



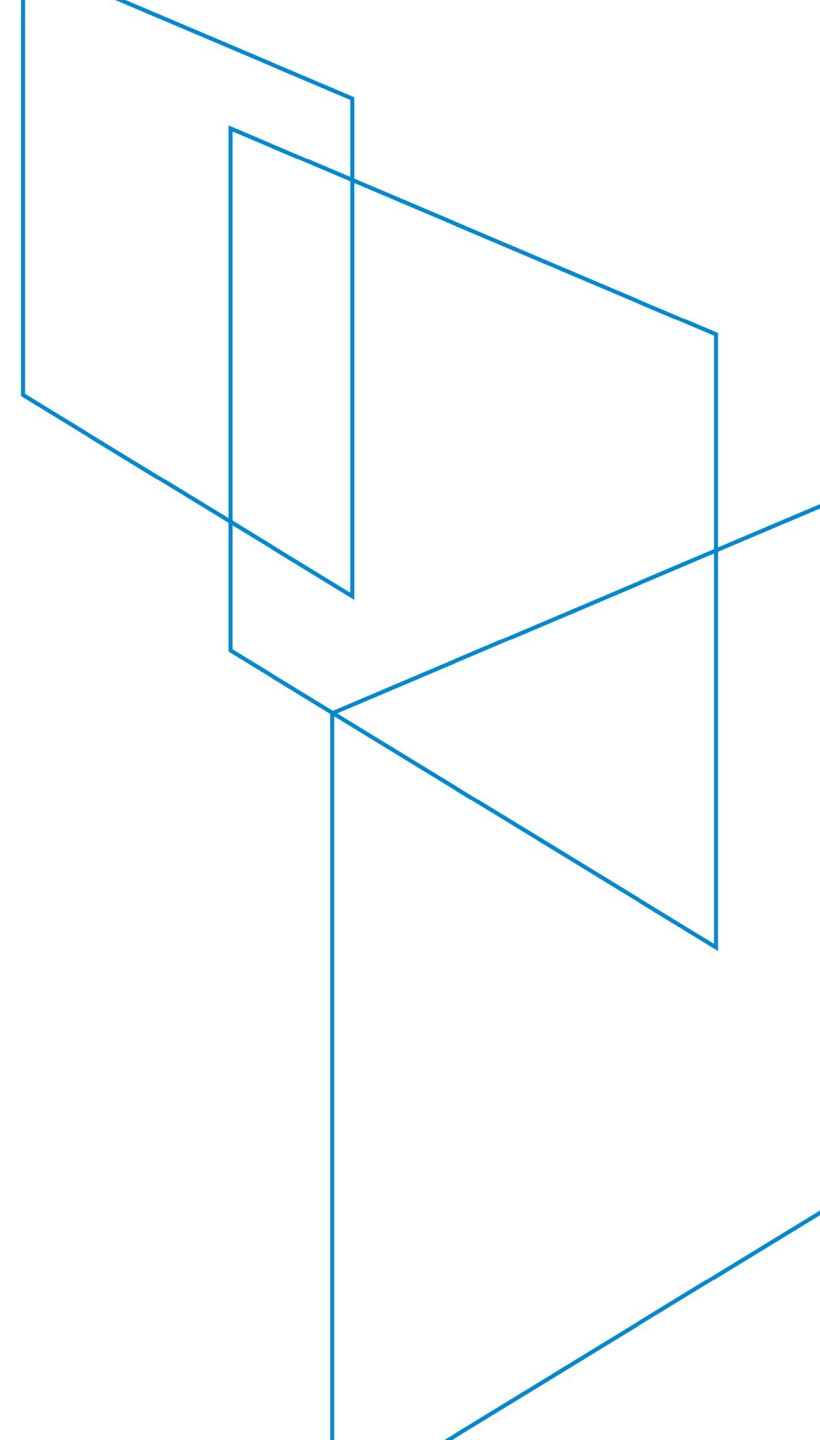
# Lupus: Dietary Factors and the Microbiome

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# Dietary Factors in Lupus

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# Disclosures

HSS educational activities are carried out in a manner that serves the educational component of our mission.

As faculty we are committed to providing transparency in any relevant external relationships prior to giving an academic presentation.

Dr. Medha Barbhैया: No relevant disclosures

# Questions we will examine

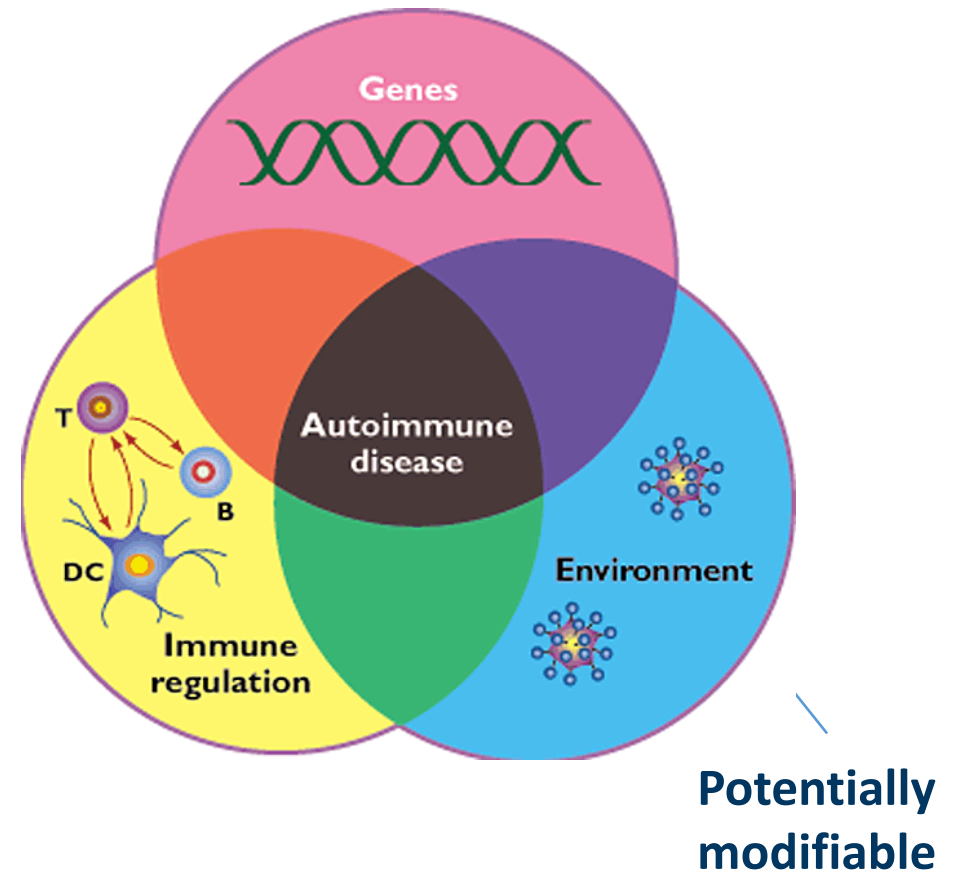
- Is diet associated with the risk of developing lupus?
- Can diet trigger, prevent or reduce lupus flares?
- How can we eat to optimize health when living with lupus?

# Why look at dietary factors in lupus?

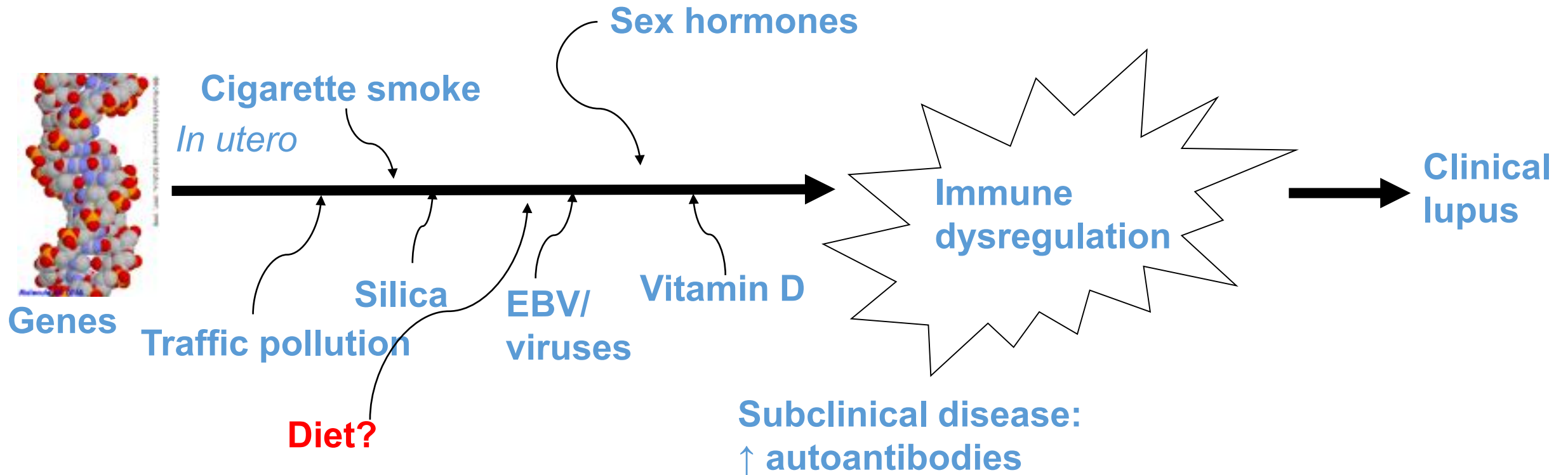
**Current thinking about lupus onset:**

## **The “Two-hit” hypothesis**

Environmental factors trigger disease in genetically predisposed individual



# Some known and possible environmental triggers



# Evidence regarding diet and disease

- Diet is known to affect risk of many chronic diseases: diabetes, cardiovascular disease, cancer
- Individual foods and nutrients have been associated with rheumatoid arthritis (RA) risk:

- **Lower RA risk:** dark meat fish, moderate alcohol consumption

- **Alcohol: 22% lower risk of RA** with moderate alcohol use
- **Fish: 24% lower RA risk** with 1 up to 3 servings per week of fish



- **Higher RA risk:** sugar-sweetened beverages (SSB)

- **63% increased risk for seropositive RA** with  $\geq 1$  serving/day of SSBs



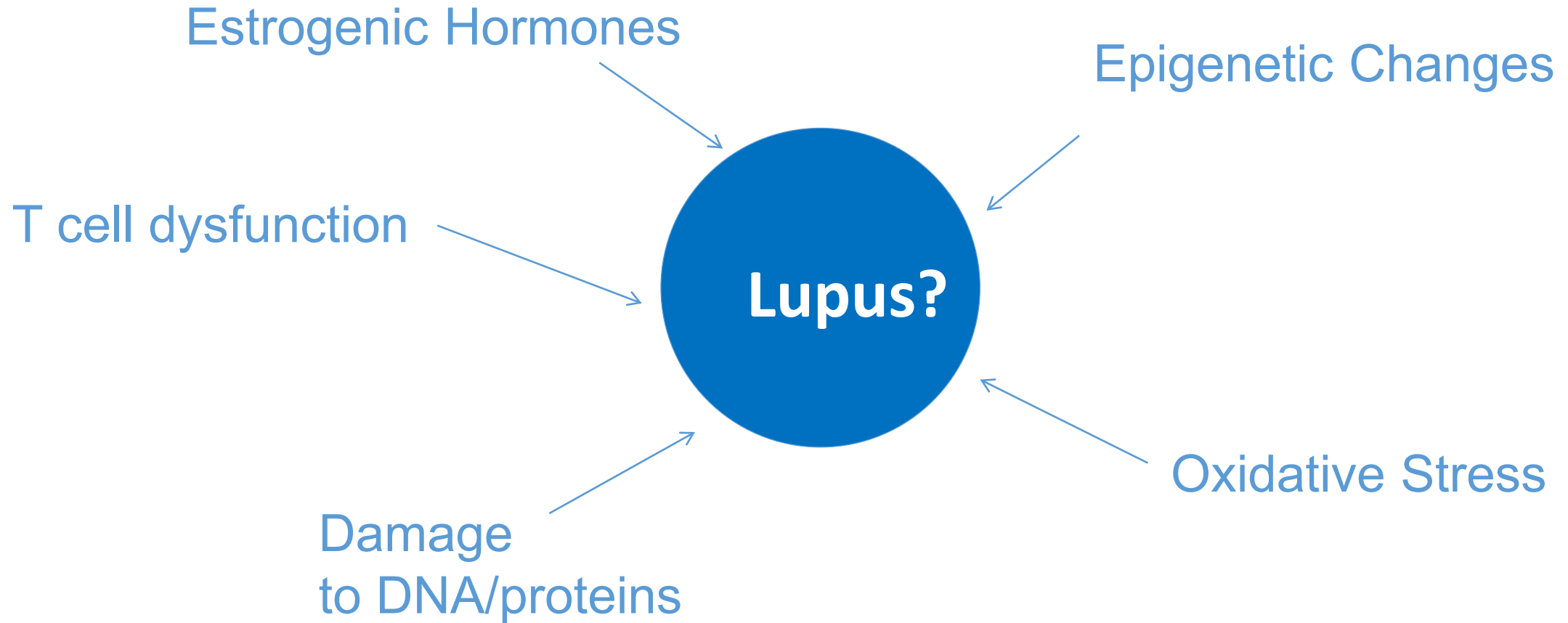
DiGiuseppe D, et al, *Arthritis Res Ther*, 2014

Lu B, et al, *Arthritis Rheumatol*, 2014

Benito-Garcia E, et al, *Arthritis Res Ther*, 2007

Hu Y, et al, *Am J Clin Nutr*, 2014

# How could diet affect lupus?





# Diet and lupus: some earlier findings

- No association found with intake of vitamin D or antioxidant vitamins

Costenbader KH et al. *Ann Rheum Dis*. 2008 Apr;67(4):530-5

Hiraki LT et al. *Arthritis Care Res (Hoboken)*. 2012 Dec;64(12):1829-36.

# Dietary factors and lupus onset: a new study

- >230,00 female nurses studied for onset of lupus for up to 29 years
- Health questionnaires every 2 years; food frequency questionnaires every 4 years
- Examined dietary patterns
  - Western dietary pattern
  - Prudent dietary pattern
- Looked at different scores of dietary quality
  - Alternative Healthy Eating Index (AHEI)
  - Alternative Mediterranean diet
  - Dietary Approaches to Stop Hypertension (DASH) diet
  - Empirical Dietary Inflammatory Pattern (EDIP)

Tedeschi SK, Barbhaiya M, et al. *Lupus*, 2019

Barbhaiya M, et al. *Arthritis Care & Research* 2020

# Conclusions of study of dietary scores/patterns

- No association between long-term adherence to four different dietary quality scores/indices and incident lupus
  - Analyses stratified by dsDNA+ and dsDNA-, revealed no differences

Tedeschi SK, Barbhaiya M, et al. *Lupus*, 2019

Barbhaiya M, et al. *Arthritis Care & Research* 2020

# Analysis of some individual foods in the AHEI

- **Nuts/Legumes:**

- Highest tertile of consumption (vs. lowest): **beneficial**

- **Polyunsaturated Fatty Acids:**

- Highest tertile of consumption (vs. lowest): **no benefit or harm**

- **Fish/Omega-3 Fatty Acids:**

- Highest tertile of consumption (vs. lowest): **no benefit or harm**

# What about alcohol?

- Moderate alcohol consumption

- Associated with reduced CVD and RA risks
- Previously unclear association with lupus

- Alcohol components (e.g., ethanol and antioxidants)

- Potentially counteract systemic inflammation

- Protective effect of long-term moderate alcohol consumption on lupus risk

- Large, longitudinal study of women

- Bear in mind

- American Cancer Society recently reversed its recommendations on alcohol intake



# Dietary factors and lupus flares: Omega-3 (fish oil) supplementation

- Double blind, placebo controlled trial, 24 weeks, 52 patients:
  - Significant improvement in lupus disease activity with omega-3 supplementation compared to placebo
- Double blind, placebo controlled trial, 24 weeks, 63 patients:
  - Significant improvement in lupus disease activity and endothelial function with low-dose omega 3 supplementation
- Randomized, placebo-controlled trial, 24 weeks, 32 patients:
  - Significant improvement in physician's assessment, quality of life, and circulating inflammatory markers
- Randomized, double-blind placebo-controlled trial, 12 weeks, 85 patients:
  - No significant association with lupus disease activity, endothelial function or inflammatory markers

Duffy et al, [\*J Rheumatol.\*](#) 2004

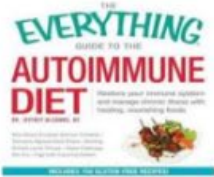
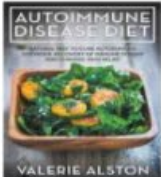

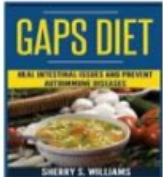
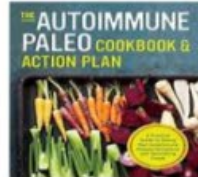
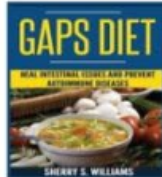


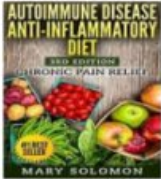
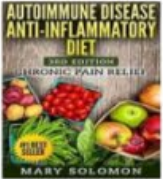
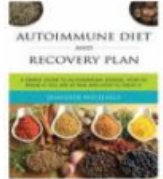
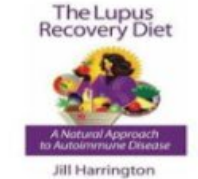
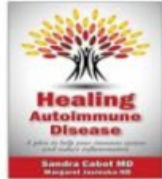

Wright SA, [\*Ann Rheum Dis.\*](#) 2008

Arriens C et al, [\*Nutr J.\*](#) 2015

Bello KJ, [\*Rheumatol Int.\*](#) 2013.

# Managing your diet with lupus

- Beware of misinformation
- Dietary changes that you make should not delay necessary treatment

 <p><b>THE EVERYTHING</b> GUIDE TO THE <b>AUTOIMMUNE</b> <b>DIET</b></p>	 <p><b>AUTOIMMUNE</b> <b>DISEASE DIET</b></p>	 <p><b>ANTI INFLAMMATORY DIET</b> <b>AUTOIMMUNE</b> <b>DINNER</b> <b>RECIPES</b></p>	 <p><b>GAPS DIET</b></p>	 <p><b>THE AUTOIMMUNE</b> <b>PALEO COOKBOOK &amp;</b> <b>ACTION PLAN</b></p>	 <p><b>GAPS DIET</b></p>	 <p><b>THE EVERYTHING</b> GUIDE TO THE <b>AUTOIMMUNE</b> <b>DIET</b></p>
<p><b>\$10.00</b> The Everything Guide To The Autoimmune Diet: Restore Your AbeBooks.com</p>	<p><b>\$5.92</b> Autoimmune Disease Diet: Natural Way To Cure Autoimmune Barnes &amp; Noble.com</p>	<p><b>\$10.99</b> Anti Inflammatory Diet: Autoimmune Dinner Recipes: 30+ Barnes &amp; Noble.com</p>	<p><b>\$29.80</b> GAPS Diet : Heal Intestinal Issues And Prevent Autoimmune Diseases Thriftbooks.com</p>	<p><b>\$11.88</b> Autoimmune Paleo Cookbook Action Plan: A Practical Guide To AbeBooks.com</p>	<p><b>\$28.45</b> GAPS Diet: Heal Intestinal Issues And Prevent Autoimmune Diseases AbeBooks.com</p>	<p><b>\$18.01</b> <del>\$18.99</del> The Everything Guide To The Autoimmune Diet: Restore Your Barnes &amp; Noble.com</p>
 <p><b>CURE</b> <b>AUTOIMMUNE</b> <b>DISEASE</b></p>	 <p><b>AUTOIMMUNE DISEASE</b> <b>ANTI-INFLAMMATORY</b> <b>DIET</b></p>	 <p><b>AUTOIMMUNE DISEASE</b> <b>ANTI-INFLAMMATORY</b> <b>DIET</b></p>	 <p><b>AUTOIMMUNE DIET</b> AND <b>RECOVERY PLAN</b></p>	 <p><b>The Lupus</b> <b>Recovery Diet</b></p>	 <p><b>Healing</b> <b>Autoimmune</b> <b>Disease</b></p>	 <p><b>THE IMMUNE SYSTEM</b> <b>RECOVERY PLAN</b></p>
<p><b>\$12.99</b> Cure Autoimmune Disease Cook Book For Beginners: The Life Barnes &amp; Noble.com</p>	<p><b>\$15.37</b> Autoimmune Disease Anti-Inflammatory Diet : Simple Steps Thriftbooks.com</p>	<p><b>\$16.05</b> Autoimmune Disease Anti-Inflammatory Diet: Simple Steps To AbeBooks.com</p>	<p><b>\$2.99</b> AUTOIMMUNE DIET AND RECOVERY PLAN: A Simple VitalSource</p>	<p><b>\$10.95</b> Lupus Recovery Diet A Natural Approach To Autoimmune Disease AbeBooks.com</p>	<p><b>\$15.57</b> Healing Autoimmune Disease: A Plan To Help Your Immune System Thinking</p>	<p><b>\$23.62</b> The Immune System Recovery Plan: A Doctor's 4-Step Program Audible.com</p>

# Managing your diet with lupus

- Look at your whole health picture
  - Your own nutritional deficiencies as determined by your doctor, e.g., Vitamin D, vitamin B12, iron, others
  - Your medications
    - Steroids can contribute to diabetes and osteoporosis
  - Your life stage, e.g., childbearing, post-menopausal
  - Your level of physical activity
  - Your smoking status



# Managing your diet with lupus

- Consider your risk for common comorbidities of lupus
  - Cardiovascular disease (CVD), high blood pressure, kidney disease, type II diabetes, osteoporosis
- Know the mortality risks for people with lupus
  - Most common cause of mortality among lupus patients is CVD

# Eat to optimize your overall health, including comorbidities

- Within your own food culture, preferences, food sensitivities and budget:
  - Emphasize:
    - Fruits and vegetables
    - Whole grains
    - Legumes and nuts
    - Seafood and lean meat and poultry
    - Unsaturated vegetable oils
    - Low- or non-fat dairy
  - De-emphasize:
    - Red and processed meats (deli meats, bacon)
    - Sugar sweetened beverages and foods with added sugar
    - Saturated (solid) fats
    - Refined grains
    - High sodium foods

Thank You



**Rheumatology Research Foundation**

Advancing Treatment | Finding Cures

# Lupus and the Microbiome

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Roberts Center for Inflammatory Bowel Disease/ Roberts Institute for IBD Research

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Dr. Randy Longman: Consultant, Pfizer, Bristol Meyers Squibb, In vitro, SAB, Ancilia

The New York Times Magazine

May 18, 2014

THE HIGH COST  
OF GETTING  
FILTHY RICH

BY ANITA KAGAN

WHY BASKETBALL  
WON'T LEAVE PHIL  
JACKSON ALONE

BY SAM ANDERSON

THE  
SECRET  
LIVES  
OF

# Germ

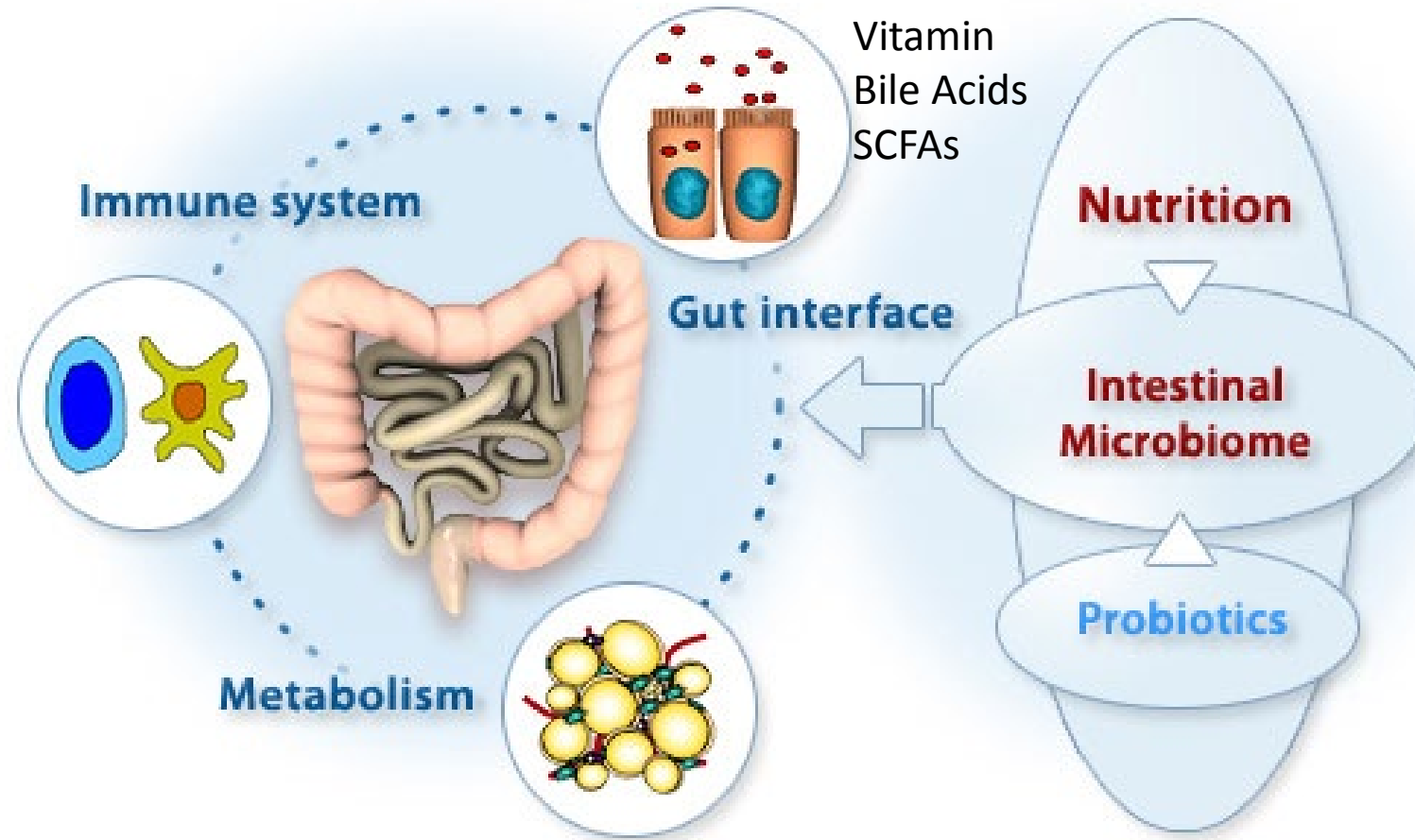
WHAT WE CAN LEARN FROM OUR MICROBIOME. BY MICHAEL POLLAN



# Defining the Microbiome

- The population of **symbiotic**, **commensal** and **pathogenic** microorganisms that live in and on the human body
  - **Symbiotic** => organisms that live in close, interdependent and cooperative relationship
  - **Commensal** => an organism that obtains food or benefit from a host without benefitting or harming the host
  - **Pathogenic** => disease-causing
- Found on the skin and in the mouth, gut and vagina

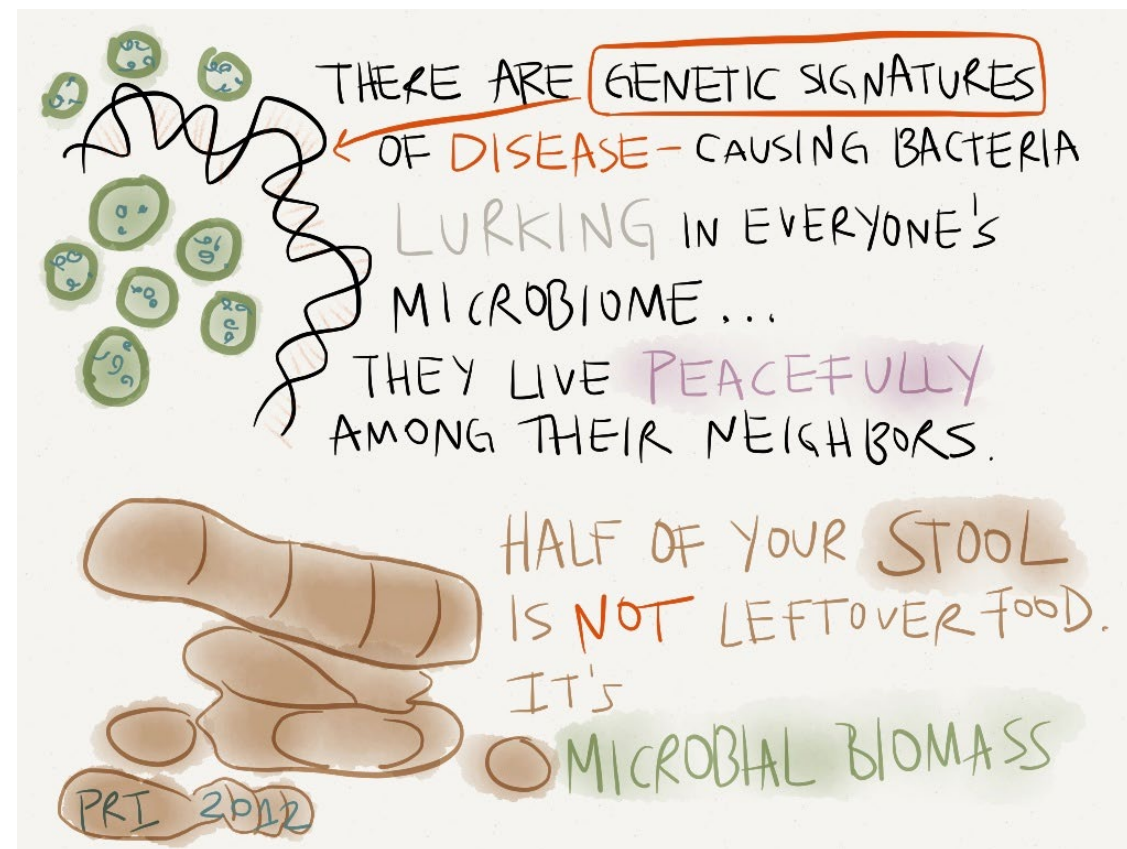
# Importance of microbiome in digestion & immunity





# Microbiome plays a big role in health & disease

- **In health:** the microbiome plays a key role in gut mucosal protection, nutrient extraction, and metabolism of foreign substances such as drugs
- Diet is a key regulator of microbiome variability and change
- **In disease:** critical changes in the microbiome correlate with lupus, RA, IBD, and obesity in genetically susceptible people
- Interactions of viruses, fungi and parasites with the microbiome can alter its effects on immunity

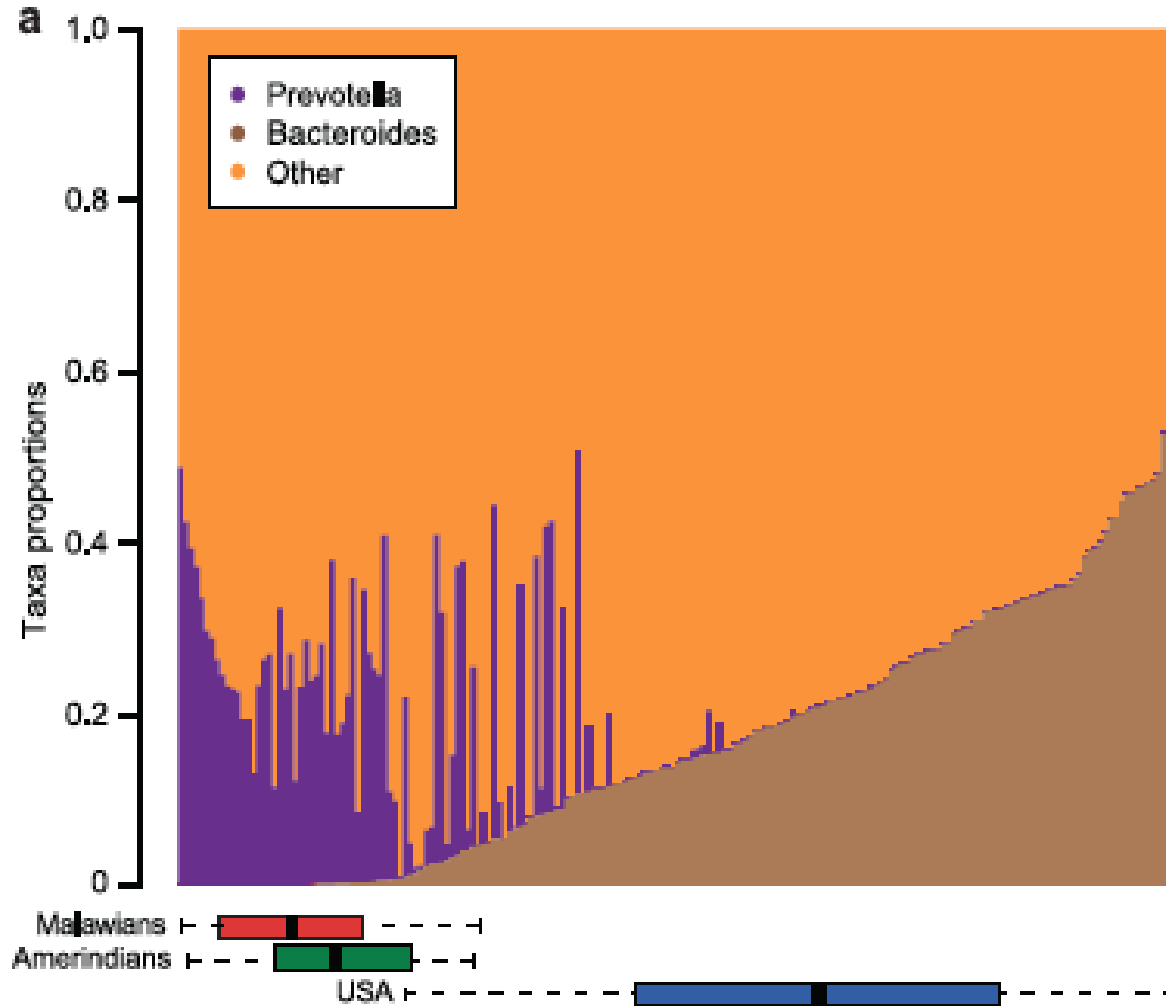


# The microbiome is bigger than us



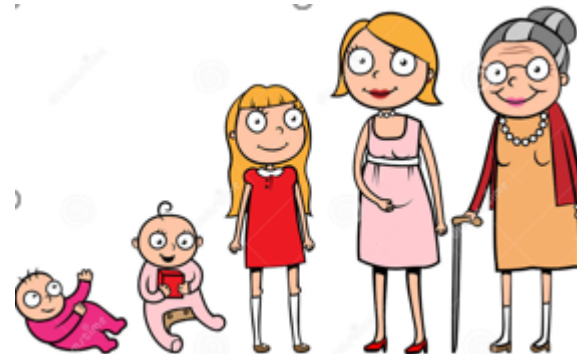
- Intestinal bacteria outnumber our human cells by 10 to 1
- The genomic material of these bacteria contains more than 300 times the number of genes in the human genome
- Common genes: secondary metabolism of carbohydrates and sugars

# Culture/Geographic Region Affects Microbiome



# Microbiome behaves differently across lifespan

- Differences in vitamin metabolism between babies and adults
- Folate made by both plants and microbes
- Babies' gut microbes are more plentiful for genes that engage in the production of folate
- Adults' gut microbes have more genes that metabolize dietary folate
- **=>Consider the microbiota when looking at nutritional needs across the lifespan**

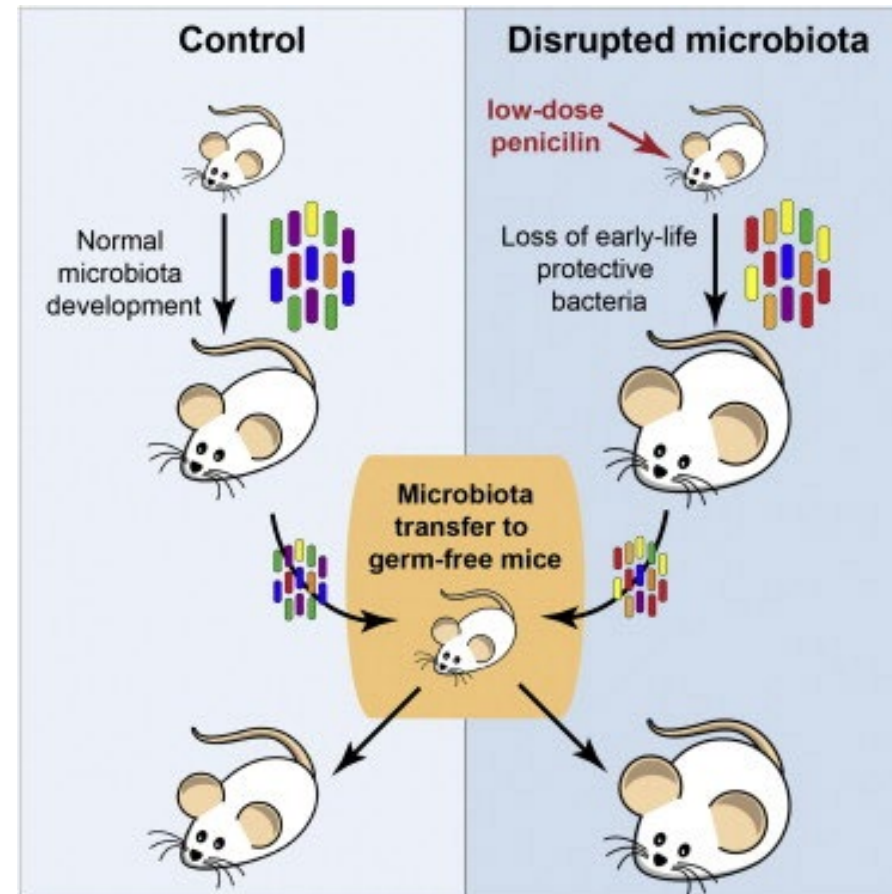


# Diet affects composition of the microbiome

- Changing one's diet can cause big changes in composition in the microbiota and relatively quickly => animal-based diet vs plant-based
- The gut community responds to what it is fed.
  - A diet high in animal products reduces the abundance of bacteria that are normally present in a diet that is high in fiber
  - Animal-based diet encourages gut bacteria that can withstand the bile acids that are more abundantly secreted to break down high dietary fat
  - Microbial metabolic activity and gene expression change with diet



# Microbiome has lasting effects on metabolism

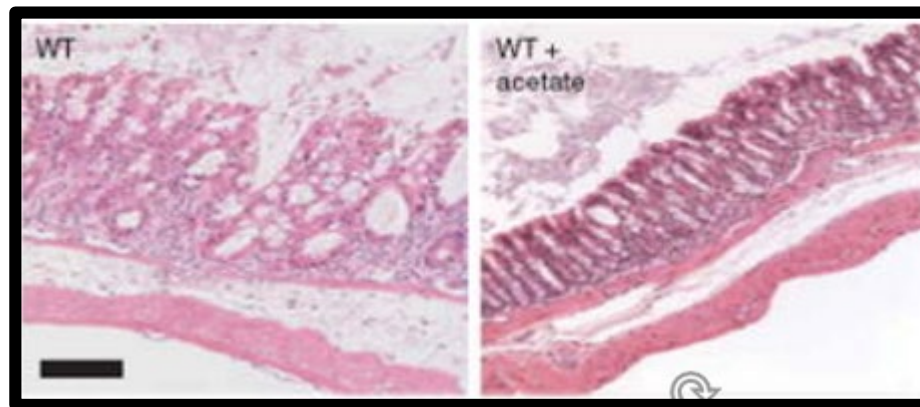


# Microbiome and Inflammatory Disease



# Short chain fatty acids (SCFA) regulate immunity

- Gut microbes help protect against inflammatory disease
- A diet high in fermentable dietary fiber (e.g., beans and legumes) feeds certain gut bacteria which ferment the fiber to produce SCFA
- SCFA help regulate immune response and reduce inflammation, thus protecting the walls of the intestines and maintaining the gut barrier

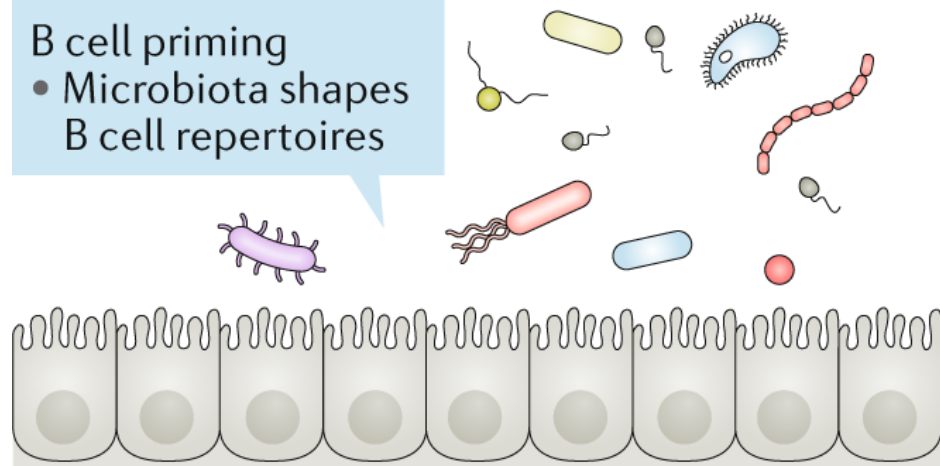




# The microbiome in lupus

## Health

B cell priming  
• Microbiota shapes B cell repertoires



Microbial translocation

Translocation to liver  
• Activation of AhR system  
• IFN-related gene expression

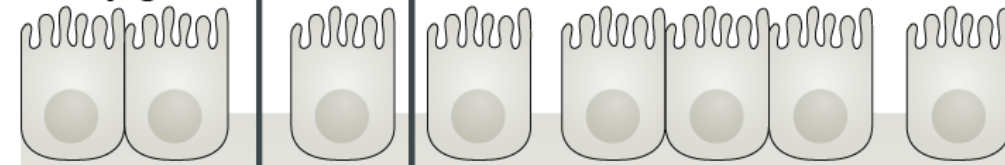
- $T_H$  17 cell responses
- Autoantibody production

## SLE

Restricted gut microbiota diversity

*E. gallinarum*

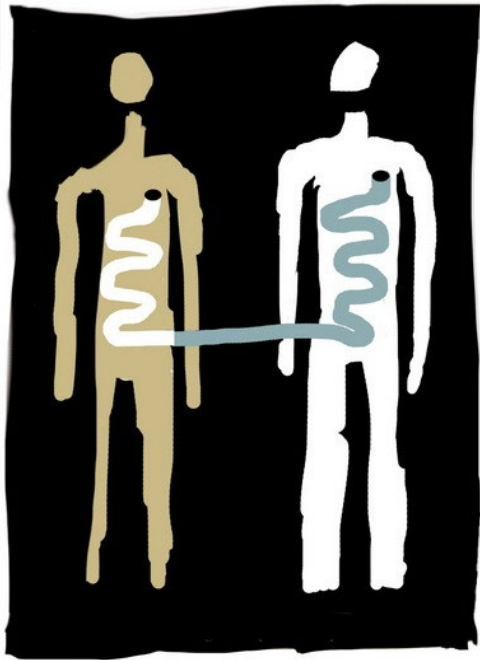
Leaky gut



Adaptive responses

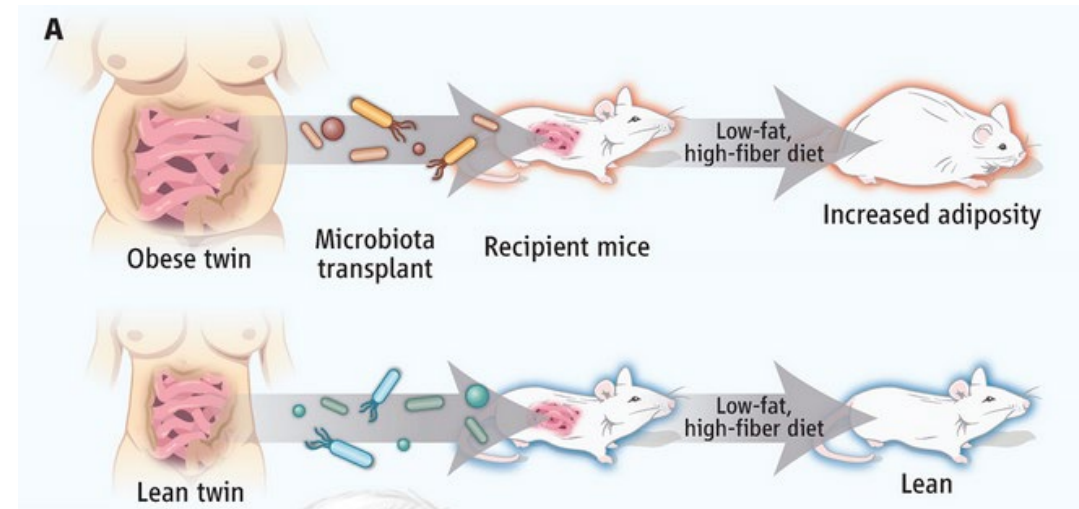
Cross-reactivity of B cell and T cell responses with bacterial orthologues and autoantigens

# Microbiome as therapy: fecal microbiota transfer (FMT)



Andrea Levy, The Plain Dealer

- The process of transferring fecal bacteria from a healthy donor to a recipient
- Ancient Chinese medicine
- 1958 used experimentally for colitis
- FMT is highly effective for the treatment of recurrent *C. difficile* colitis
- Efficacy in patients with IBD remains under investigation
- FDA classifies as an Investigational New Drug (IND)



Ridaura et al Science 2013

# Future implications for microbiome science

- Specific diets to reduce genetically or metabolically predisposed risk
- Diets to enhance/promote therapeutic efficacy of medicines
- Fecal transplant to modulate the microbiome, disease susceptibility and metabolic function
- Improved diagnostics for more precise dietary intervention.