National Institutes of Health
Office of Dietary Supplements

Diet, Microbiome and Health

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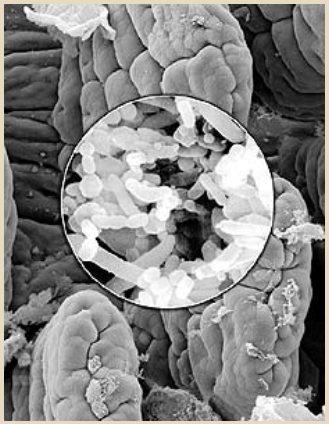
Outline

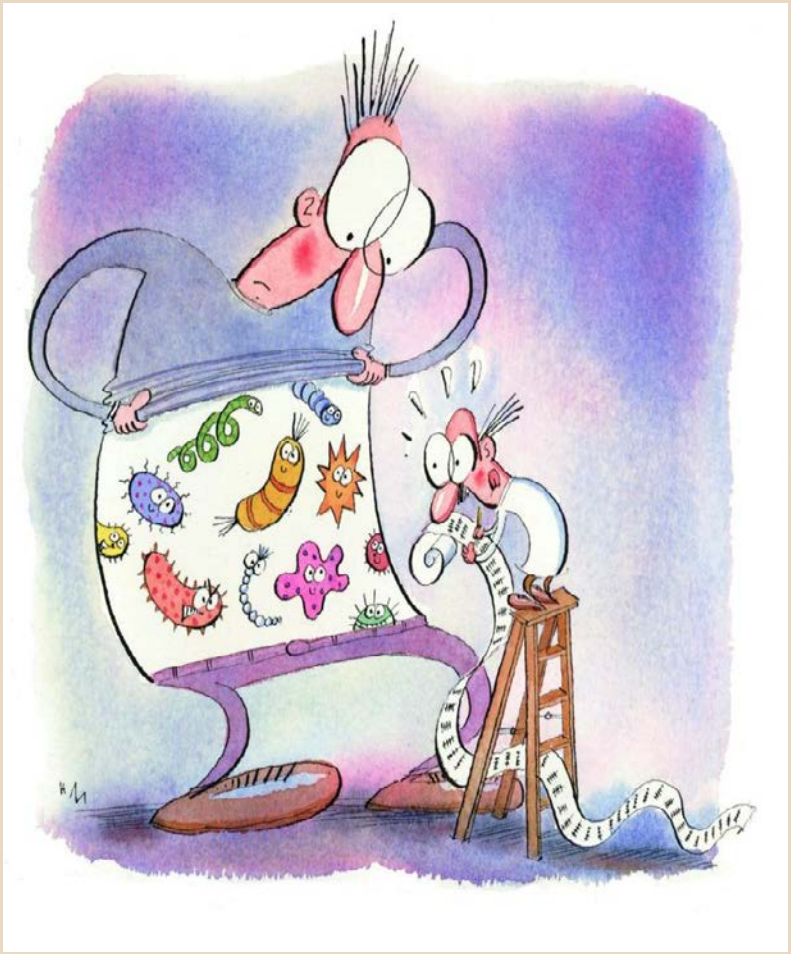
1. What is the microbiome?
2. How does it vary over the lifespan?
3. What is the evidence that diet can influence the microbiome?
4. How can the microbiome influence the response to dietary components?
5. What is the relationship between diet, the microbiome and disease risk?

The Human Microbiome

- We are a composite of species: human, bacterial, viral- up to 10x more microbial cells than human
- Gut Microbiota= microbes in our GI tract, ~100 trillion organisms
- Microbiome= their collective genome, >100 times as many genes as human genome

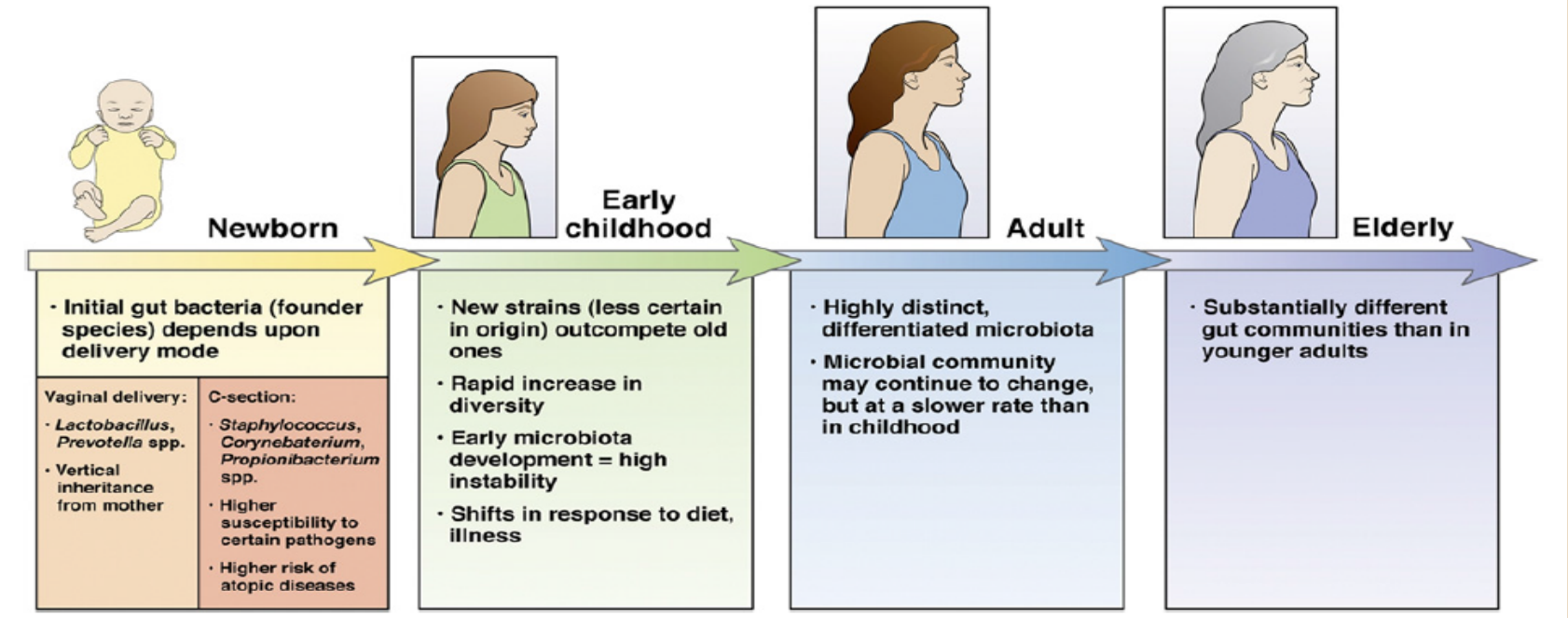


What Do Microbes Do For Us?



- Provide ability to harvest nutrients
- Produce additional energy otherwise inaccessible to the host
- Produce vitamins
- Metabolize carcinogens
- Prevent colonization by pathogens
- Assist in the development of a mature immune system

Human Intestinal Microbiota over the Lifespan

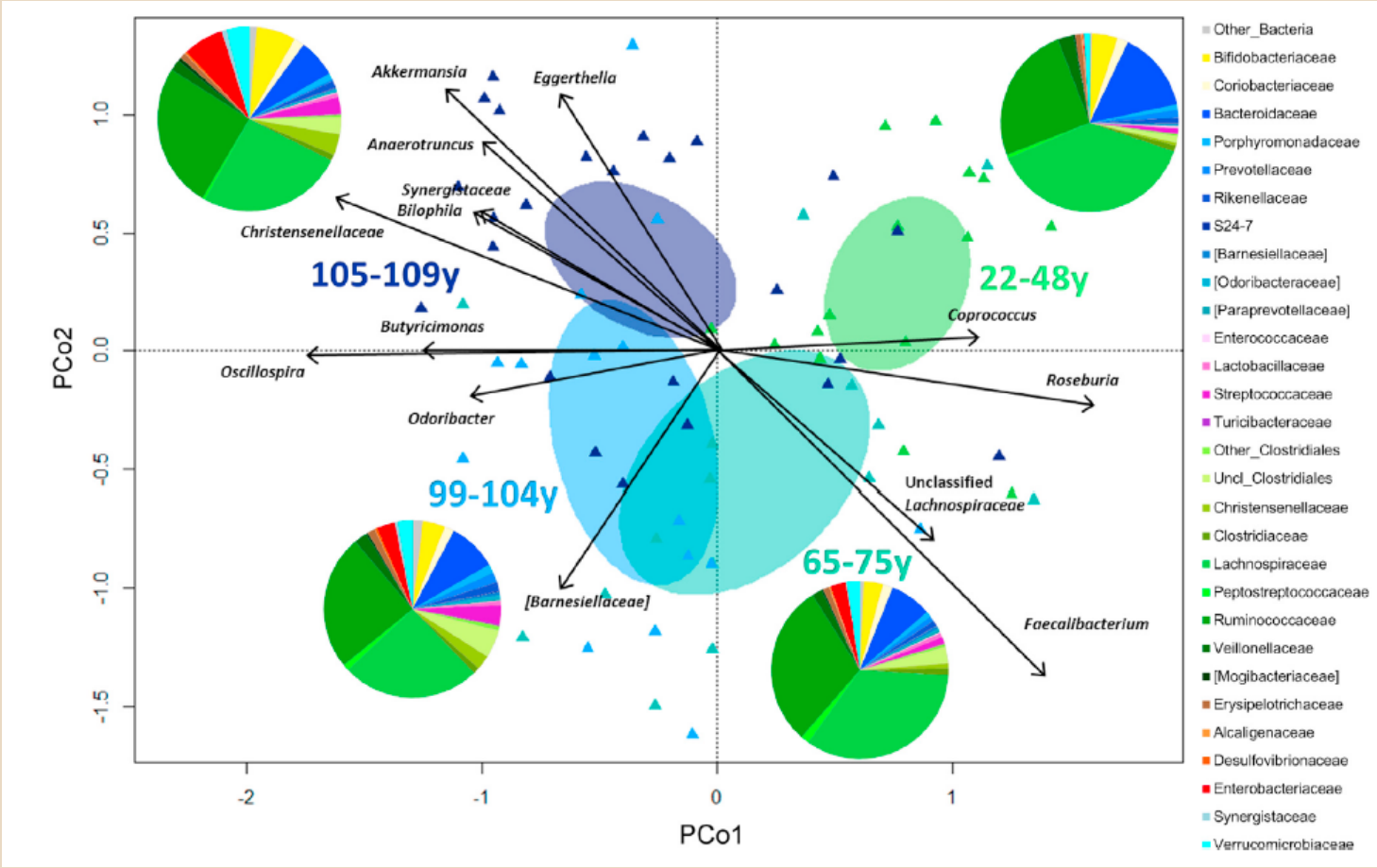


Dominguez-Bello M.G. et al. Gastroenterology 14: 1713-1719, 2011

Kostic et al. Genes and Development 27:701-718, 2013

Gut Microbiota and Extreme Longevity

Longevity is associated with enrichment of subdominant taxa that appear to be associated with health- *Akkermansia, Bifidobacterium* and *Christenseneliaceae* (n=24 for 105-109 years and n=15 for other age groups)



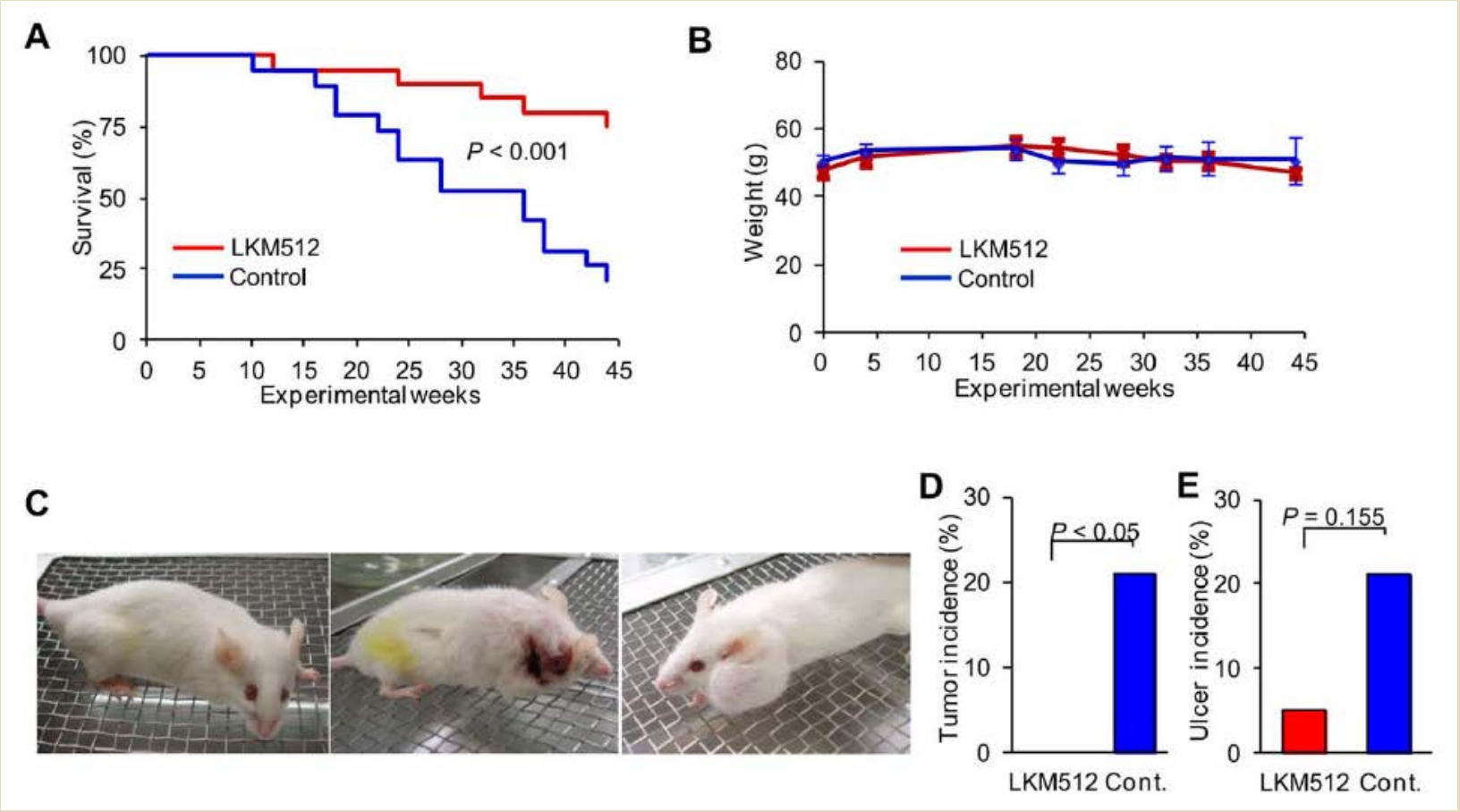
Biagi et al. Current Biology 26:1480-1485, 2016

Dietary Modulation of Gut Microbiota

- **Probiotics:** foods or dietary supplements that contain live bacteria
- **Prebiotics:** nondigestible food ingredient, which selectively stimulates the growth of gut bacteria
- **Synbiotics:** combination of a probiotic with a prebiotic
- **Other factors:** tea, cocoa, wine polyphenols, spices

Continuous Probiotic Exposure Increases Longevity in Mice

10 month female ICR mice fed a chow diet and gavaged with *Bifidobacterium animalis* subsp. *lactis* LKM512 or vehicle daily for 11 months



Matsumoto et al. PloS One 6:e23652, 2011

The Prebiotic High-Amylose Starch (HAS) Might Increase Longevity

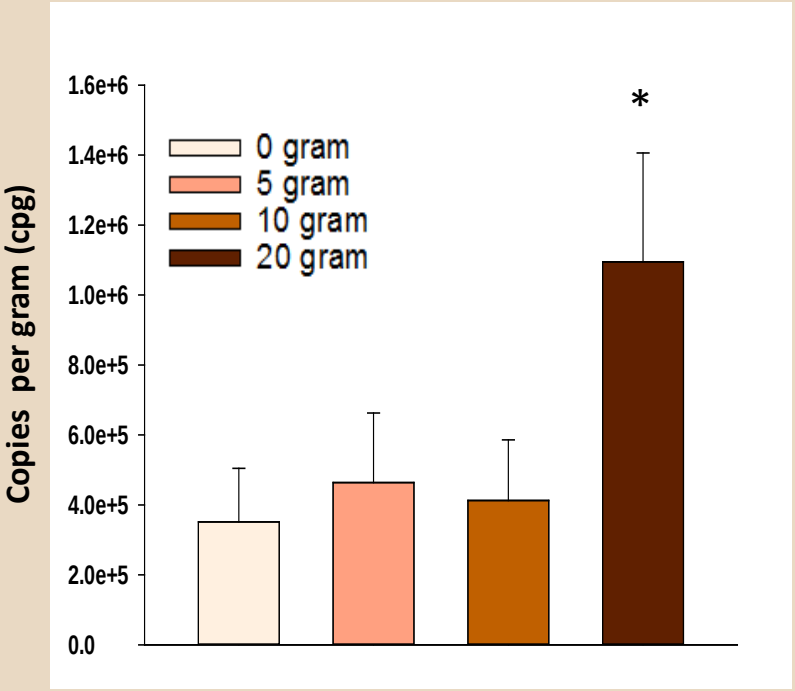
Table 2 Summary of the effects of diet restriction and high-amylose starch

	Diet restriction	High-amylose starch	HAS references
Longevity	↑	?	
Inflammation	↓	↓	Zhou et al. 2012; Le Leu et al. 2013
Glucose clearance	Improved	Improved	Zhou et al. 2008; Shen et al. 2011
Insulin sensitivity	Improved	Improved	Robertson et al. 2005; Johnston et al. 2010; Robertson 2012
Blood lipids	↓	↓	Keenan et al. 2006, 2013; DeJonge et al. 2009
Oxidation of fatty acids	↑	↑	Higgins et al. 2004; Zhou et al. 2009
Lipogenesis	↓	↓	Higgins et al. 2006; Higgins and Brown 2013
Body fat	Reduced	Reduced	Keenan et al. 2006, 2013; Charrier et al. 2014
Cancer risk	↓	↓	Toden et al. 2007; Clarke et al. 2008
Oxidative Stress	↓	↓	Kwak et al. 2012

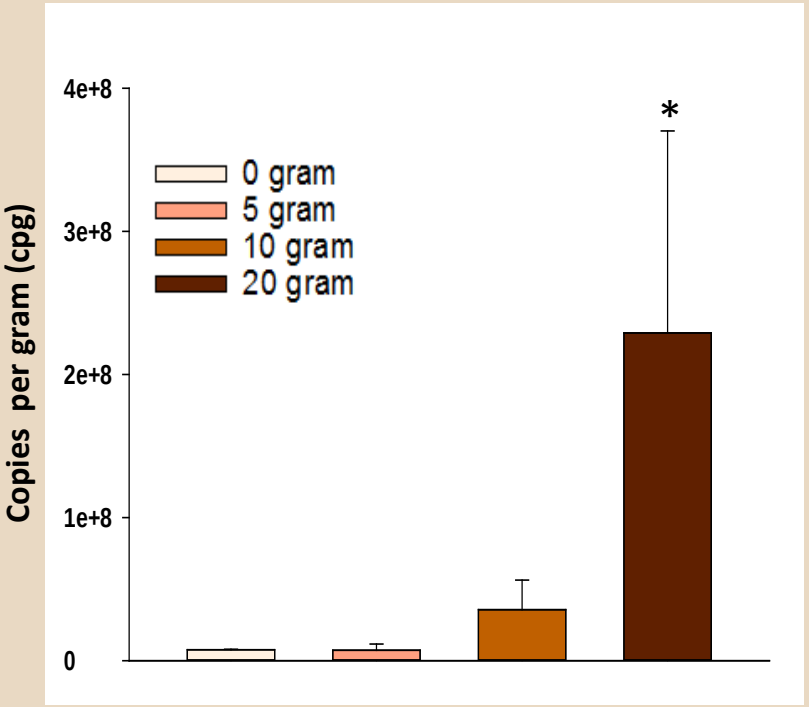
Keenan et al. AGE 37:98-108, 2015

Change in Bacterial Abundance After Consumption of Cocoa-Derived Flavanols

Bifidobacterium spp **(Feces)**



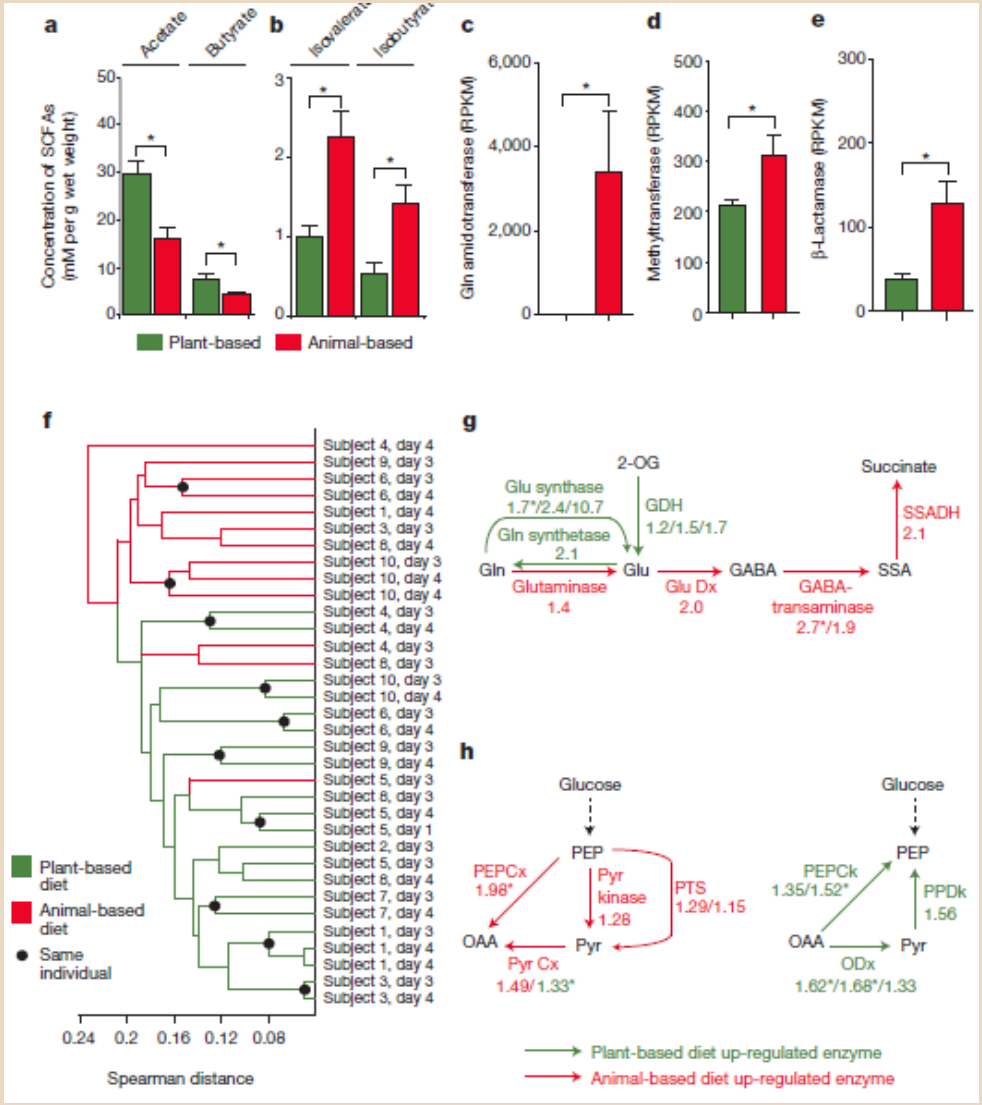
***Lactobacillus* (*casei* group)** **(Distal colon contents)**



Cocoa powder consumption decreased TNF-α and TLR-2, -4 and -9 gene expression in intestinal tissues

Jang, S. et al., J. Nutr., 2016

Diet Alters Microbial Activity and Gene Expression



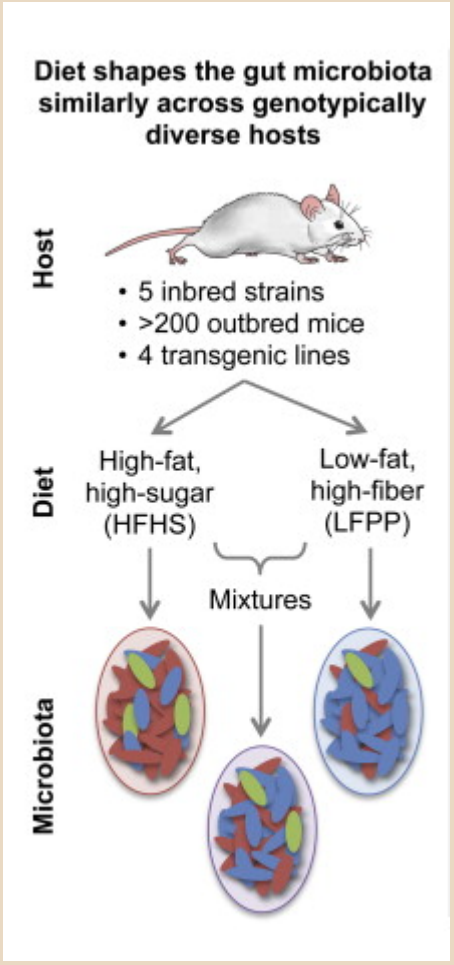
Short- term consumption of diets composed entirely of animal or plant products:

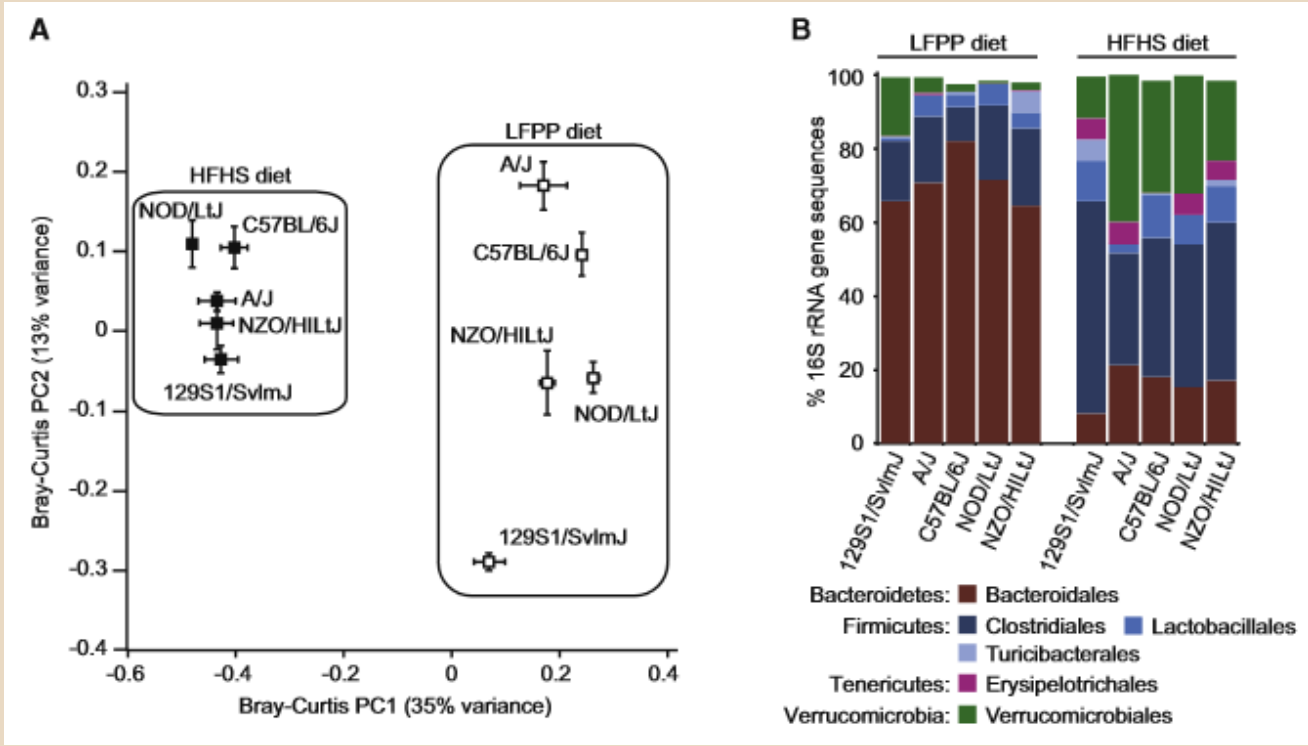
- Alters microbial community structure
- Overwhelms inter-individual differences in gene expression
- Modifies metabolic pathways

David, L.A. et al., Nature, 505: 559-563, 2014

Diet Dominates Host Genotype in Shaping the Mouse Gut Microbiota

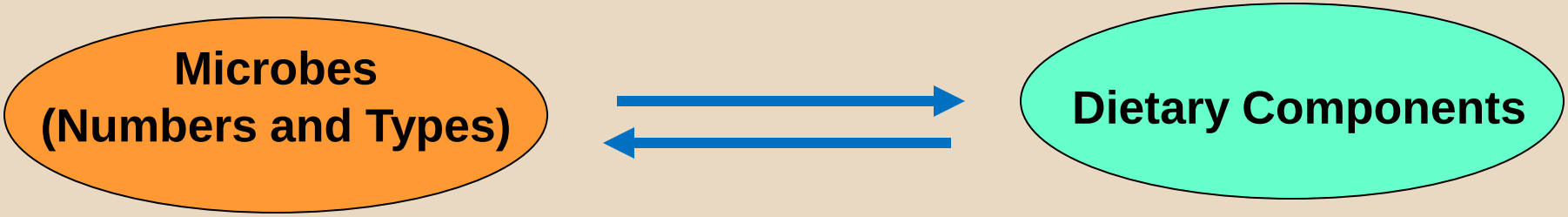
5 Inbred and >200 outbred mouse strains were fed a low fat, high-plant polysaccharide diet (LFPP:22.2%KCAL protein, 16% fat, 61% CHO) and a high fat, high-sugar diet (HFHS: 14.8% KCAL protein, 40.6% CHO, 44.6% fat)





Carmody et al., Cell Host & Microbe 17:72-84, 2015

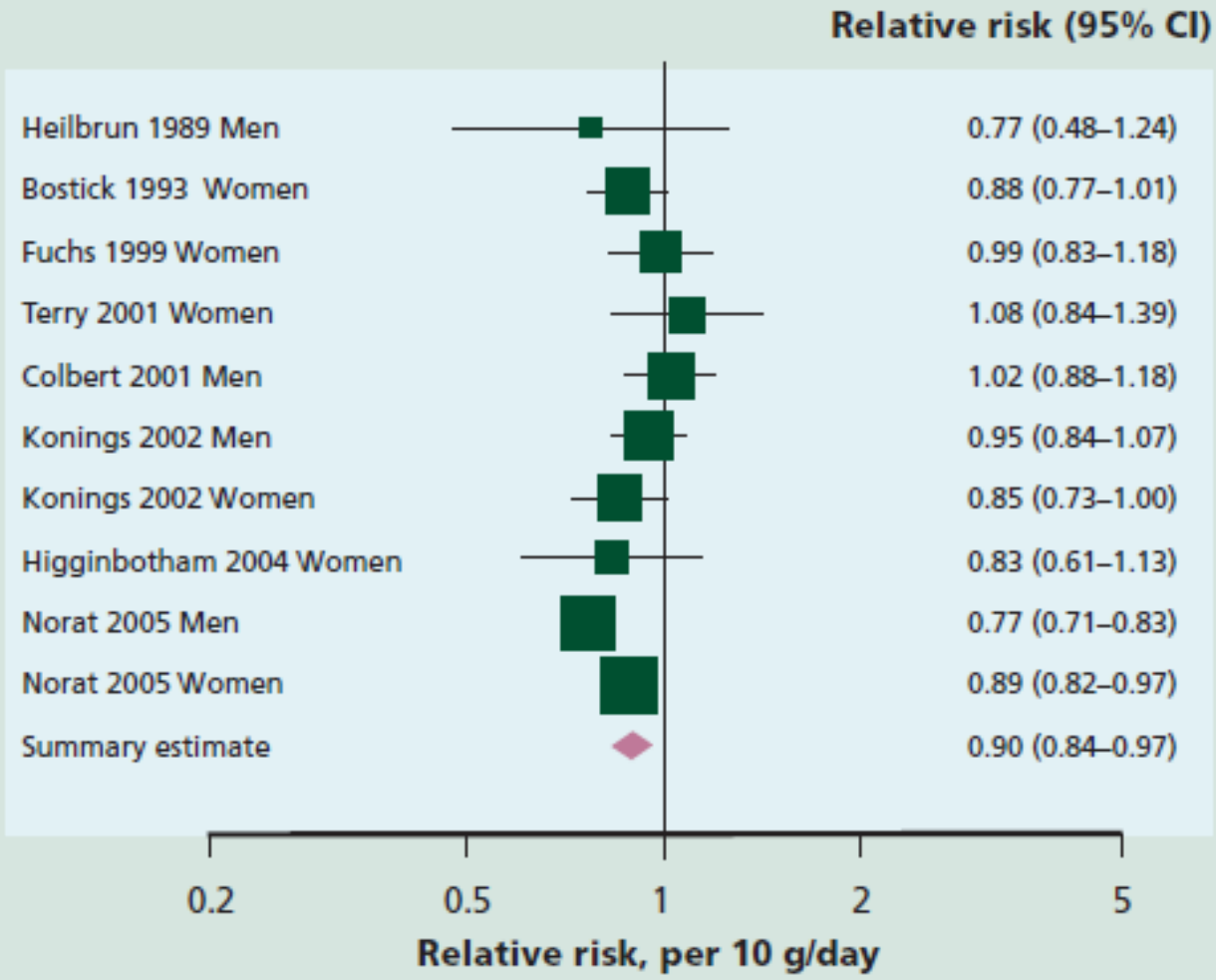
Diet and the Microbiome: A Two-Sided Relationship



Bacteria Can Generate New Metabolites from Dietary Components

Food Component	Bacterial Metabolite
Soy	Equol
Fiber	Butyrate
Plant Lignans	Enterodiol, Enterolactone
Ellagic Acid	Urolithins A and B
Hops	8-Prenylnaringenin
Linoleic Acid	Conjugated Linoleic Acid

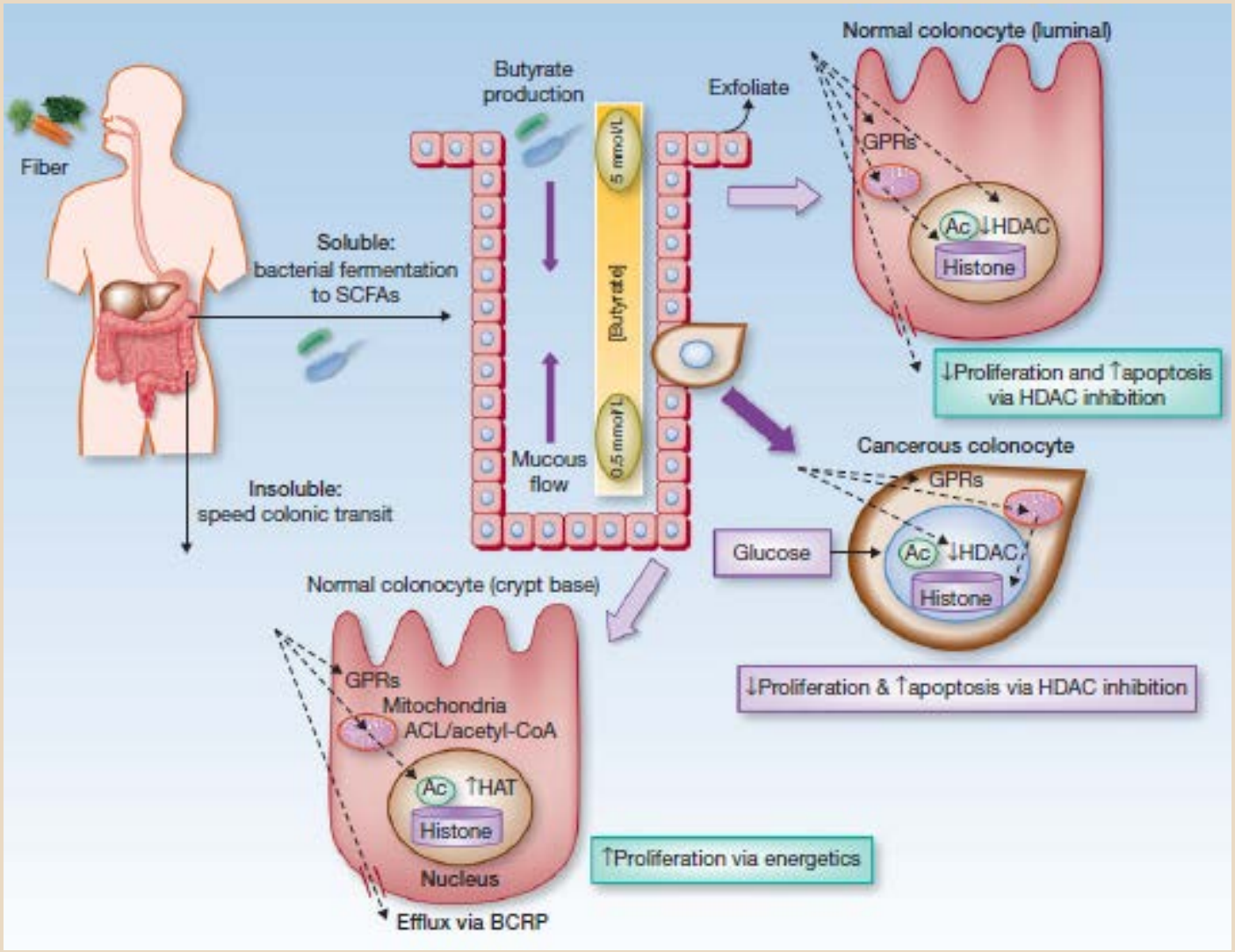
Figure 4.1.2 Dietary fibre and colorectal cancer; cohort studies



Dietary Fiber and Cancer

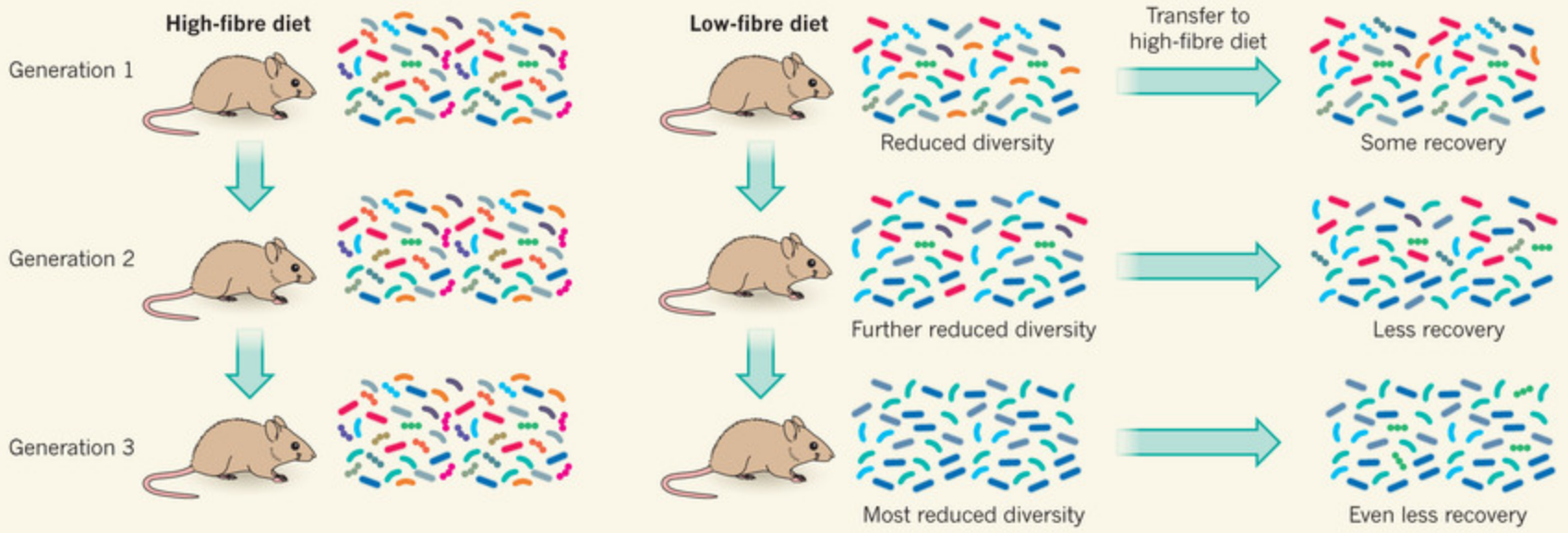
- Dietary fibers are fermented by colonic bacteria to form short chain fatty acids
- Butyrate is the most widely studied and the preferred energy source of colonocytes
- Butyrate has differential effects in normal versus cancer cells
- Human and animal studies of butyrate production and cancer risk are difficult to perform

Dietary Fiber and Colon Cancer



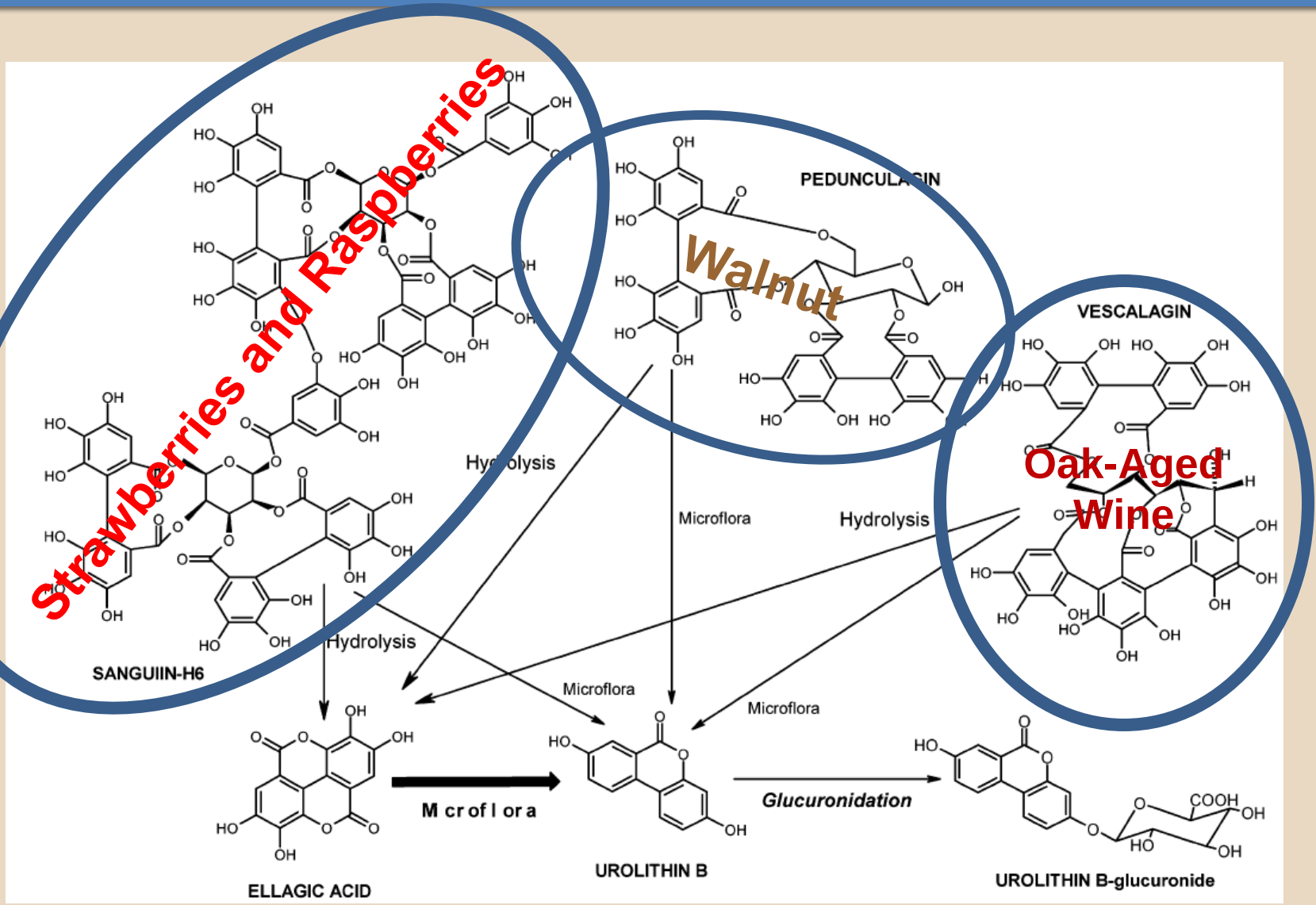
Bultman, S.J. Clin. Canc. Res., 20:1-5, 2013

Dietary Fiber and Bacterial Diversity



Martens E. Nature 529:158-159, 2016
Sonnenburg, E. et al. Nature 529: 212-215, 2016

Metabolism of Ellagitannins



Cerda et al. J Agric Food Chem 53:227-235, 2005

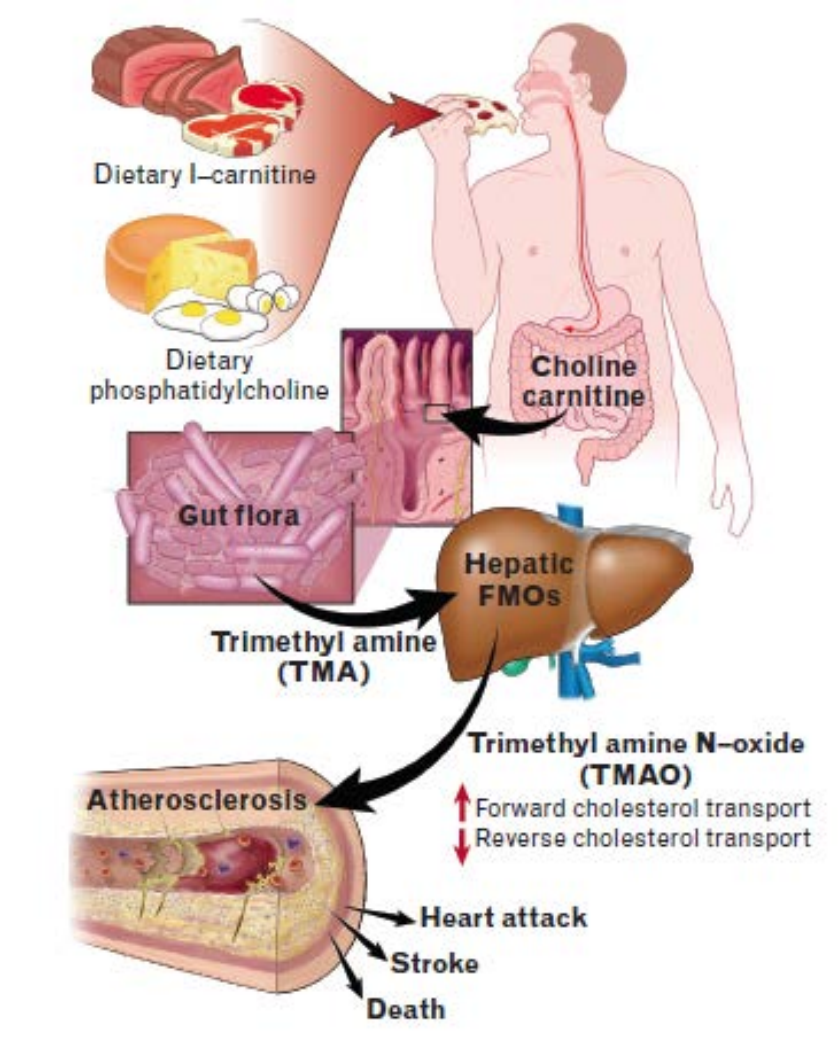
Urolithin Excretion After Intake of Different Ellagic Acid Containing Foods

Food	Excretion (%)
Strawberry (250 g)	0.06-6.3
Raspberry (225 g)	0.21-7.6
Red wine (300 ml)	1.8-7.4
Walnut (35 g)	1.2-81.0

N=10 volunteers

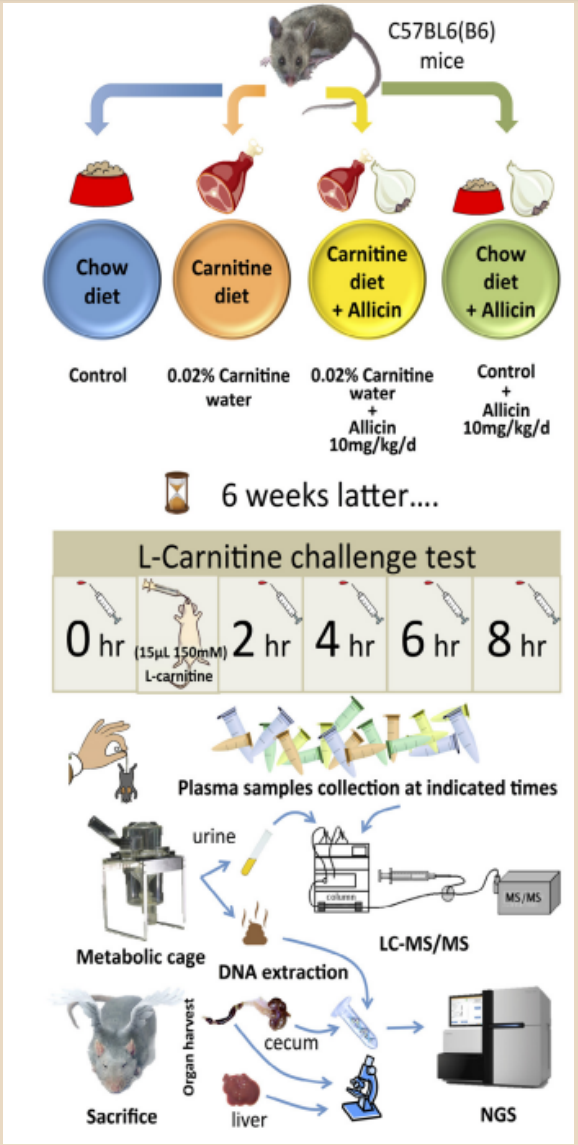
Cerda et al. J Agric Food Chem 53:227-235, 2005

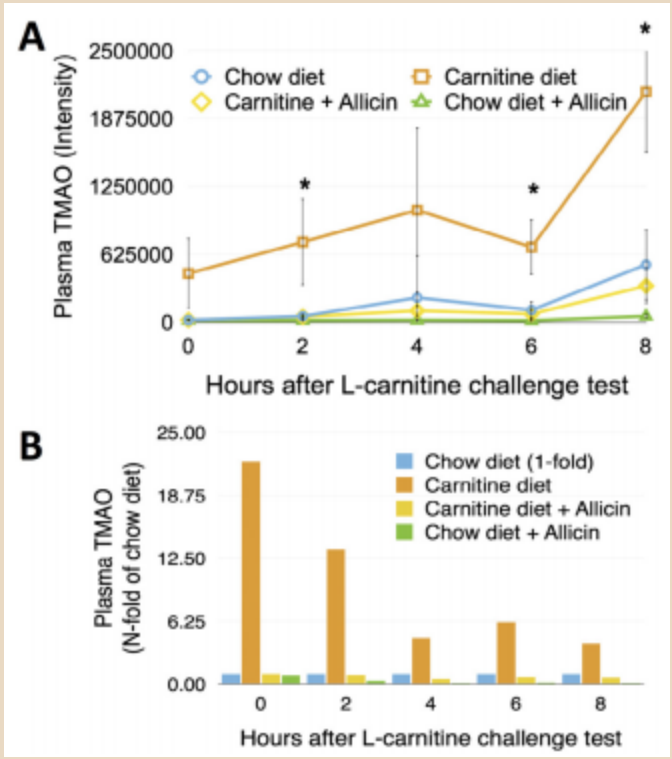
Diet, Microbial Metabolism and Cardiovascular Disease



Hazen, S.L. Curr. Opin. Lipidol. 25: 48-53, 2014

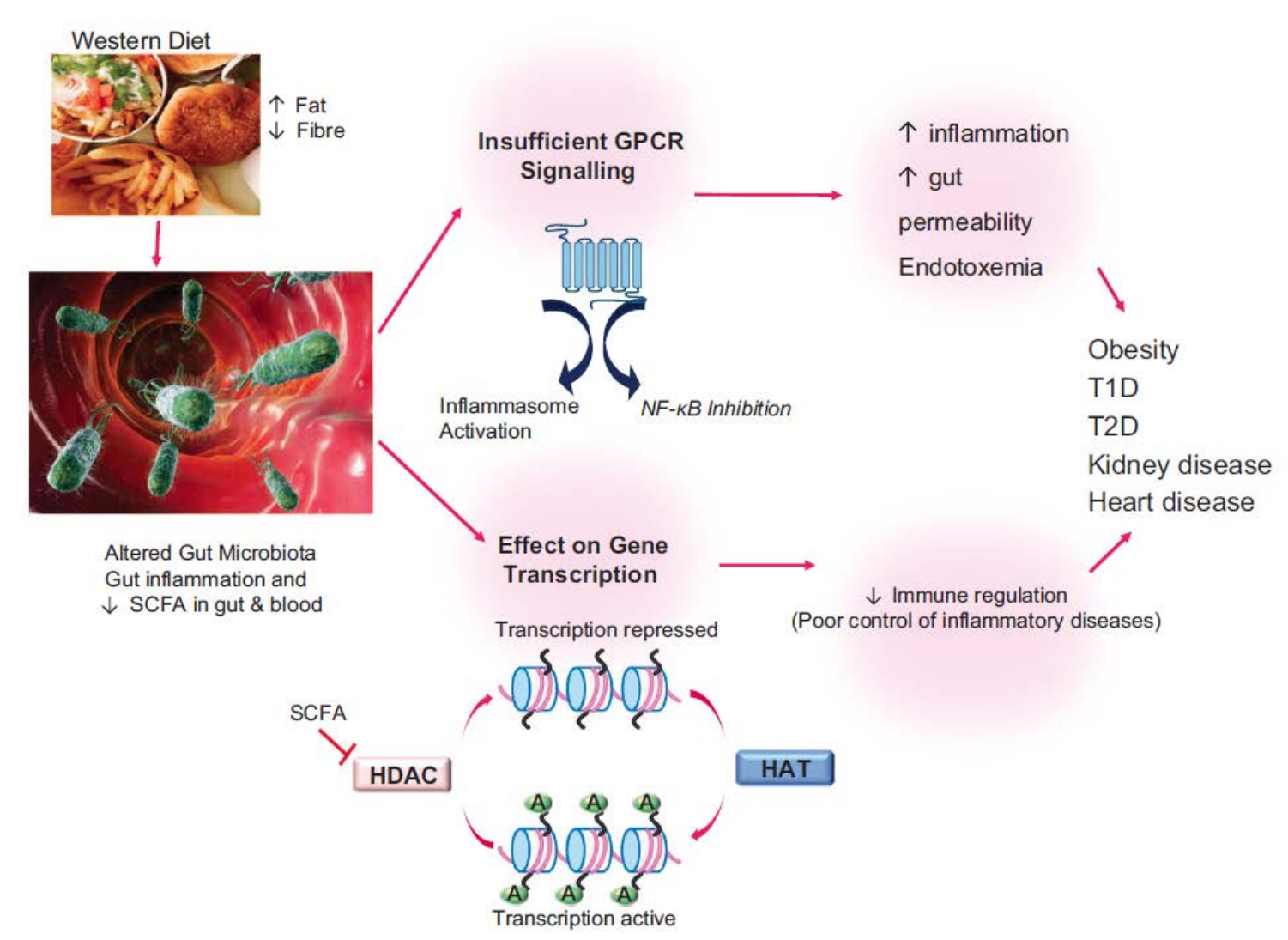
Dietary Allicin Reduces Metabolism of L-Carnitine to TMAO



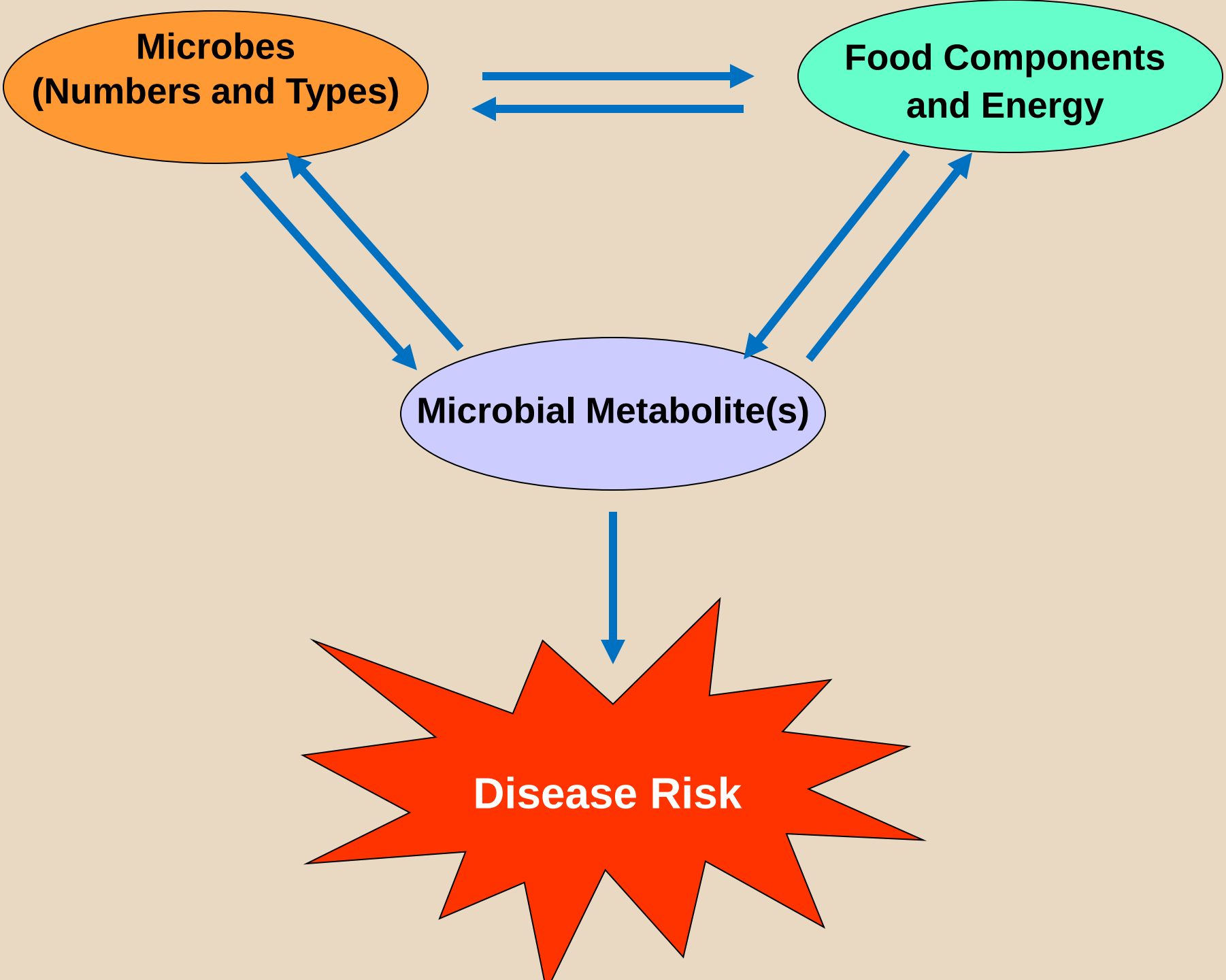


Wu et al. J. Functional Foods 15:408-417, 2015

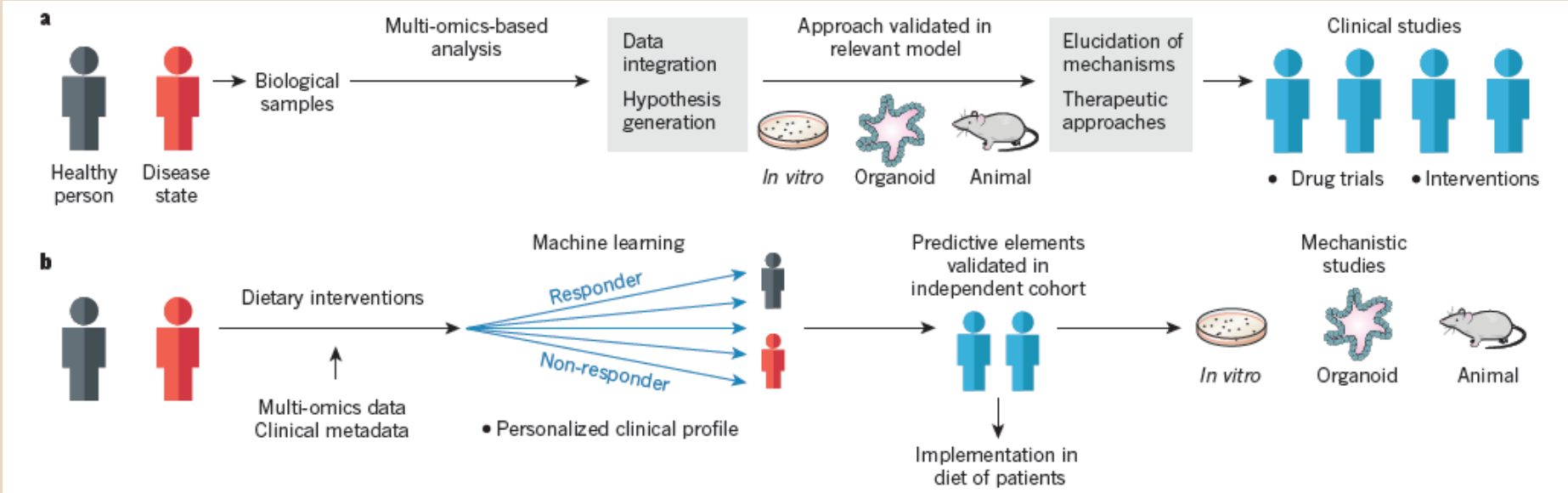
How Diet May Be Contributing to Human Inflammatory Diseases



Richards et al. Clin. Transl. Immunol. 5: e82, 2016

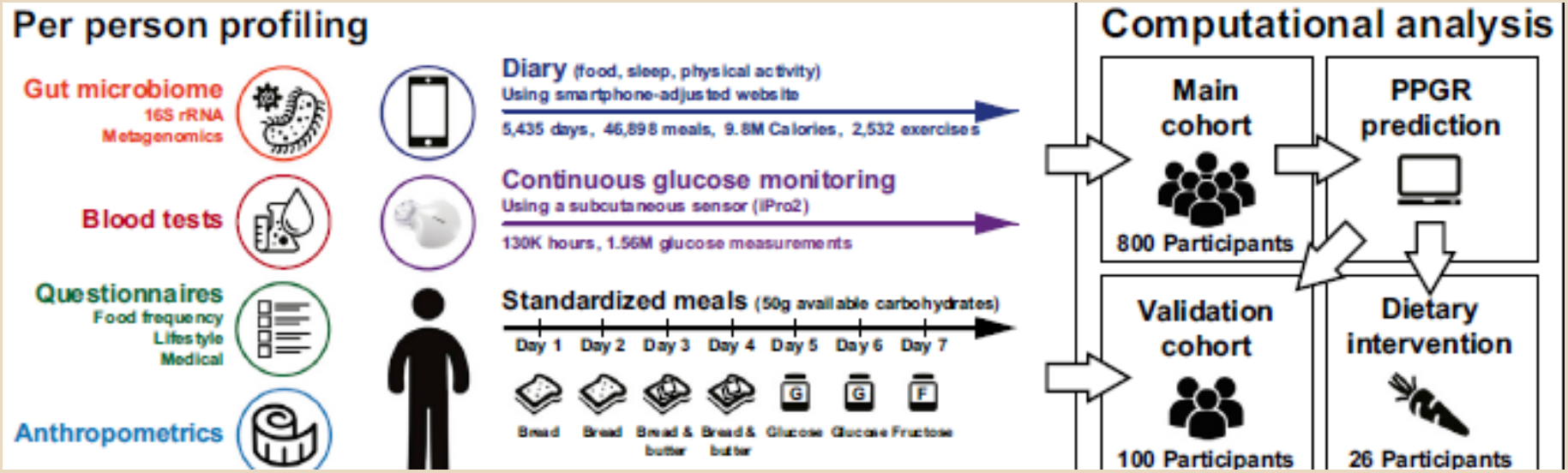

Microbes
(Numbers and Types)
Food Components
and Energy
Microbial Metabolite(s)
Disease Risk

Strategies for Modulating the Gut Microbiota to Improve Human Health



Sonnenburg and Backhed Nature 535:56-64, 2016

Can Your Microbiome Tell You What to Eat?



- High interpersonal variability in post-meal glucose observed in an 800-person cohort
- Using personal and microbiome features enables accurate glucose response prediction
- Prediction is accurate and superior to common practice in an independent cohort
- Short-term personalized dietary interventions successfully lower post-meal glucose

Zeevi D., et al. Cell 163:1079-1094, 2015

A Metagenomic View of our Dinner Plate

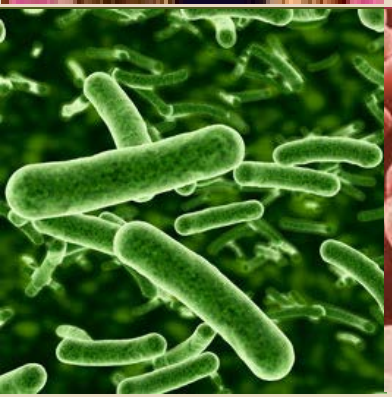
Dutton and Turnbaugh, Curr. Opinions Clin. Nutr. and Metabolic Care 15:448-454, 2012

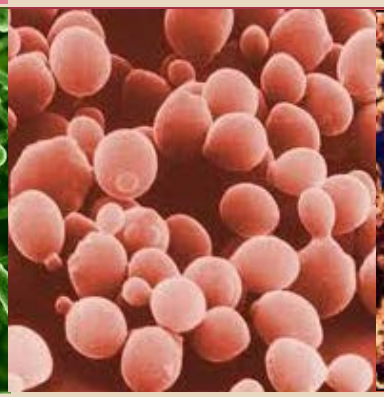

I'll have the Garden Salad, please
We'll have the Cheeseburger and fries!
FLO
P
S
Max's Cafe
MORRIS

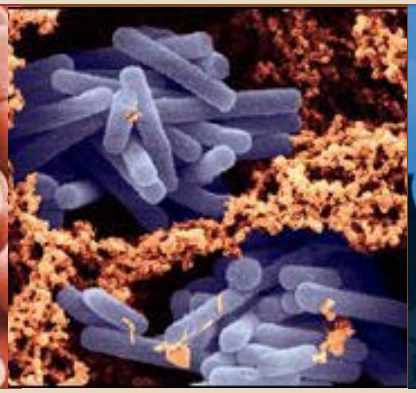
Cindy D. Davis

davisci@mail.nih.gov

http://ods.od.nih.gov







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