THE MICROBIOME

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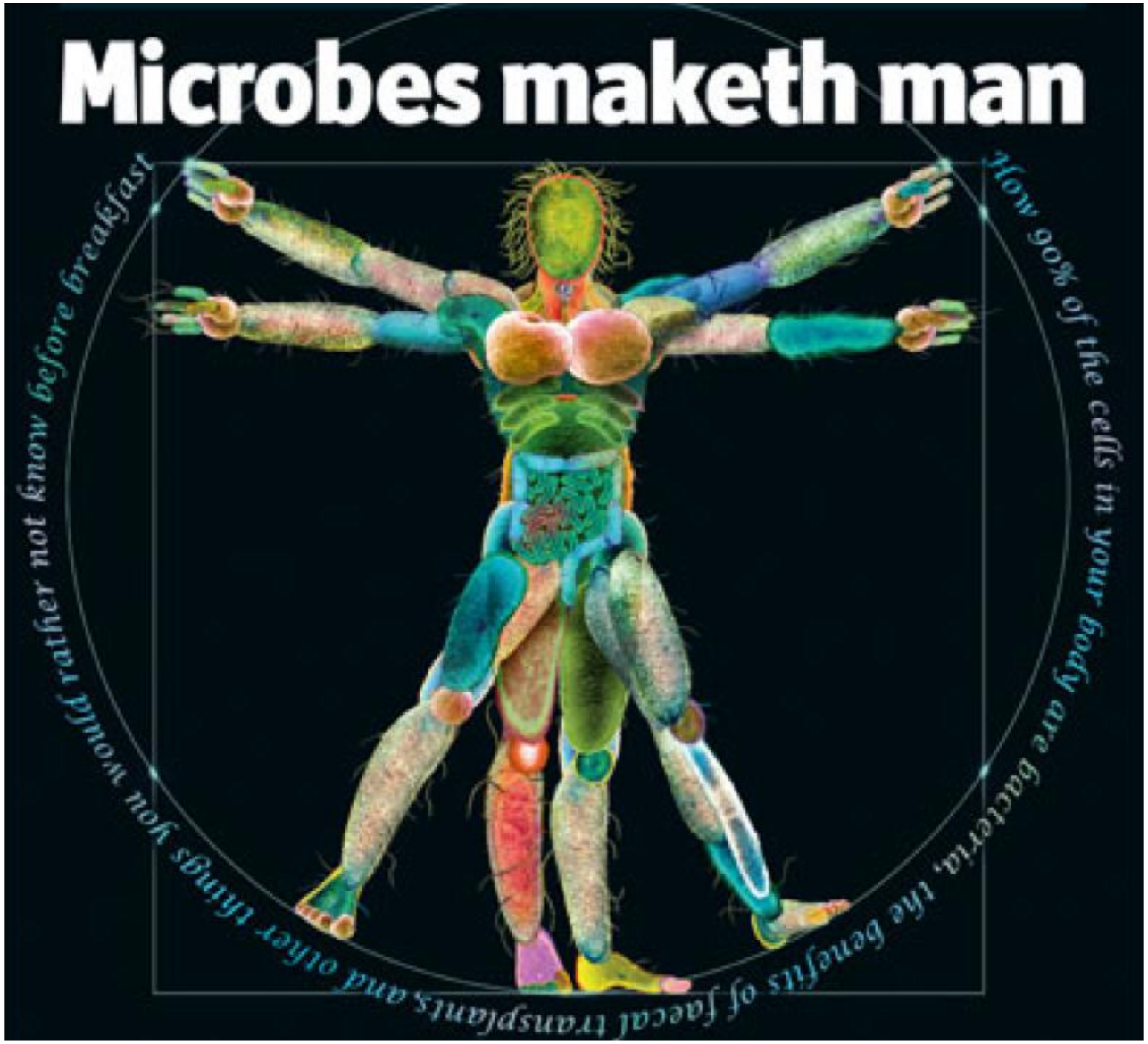
NO DISCLOSURES

OBJECTIVES

1. DEFINE THE MICROBIOME
2. LEARN THE BENEFITS OF THE MICROBIOME
3. UNDERSTAND THE RELATIONSHIP BETWEEN MICROBIOME AND GI DISEASE
4. UNDERSTAND THE RELATIONSHIP BETWEEN THE MICROBIOME AND OBESITY
5. LEARN WHAT BACTERIA MAY OFFER AS THERAPY

Microbes maketh man

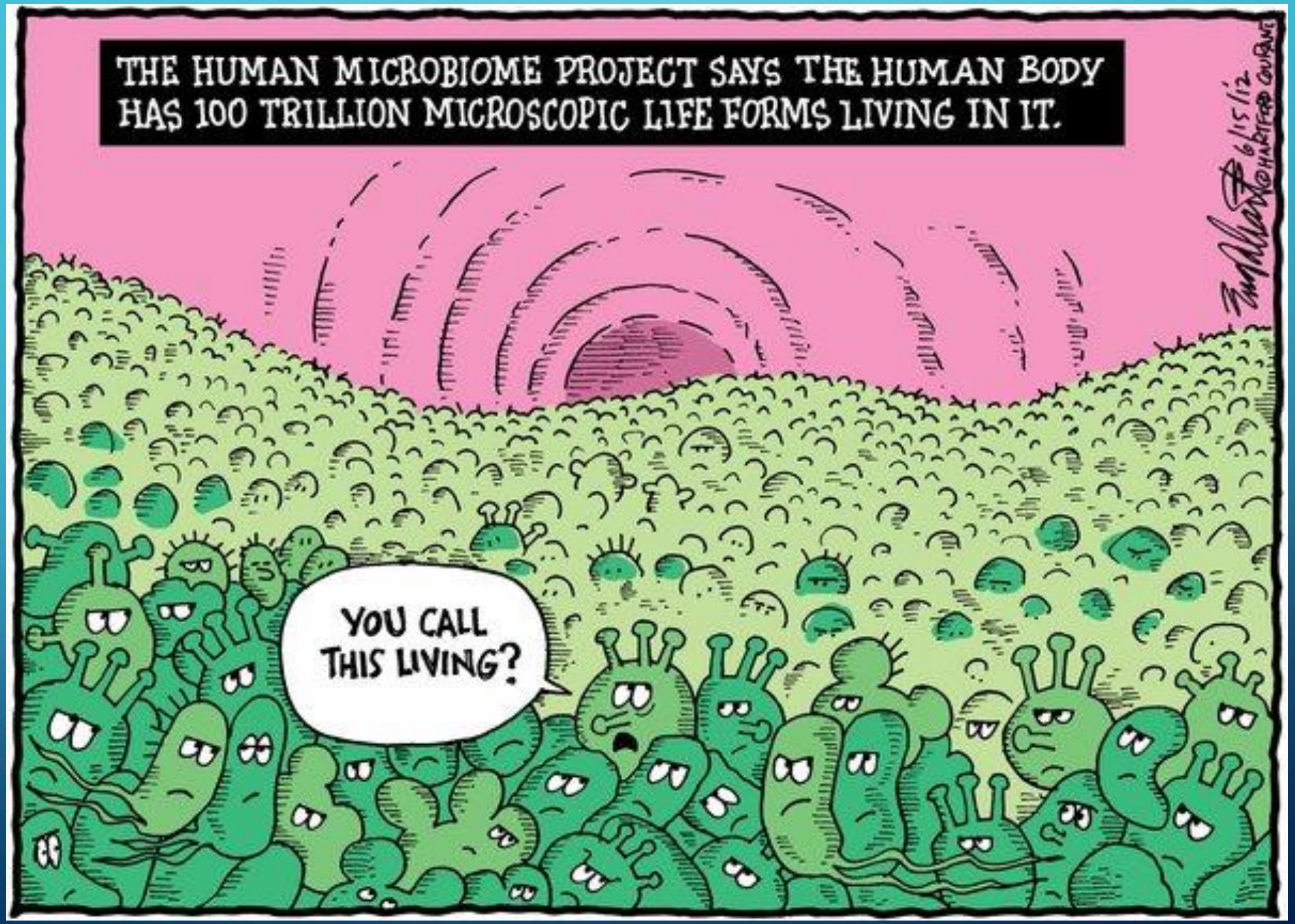


MICROBIOME - HISTORY

- Antonie van Leeuwenhoek (Dutch) created the term “animalcules” in 1675
- These “animalcules” are learned to be ubiquitous in habitation
- Centuries later term “microbiome” was coined to describe the collective community of bacteria, viruses, fungi and other microbes that colonize an ecosystem
- Nobel Laureate and Microbiologist Joshua Lederberg in 2001

MICROBIOME

- The word microbiome represents the unexplored worlds of bacteria, viruses, fungi and other microorganisms
- The ecological community of commensal, symbiotic and pathogenic microorganisms
  - Inhabit every corner of the planet
  - Share our body
- Consists of about 100 trillion microbial cells
- Accounts for ~1-3% total body mass (ranging as high as 3 pounds)


THE HUMAN MICROBIOME PROJECT SAYS THE HUMAN BODY HAS 100 TRILLION MICROSCOPIC LIFE FORMS LIVING IN IT.
YOU CALL THIS LIVING?
6/15/12
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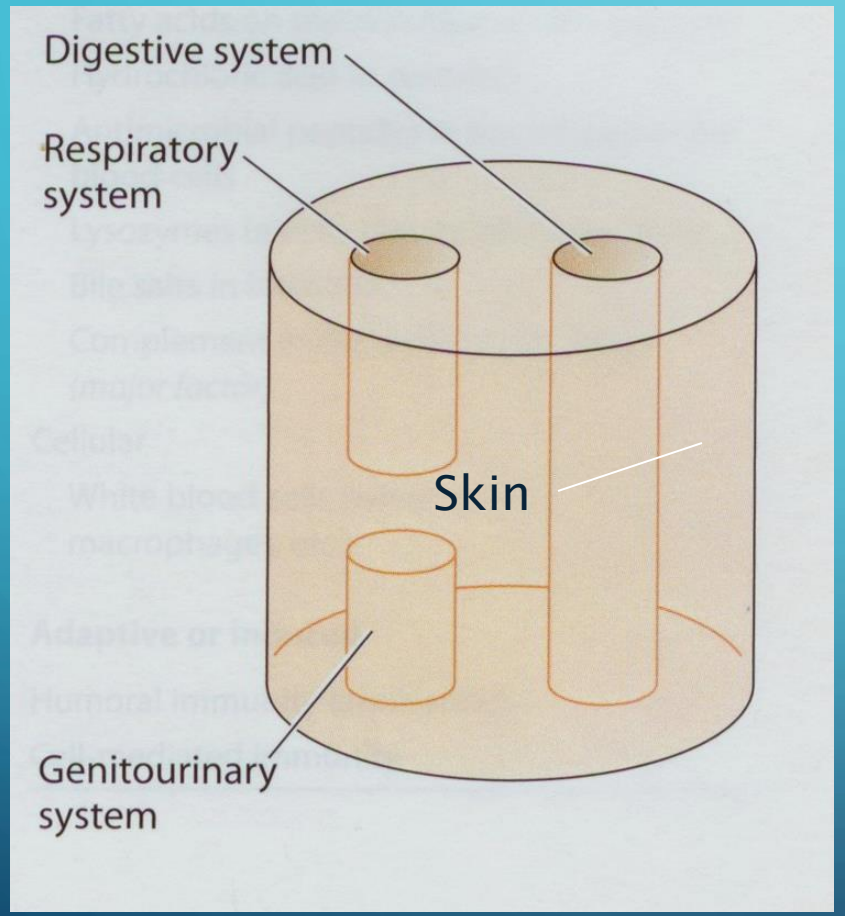
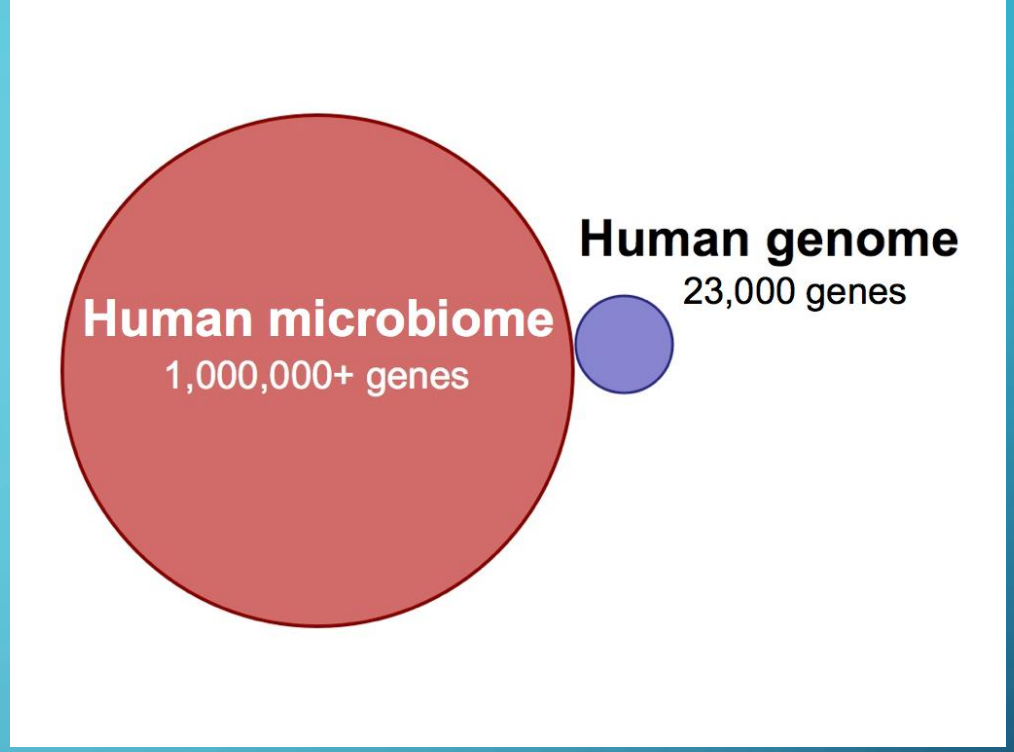
A microbe's view of us



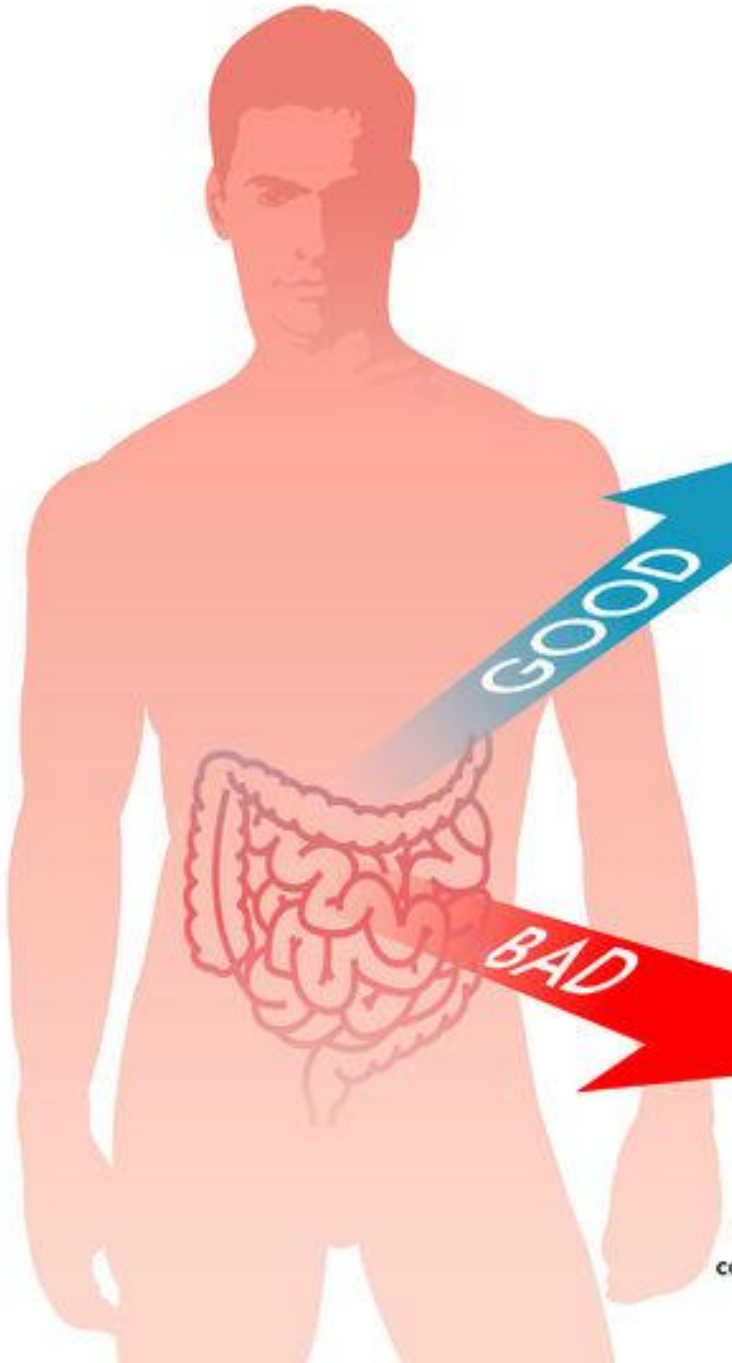


Bacterial cells exceed human body cells by 10:1 and comprise up to 4-6 lbs. of body mass

MICROBIOME

- Bacteria form tiny ecosystems side by side with our own cells
- Are all bacteria bad?

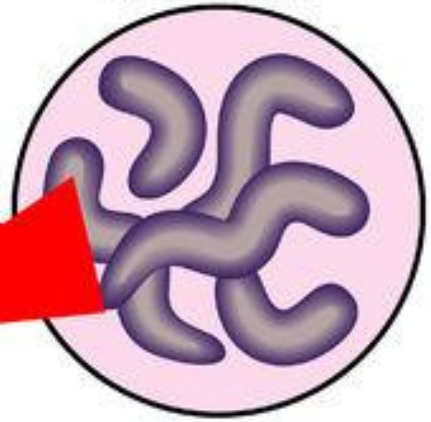
Good and Bad Bacterial Flora



BIFIDOBACTERIA
The various strains help to regulate levels of other bacteria in the gut, modulate immune responses to invading pathogens, prevent tumour formation and produce vitamins.

ESCHERICHIA COLI
Several types inhabit the human gut. They are involved in the production of vitamin K2 (essential for blood clotting) and help to keep bad bacteria in check.
But some strains can lead to illness.

LACTOBACILLI
Beneficial varieties produce vitamins and nutrients, boost immunity and protect against carcinogens.



CAMPYLOBACTER
C Jejuni and C coli are the strains most commonly associated with human disease. Infection usually occurs throught the ingestion of contaminated food.

ENTEROCOCCUS FAECALIS
A common cause of post-surgical infections.

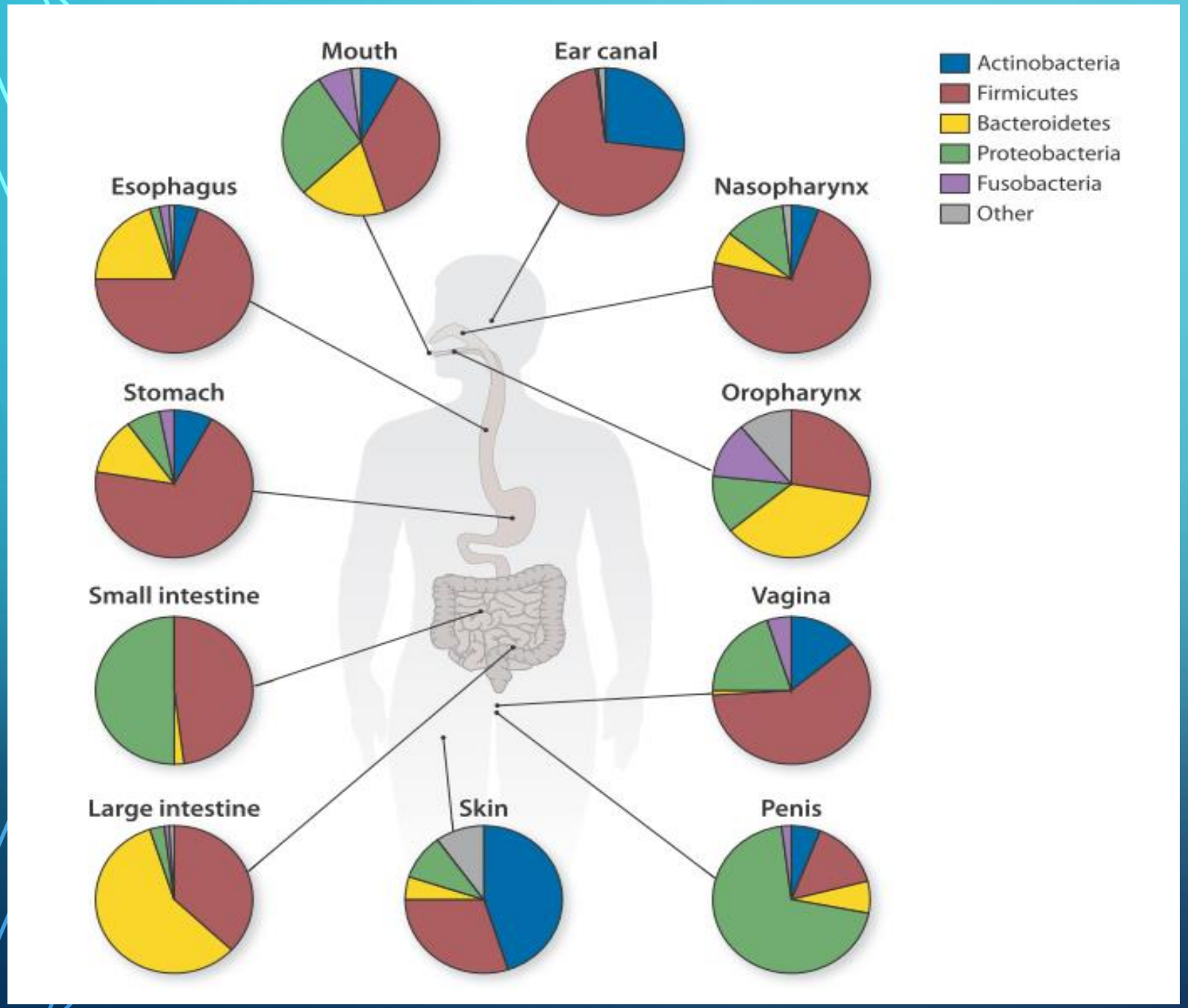
CLOSTRIDIUM DIFFICILE
Most harmfull following a course of antibiotics when it is able to proliferate.

MICROBIOME

- Research into the role that microbiota in the gut might play in the human immune system started in the late 1990s
  - Shape our metabolism
  - Makes us susceptible to allergic and inflammatory diseases
  - Implicated in some reactions to medical treatment

BENEFITS OF THE MICROBIOME

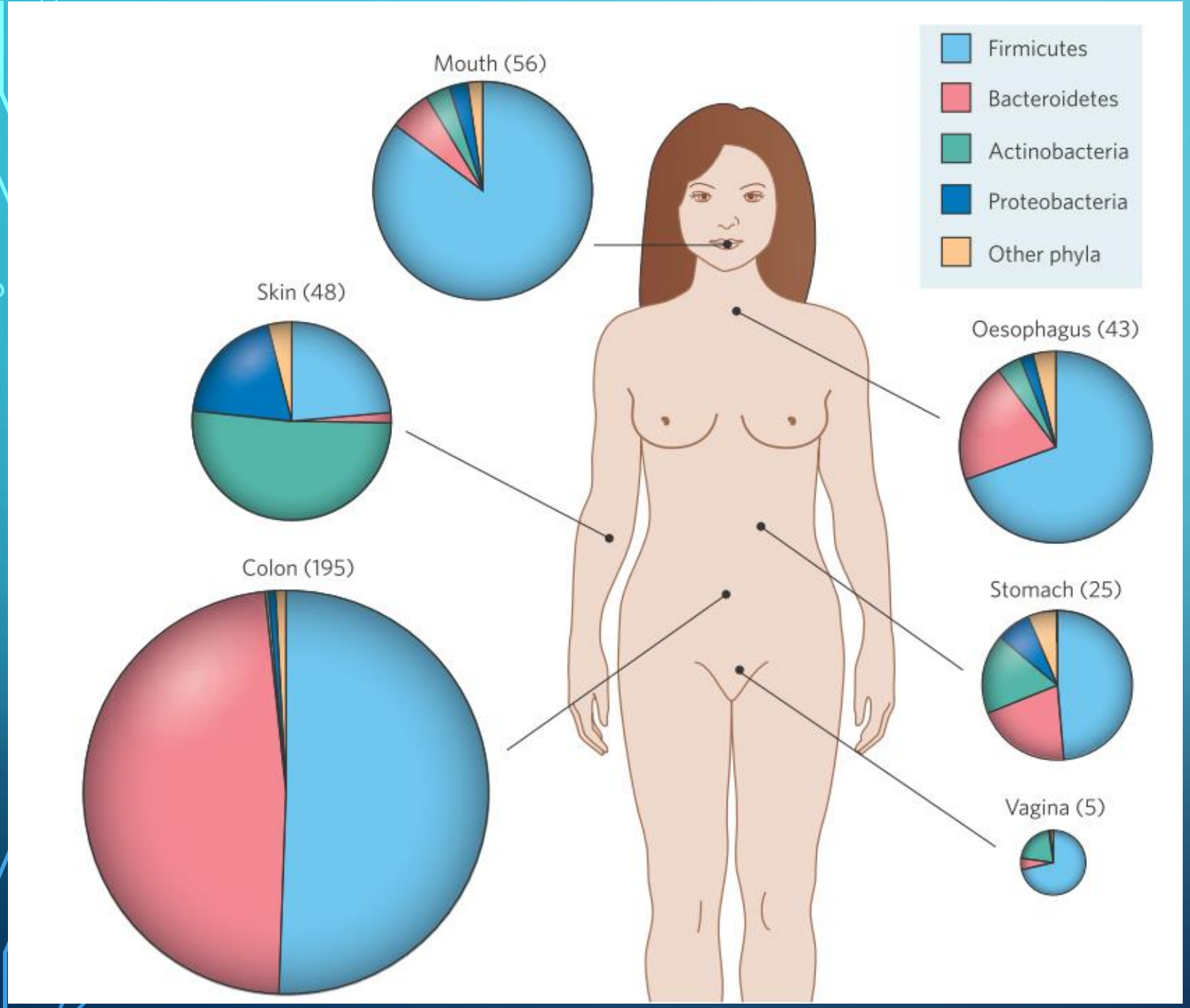
- **Synthesize vitamin** K and Vitamin B12
- **Prevent colonization of pathogens**
  - Competing for attachment sites
- **May antagonize other bacteria**
  - Production of substances which inhibit or kill non-indigenous species
    - Nonspecific fatty acids, peroxides, bacteriocins
- **Stimulate development of certain tissues**
  - Intestines, certain lymphatic tissues, capillary density
- **Stimulate production of cross-reactive antibodies**



Bacterial phyla by location in the body

(Fierer et al 2012)

Bacterial phyla distributed in the GI tract



Dethlefsen, McFall-Ngai and Relman 2007

MICROBIOME - ACQUISITION

- Delivery: The gut flora of vaginally-delivered babies differs from babies delivered by C-section
  - The vaginal microbial community of pregnant women contains **bacteria involved in digesting milk** (*Lactobacillus)*
- Feeding: The nature of the flora colonizing the intestines changes depending on form of feed
  - Breastmilk vs Bottle

MICROBIOME

- Millions of microbes in the large intestine exchange chemical signals with the body's cells and help digest nutrients
- Form a symbiotic relationship with the body
- Contribute to the normal functioning of the digestive system
- Impact on GI track first documented by Dr. Gordon at Washington University
  - Studied the gut microbiome to understand the nuanced relationship between microbes and their hosts

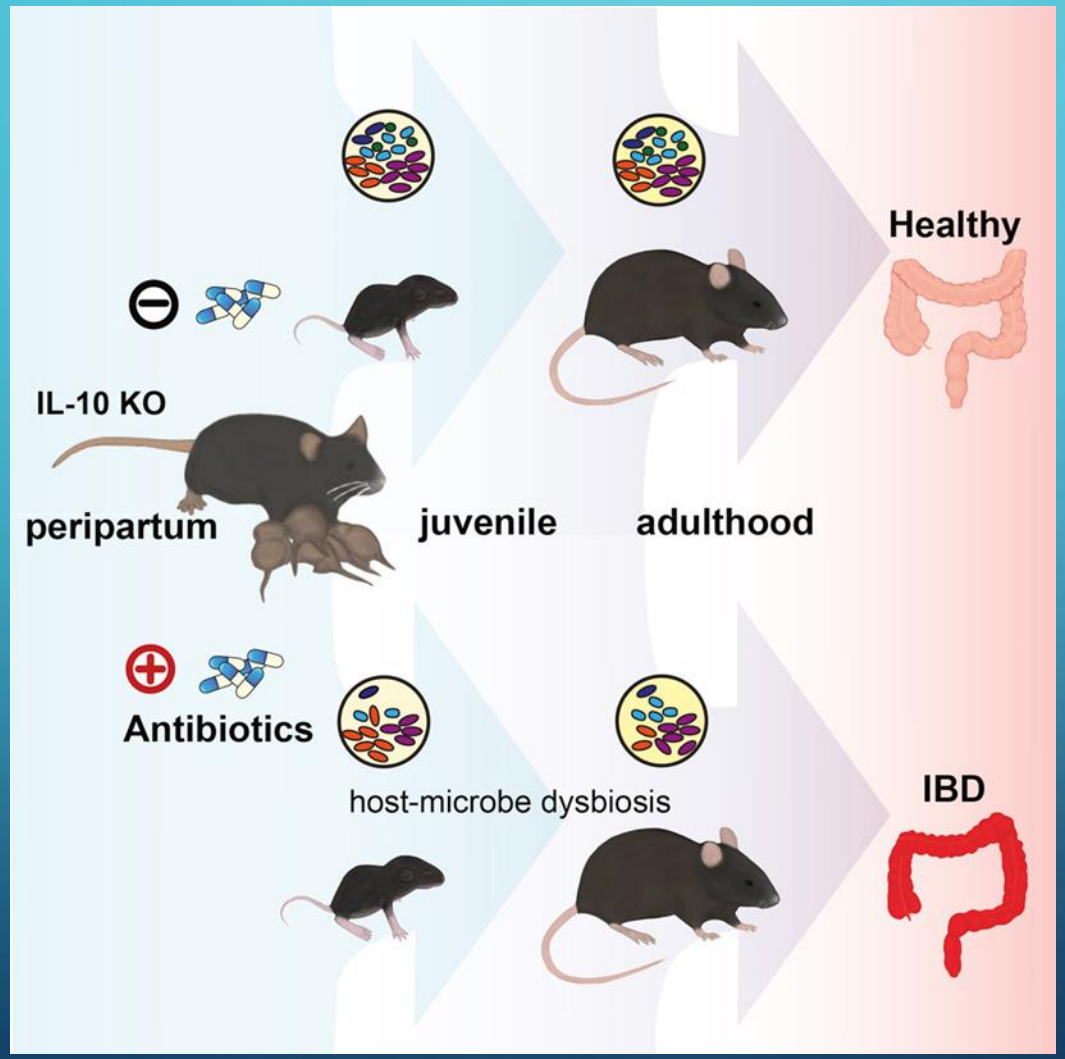
MICROBIOME AND HEALTH

- Gordon's research
  - Transplanted gut microbes from both genetically obese mice and lean mice into germ-free mice
  - All the mice ate the same diet and the mice who received microbes from obese mice gained more weight
- Gordon's research demonstrated the gut microbiome of obese humans changed as they consumed low-calorie diets and lost weight
- "The Father of the Microbiome"

MICROBIOME AND GI DISEASE - IBD

- Research demonstrates a high-fat, high-calorie diet maybe partially responsible to the rise in inflammatory bowel disease
  - Highly saturated fats alter the composition and functional properties of bacteria in the intestines
  - These distortions disrupt the advantageous mix of gut microbes and cause an emergence of microbes that induce inflammation

PERIPARTUM ANTIBIOTICS AND GUT DYSBIOSIS



Cell Reports 2017

PERIPARTUM ANTIBIOTICS AND GUT DYSBIOSIS

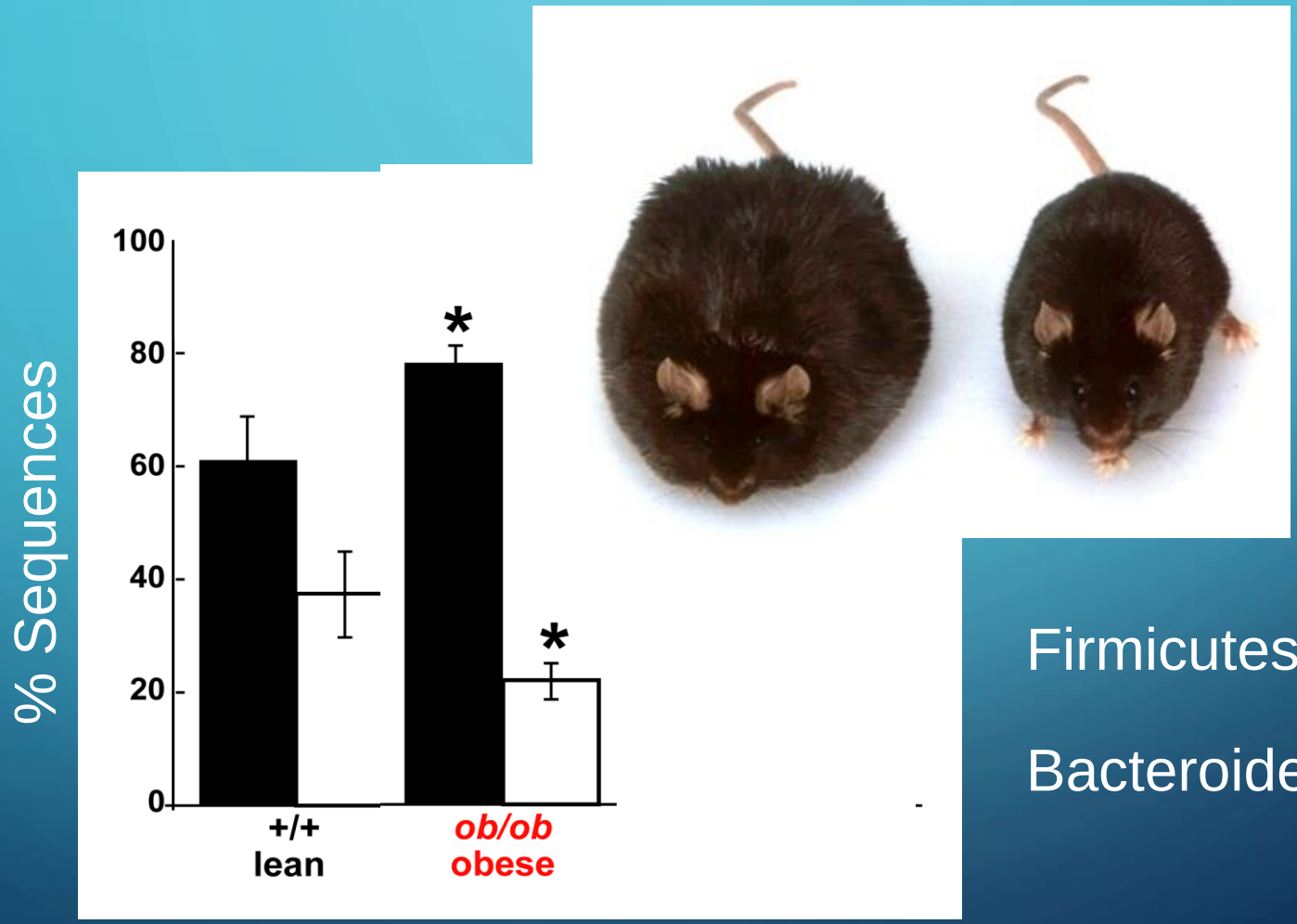
- Peripartum antibiotics promote offspring gut dysbiosis, immune dysfunction, and IBD
- Antibiotics given after the developmental period do not increase IBD
- Antibiotic-perturbed maternal microbiota likely contribute to neonatal gut dysbiosis
- Gut dysbiosis from peripartum antibiotics and genotype may be useful markers for IBD

Cell Reports 2017

MICROBIOME AND OBESITY

- A calorie-rich diet can induce proliferation of microbes studied to favor digestion of high-fat foods
- The stable presence of these types of microbes have demonstrated to contribute to over-nutrition and obesity

DIFFERENT GUT MICROBIAL COMMUNITY STRUCTURE IN OBESE MICE

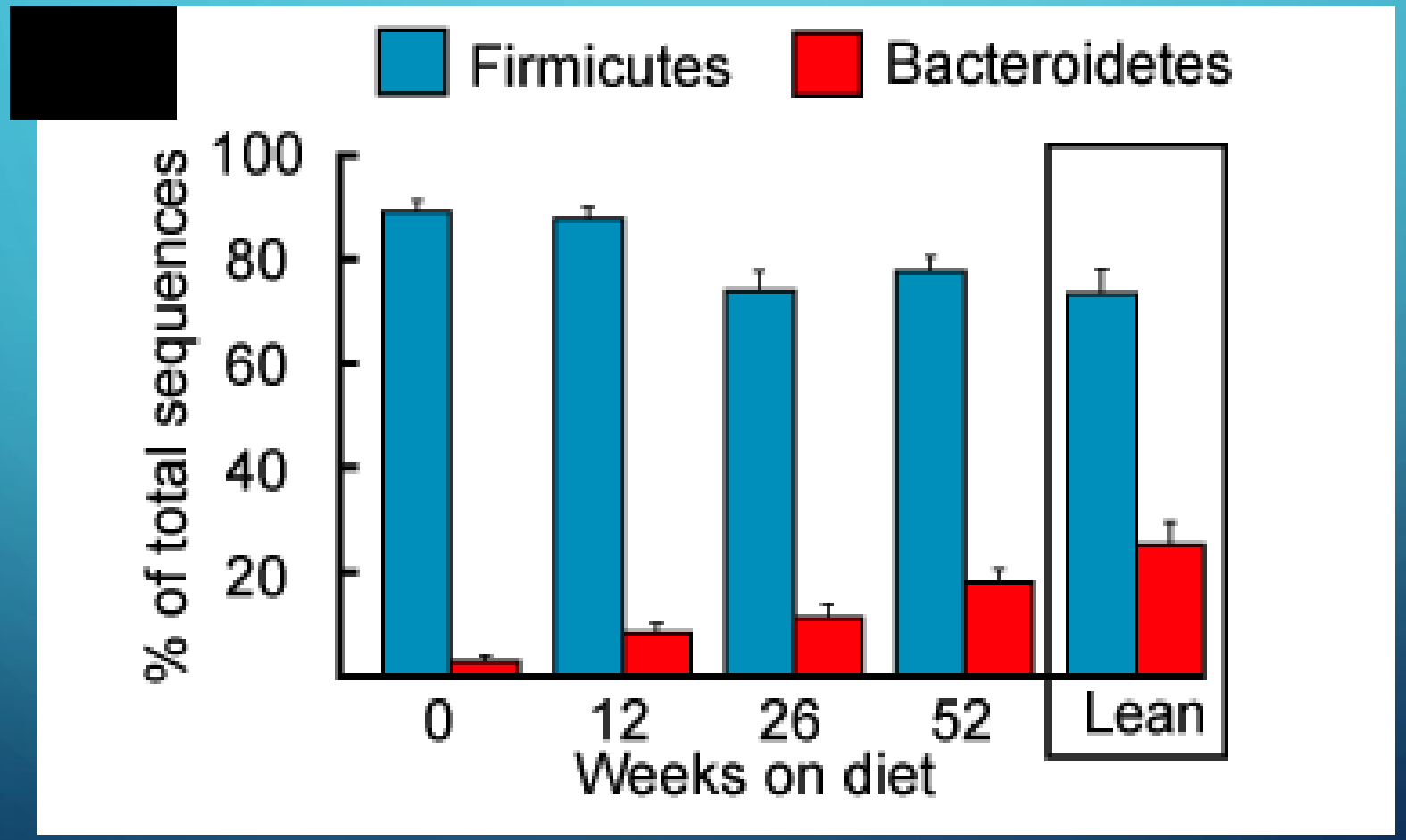


Firmicutes

Bacteroidetes

Ley *et al.*, PNAS 102: 11070-5 (2006)

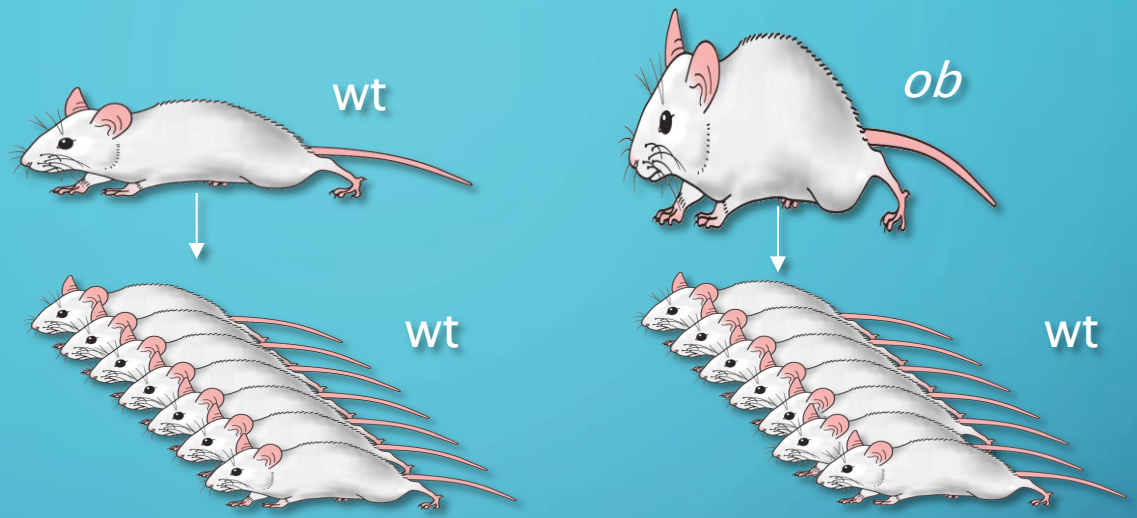
EFFECTS OF DIETING AND MICROBES



Ley *et al*. Nature 444: 1022 (2006)

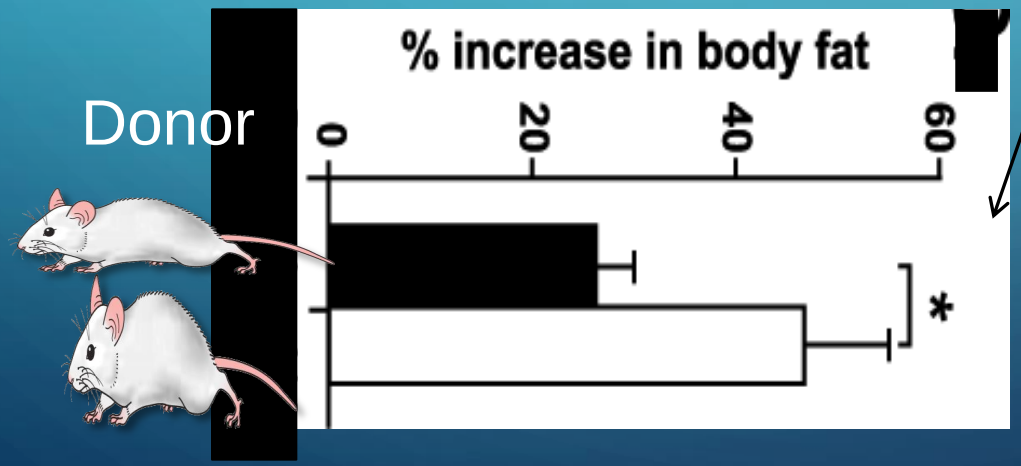
MICROBIOTA FECAL TRANSPLANTATION AND OBESITY

Conventionally raised donors



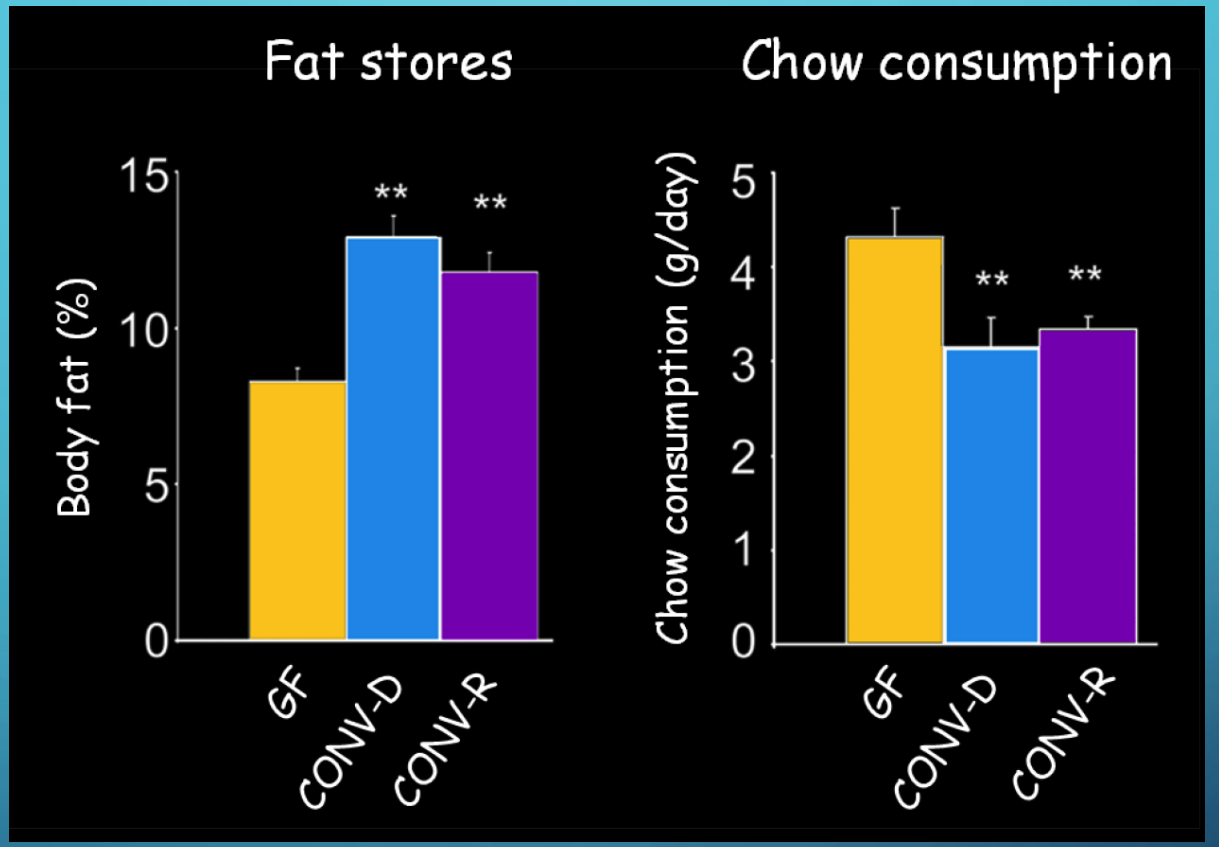
Germ-free Wild type recipients

Donor



Turnbaugh *et al.*, Nature 444: 1027-1031

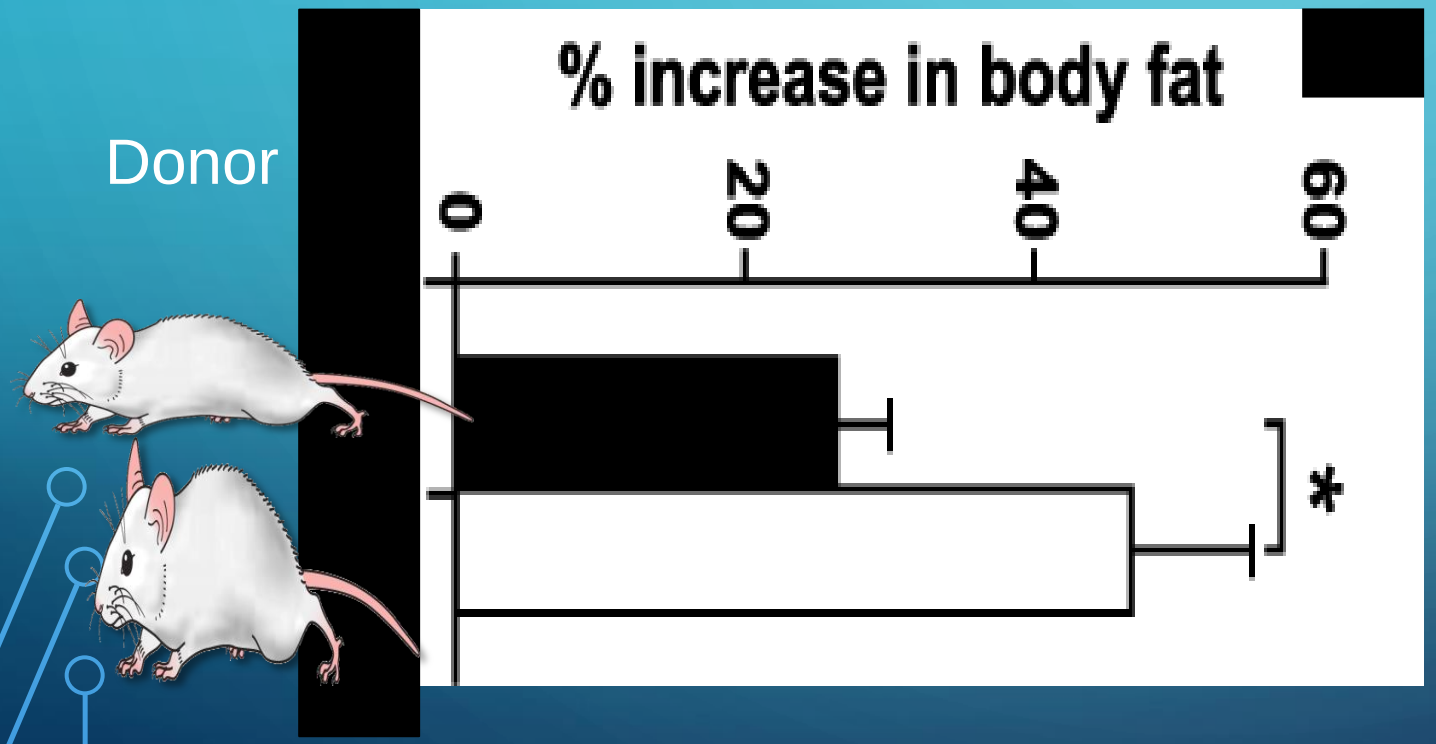
MICROBIOTA FECAL TRANSPLANTATION AND OBESITY

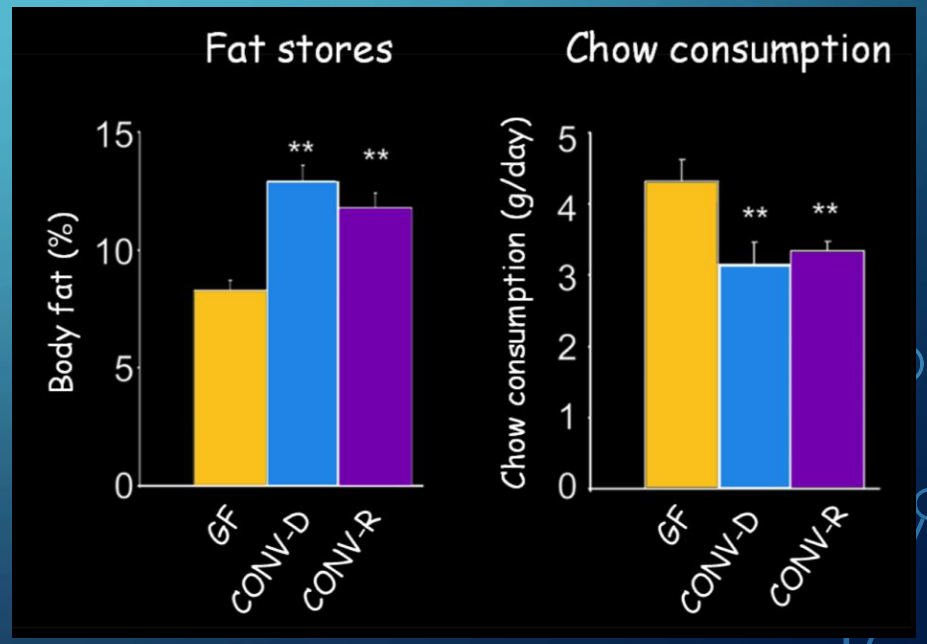


Conventionalized mice (CONV-D) are formerly germ-free (GF) recipients of a gut microbiota transplant from conventionally-raised (CONV-R) donors

Microbiota fecal transplantation and obesity

Donor





MICROBIAL ECOLOGY

- Metagenomic analysis of obese/lean mouse gut microbiotas
  - Obese gut microbiome contains more genes predicted to harvest energy from polysaccharides
- Hypothesis:
  - Differences in gut microbial ecology among humans affects the efficiency of their energy harvest/storage when consuming a given diet

Turnbaugh *et al*., Nature 444: 1027-1031

BACTERIOTHERAPY – NOT ALL BACTERIA ARE BAD

CASE REPORT

Changes in the Composition of the Human Fecal Microbiome After Bacteriotherapy for Recurrent *Clostridium difficile*-associated Diarrhea

Alexander Khoruts, MD, Johan Dicksved, PhD,† Janet K. Jansson, PhD,‡ and Michael J. Sadowsky, PhD§*

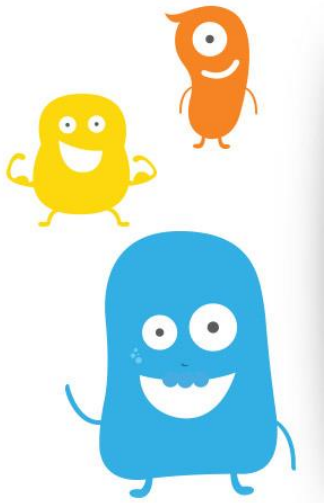
Clostridium difficile-associated diarrhea (CDAD)

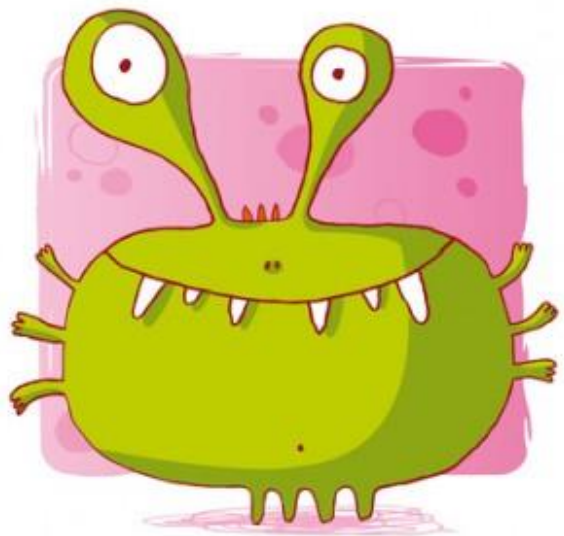
- Usually results from prior antibiotic treatment
- Persistent disruption of gut microbiota
  - can be severe, even causing death

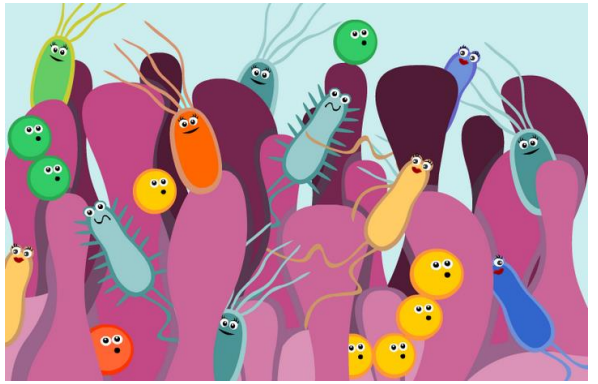
J Clin Gastroenterology (2010) 44:354-360

RESOURCES

- Devkota, S., Wang, Y., Musch, M., Leone, V., Fehlner-Peach, H., Nadimpalli, A., Antonopoulos, D., Jabri, B., & Chang, E. (2012). Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in Il10-/- mice Nature DOI: 10.1038/nature11225
- Miyoshi, J., Bobe, A., Miyoshi, S., Chang, E. (2017). Peripartum Antibiotics Promote Gut Dysbiosis, Loss of Immune Tolerance, and Inflammatory Bowel Disease in Genetically Prone Offspring. Cell Reports DOI: https://doi.org/10.1016/j.celrep.2017.06.060
- J Clin Gastroenterology (2010) 44:354-360
- Turnbaugh *et al*., Nature 444: 1027-1031







THANK YOU