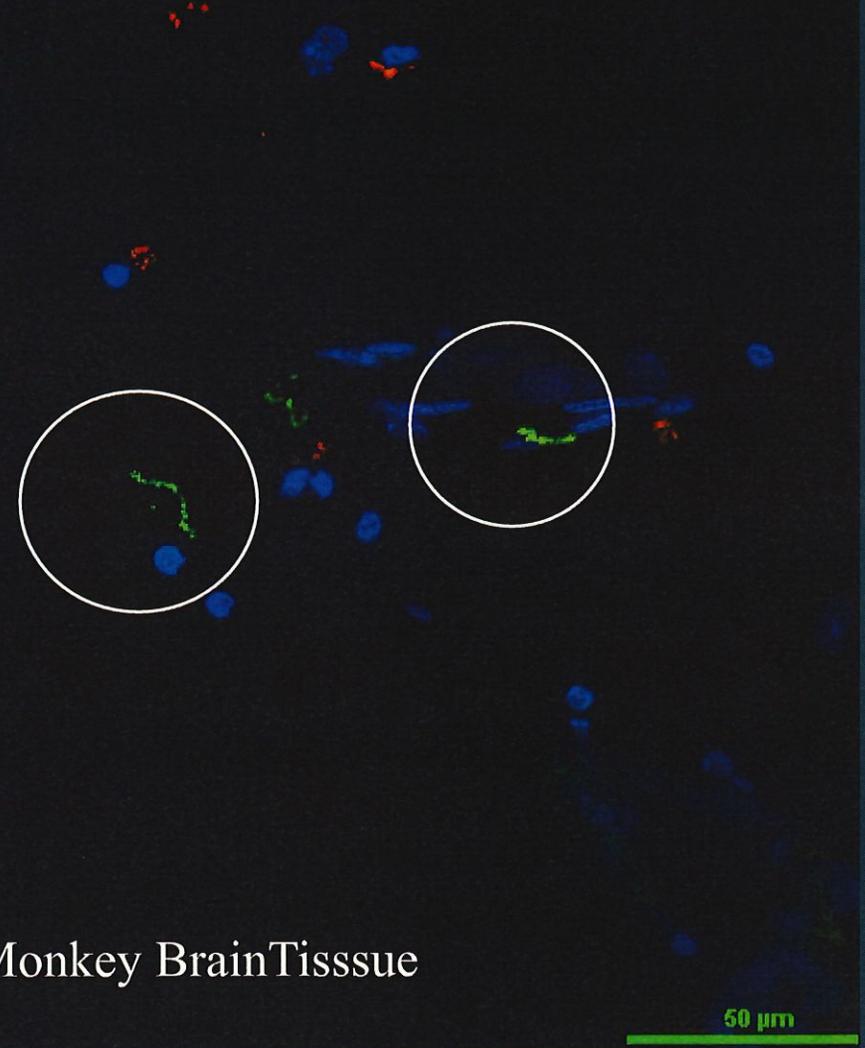
- Monica Embers

## □ Southern Research Institute/GLA

- Tim Sellati

## □ Collaborators

- Ken Liegner
- Judith Miklossy



Monkey Brain Tissue

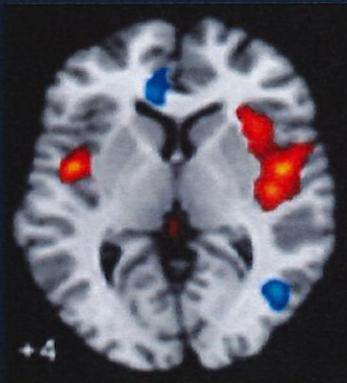
50 μm

# Current Research: Are the brain's neural circuits or chemistry altered?

A Columbia study of Post-treatment Lyme patients

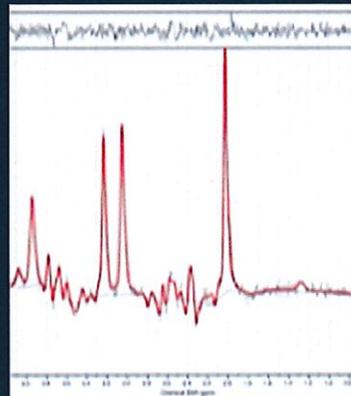
## Functional Magnetic Resonance Imaging

- Does the brain show central sensitization – hyperactivated pain circuits compared to healthy controls?



## Magnetic Resonance Spectroscopy

- Is the brain neurochemistry different from healthy controls?



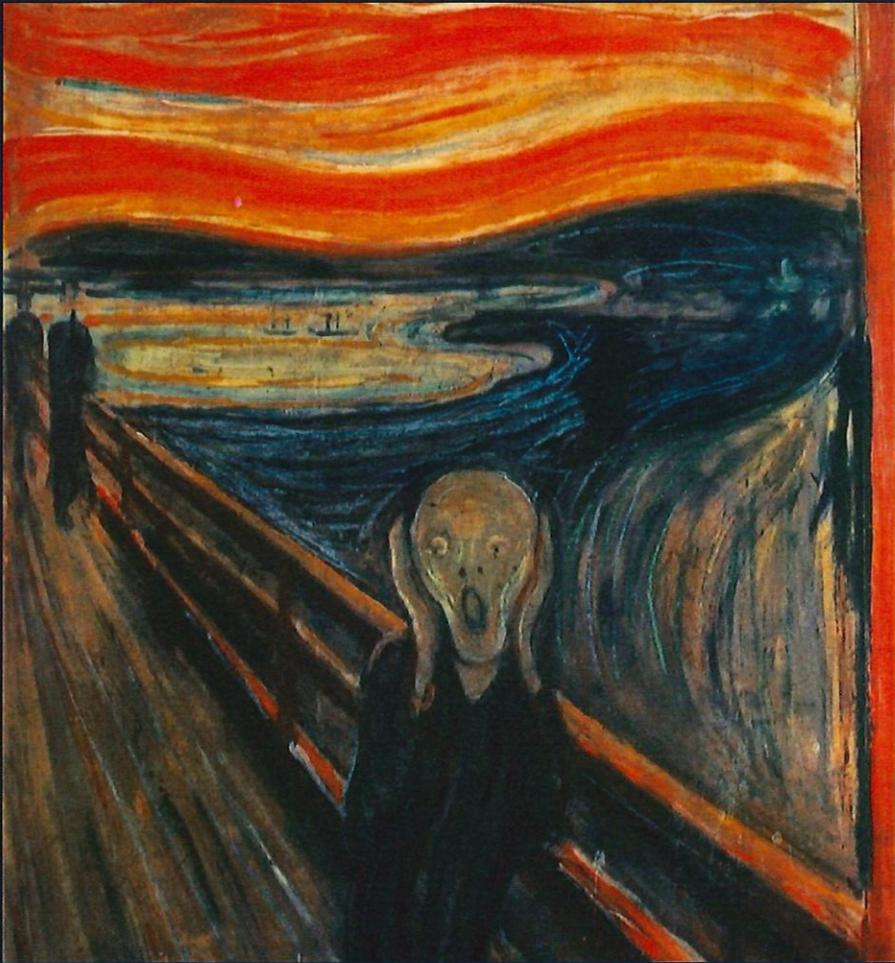
Alla Landa,  
PhD

# Prevention is key

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# What is the patient's experience?



Eduard Munch: Sensory Hyperarousal



William Blake: Job Being Accused"

# New Columbia Lyme Center Pediatric Research Outreach

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- Joining forces with Columbia Neurology
- Focus on infection-triggered and immune-triggered neuropsychiatric disorders



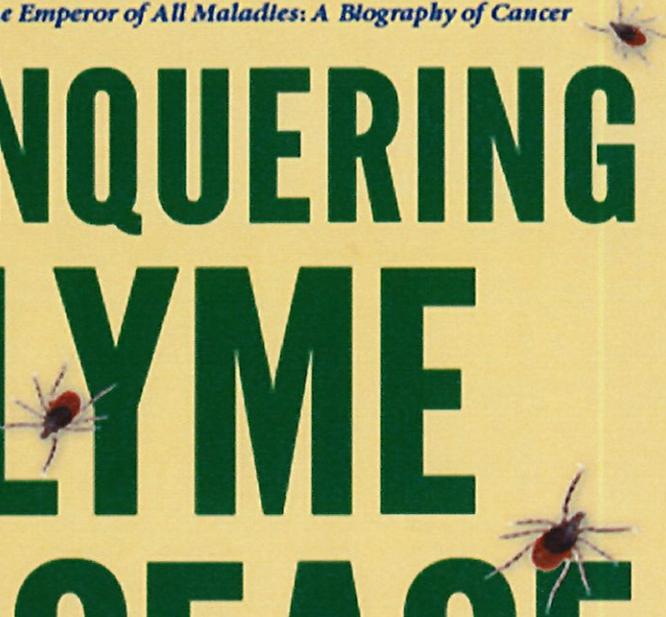
Shannon Delaney (Child Psychiatry), Wendy Vargas (Pediatric Neurology), Dritan Agalliu (Neurology, Pathology, Cell Biology)

So...is there reason for hope?  
Yes, Science is creating a bridge  
across the great Lyme Divide



"A lucid and important book, filled with moving case histories and vignettes,  
about an infectious illness that is threatening many lives."

—SIDDHARTHA MUKHERJEE,  
author of *The Emperor of All Maladies: A Biography of Cancer*



# CONQUERING LYME DISEASE

SCIENCE BRIDGES THE GREAT DIVIDE



**BRIAN A. FALLON, MD  
AND JENNIFER SOTSKY, MD**

With:

Carl Brenner

Carolyn Britton, MD

Marina Makous, MD

Jenifer Nields, MD

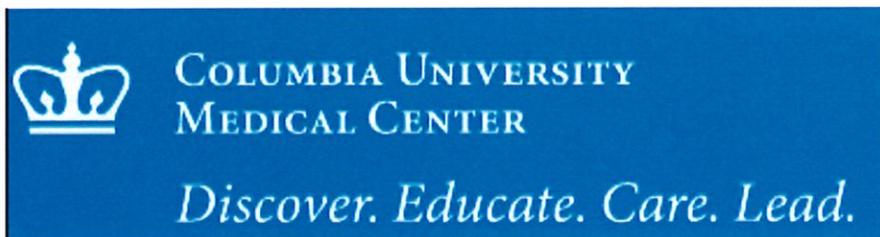
Barbara Strobino, PhD

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# Thank you from our team



**Columbia Lyme & Tick-Borne  
Diseases Research Center**

