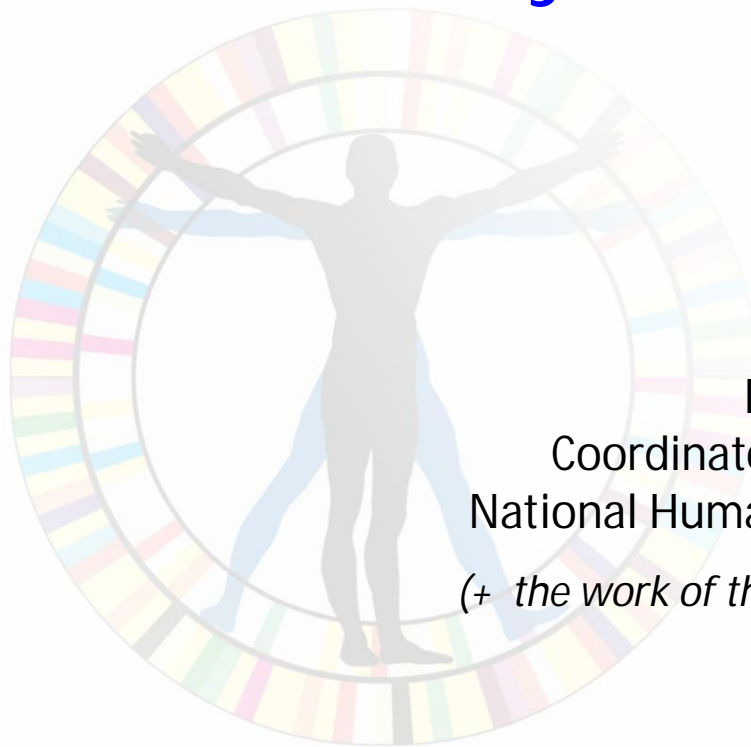


The NIH Human Microbiome Project: Catalyst for an Emerging Field



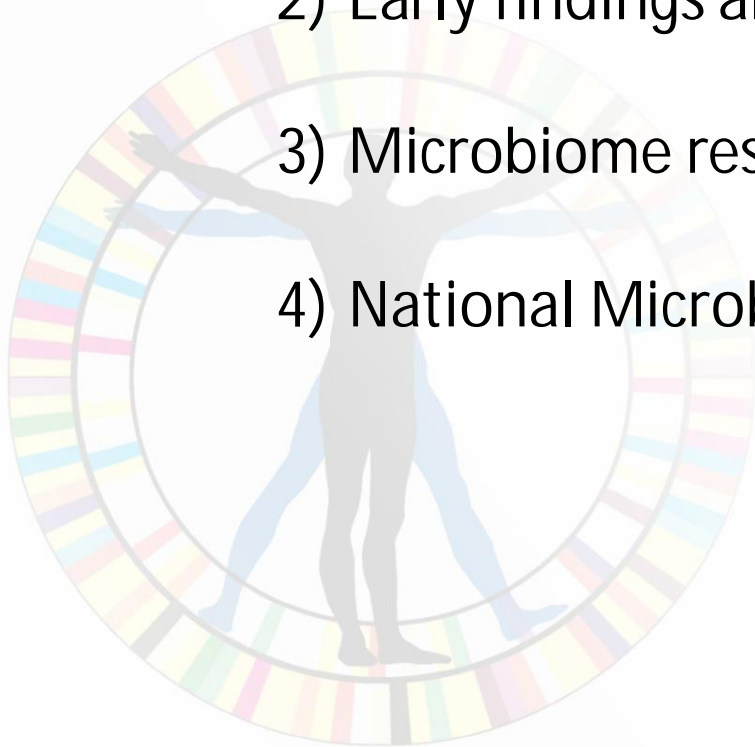
Lita M. Proctor, Ph.D.
Coordinator, Human Microbiome Project
National Human Genome Research Institute, NIH
(+ the work of thousands of scientists in US and abroad)

CHE webinar
May 24, 2016



Topics in this talk

- 1) Impetus for and goals of the HMP
- 2) Early findings about the human microbiome
- 3) Microbiome research beyond the HMP
- 4) National Microbiome Initiative





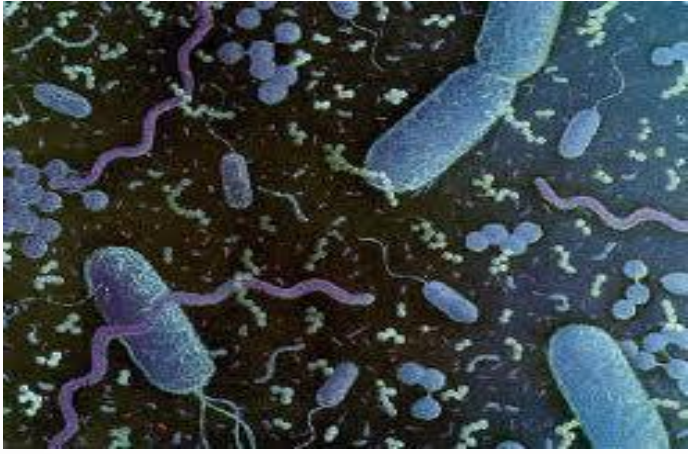
“microbiome”
“microbial organ”
“human superorganism”
“good germs”
“our second genome”



Society's war against infectious disease

(bubonic plague, smallpox, scarlet fever, yellow fever, tuberculosis, malaria, diphtheria, dysentery, leprosy, typhoid fever...)





~1400 species of human pathogens

vs.

~1 - 10 million microbial species on Earth

The **MAJORITY** (>> 99%) of microbes (bacteria, viruses, fungi) do not cause disease; many are beneficial. Microbes on Earth:



- ▶ Soil production/regeneration
- ▶ Oxygen production
- ▶ Base of food webs (ocean, forests, etc)
- ▶ Support plant, animal & human health



Human Microbiome Project: 2008 to Present

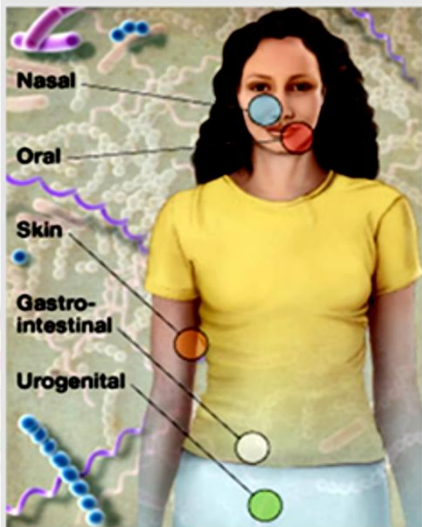


Human Microbiome Project, Phase One: *a community resource* (<http://commonfund.nih.gov/hmp>)

Phase 1 (\$181M): Survey of the microbiome in humans

“Who’s there?”

Healthy cohort study



Clinically healthy

300 male/female

18-40 y.o.

5 major body regions
(18 body sites)

Up to 3 visits in 2 yrs

No antibiotics, probiotics,
immunomodulators

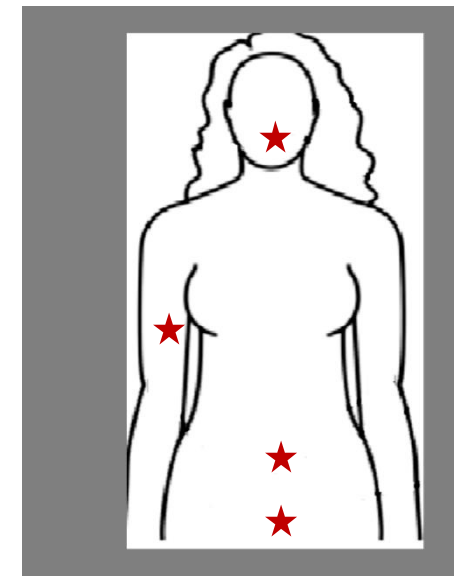
Microbiome-associated conditions

Skin: eczema, psoriasis, acne

GI/oral: esophageal adenocarcinoma, necrotizing enterocolitis, pediatric IBS, ulcerative colitis, Crohn’s Disease

Urogenital: bacterial vaginosis, circumcision, sexual histories

Demonstration Projects



case:control



Human Microbiome Project, Phase Two: *a community resource* (<http://hmp2.org>)

Phase 2 (to date, ~\$35M): Integrative HMP “iHMP”

“What are they doing?”

Analyse biological properties of both *microbiome & host over time* to look for biomarkers of health and disease.

Three “model” microbiome-associated conditions:



Pregnancy & Preterm Birth

Multi-Omic Microbiome Study: Pregnancy Initiative (MOMS-PI)



Inflammatory Bowel Disease

Characterizing the gut microbial ecosystem for diagnosis and in therapy in IBD



Prediabetes

Microbiome and host changes during respiratory and other stress conditions in individuals at risk for type 2 diabetes

longitudinal studies

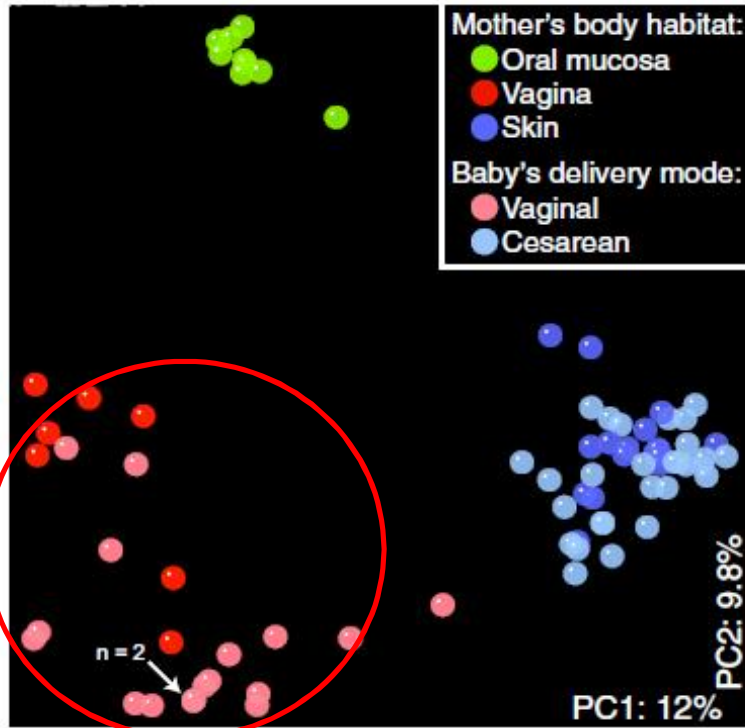


Early findings about the microbiome

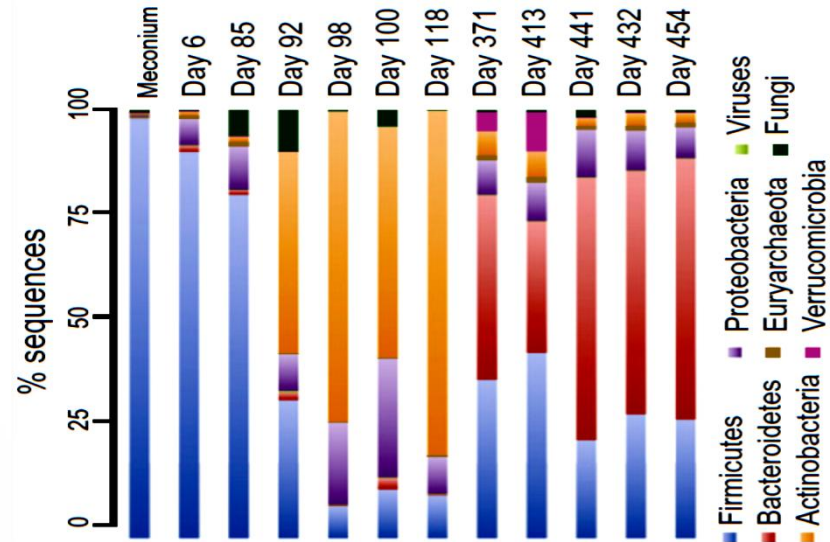


Microbiota acquired anew each generation.

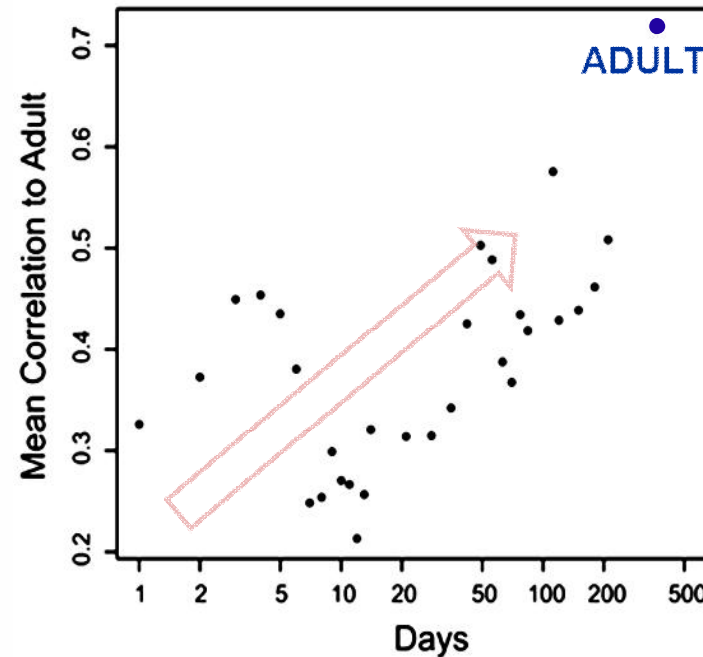
Dominguez-Bello et al. (2010).



- 1) Infants obtain inoculum from mother or environment.
- 2) Microbial succession over ~1-2 yrs.
- 3) Microbiome becomes "adult-like" in ~1-2 yrs.



Koenig et al. (2010)



Palmer et al. (2007)

Development of the immune system



newborn

three month old

one year old

six years old

Maternally-acquired (passive) immunity →

← Adaptive immunity →

Maternal immune properties transferred *in utero*.

Infant begins producing antibodies.

Antibodies at 15-20% of adult levels.

Normal antibody levels.



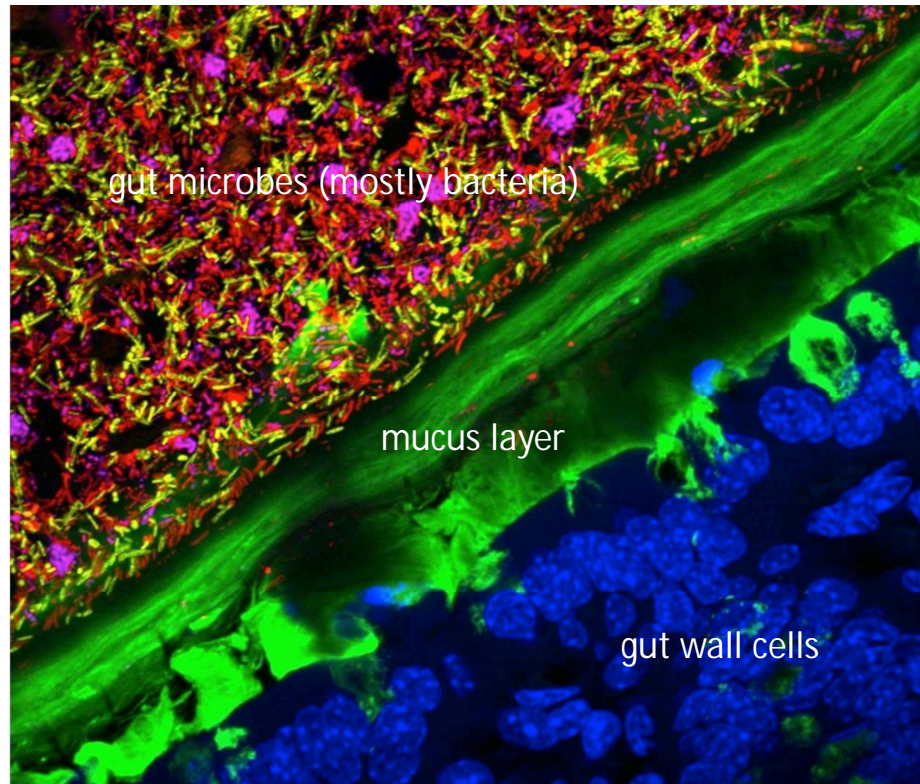
Sources of microbes to the newborn, infant and child



newborn	three month old	one year old	six years old
Uterus		Breastmilk, food	Food
Amniotic fluid		Family members	Other humans
Vagina		Pets/animals	
Breastmilk			
Skin			
Environment	Environment Environment

We co-evolved with our microbiome: Immune system cannot mature without specific microbes.

Some bacteria induce host *pro-inflammatory* response to protect against infection.



Others bacteria induce host *anti-inflammatory* response to restore immune system balance.

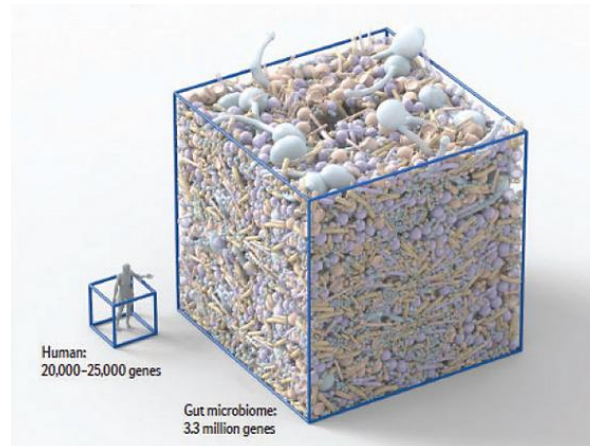
Cross section of gut epithelium and bacterial community.
(blue = gut wall cells green = mucous layer yellow and fuschia = bacteria)

micrograph from Earle et al. (2015)



Each of us host ~4000 bacterial species,
which include ~4,000,000 bacterial genes.

Human genome? 20,000-23,000 genes

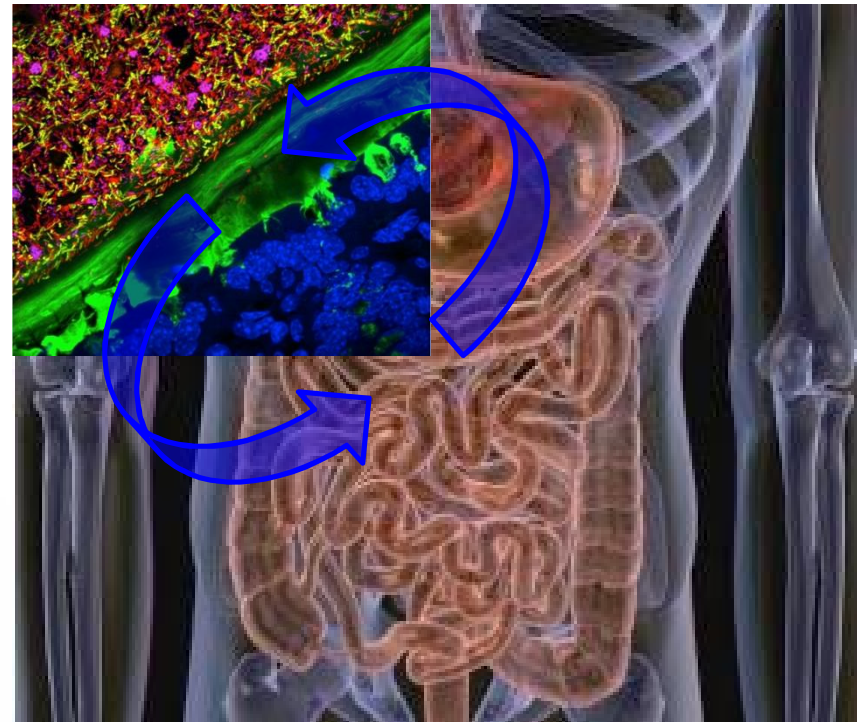


*100-200x more
bacterial genes
than human genes
in human
ecosystem.*

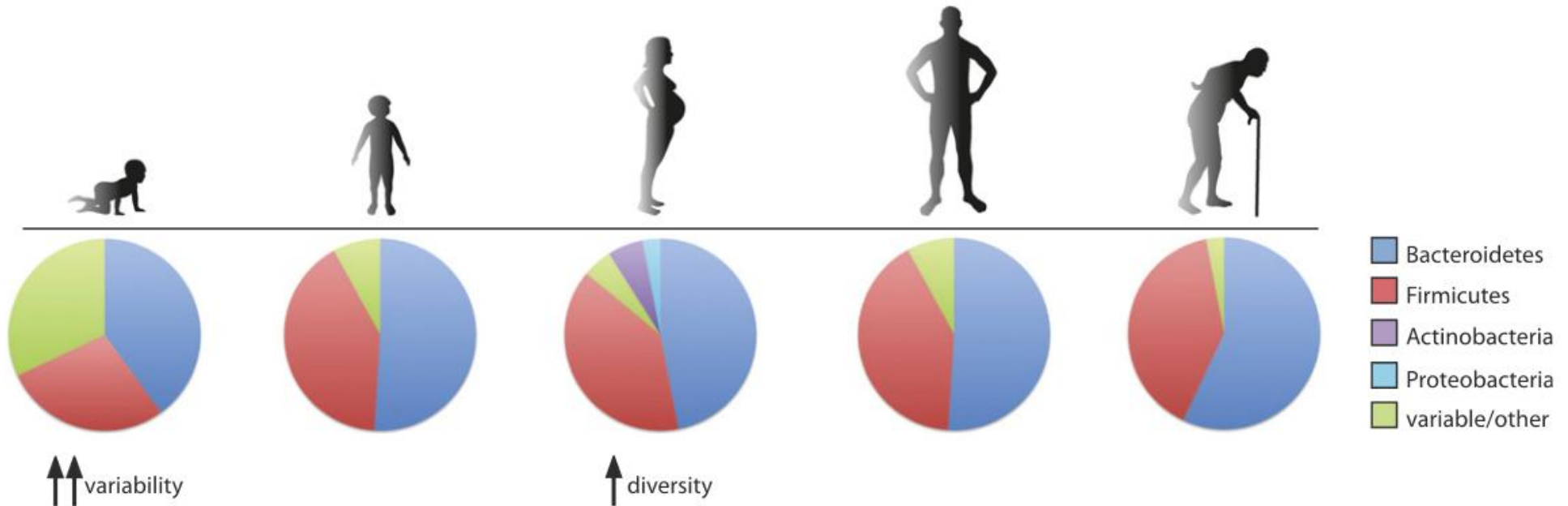


Microbiota and host *interact* to regulate human health.

- ✓ 'educates' the immune system to recognize self from nonself,
- ✓ digests the 'indigestables' (ex. plant material, host cells, mucus),
- ✓ produces energy substrates for host cells (ex. SCFAs),
- ✓ metabolizes drugs,
- ✓ produces beneficial compounds (ex. vitamins, antimicrobials)
- ✓ produces signaling molecules which communicate with the host,
- ✓ gut microbiota communicate with the brain



Though the human microbiome is a fixed feature,
it is also a variable trait.

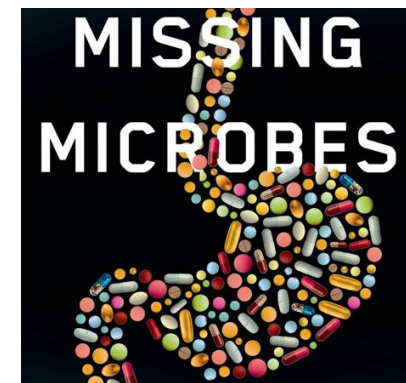
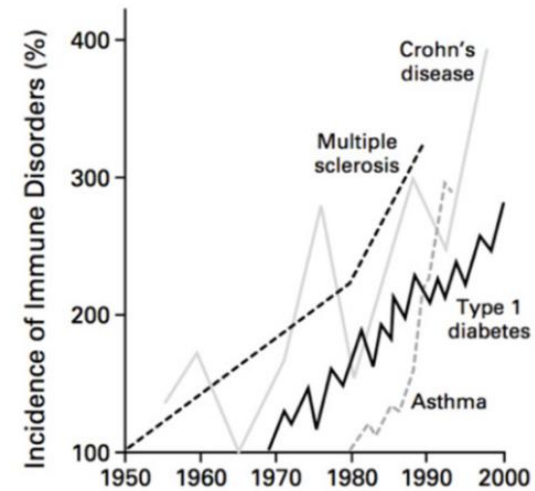


- ✓ Between generations
- ✓ Throughout our lifetimes
- ✓ Between health and disease

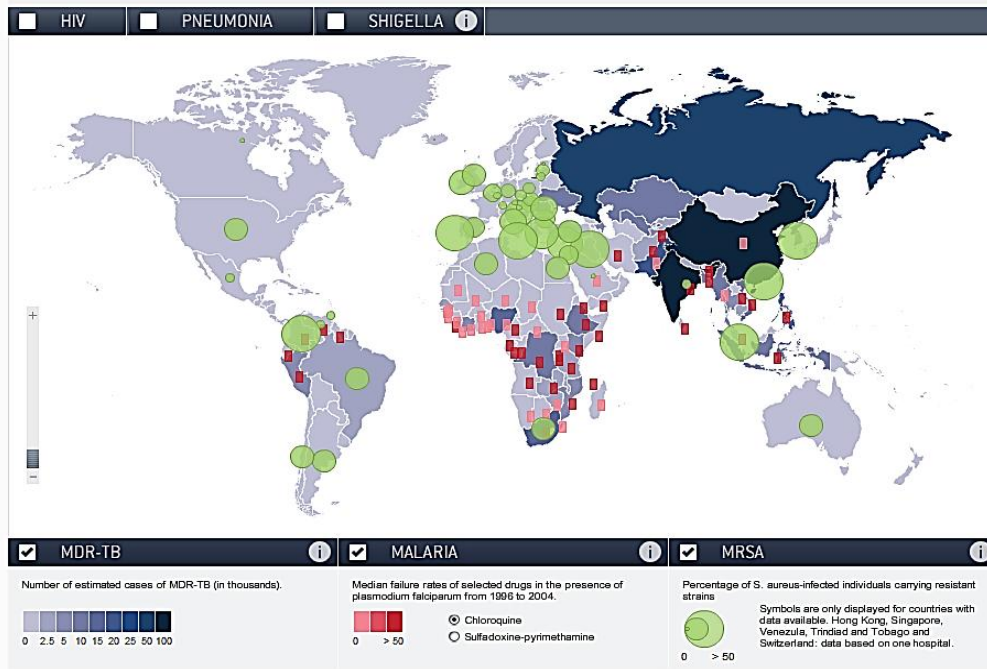
Unlike the human genome, the microbiome is naturally mutable.



Disturbances to our microbiomes and modern diseases?



DOCUMENTED EXAMPLES OF DRUG RESISTANCE BY DISEASE



From Center for Global Development



The list of potential microbiome-associated diseases/disorders is growing....

Brain/behavior: general brain function, epilepsy, Alzheimer's, psychiatric disorders

Heart: cardiovascular diseases

Gut: irritable bowel disease (IBD), ulcerative colitis, Crohn's disease, GERD, necrotizing enterocolitis (NEC)



Skin: eczema, psoriasis, acne
Lung: asthma, cystic fibrosis

Vagina: bacterial vaginosis, preterm birth

Liver: non-alcoholic liver disease (NAFLD), alcoholic steatosis

Cancers: esophageal cancer, colorectal cancer, Hodgkin's lymphoma, cervical cancer, liver cancer, gastric cancer

Systemic: obesity, metabolic syndrome, rheumatoid arthritis, multiple sclerosis, autism, type 1 diabetes, type 2 diabetes



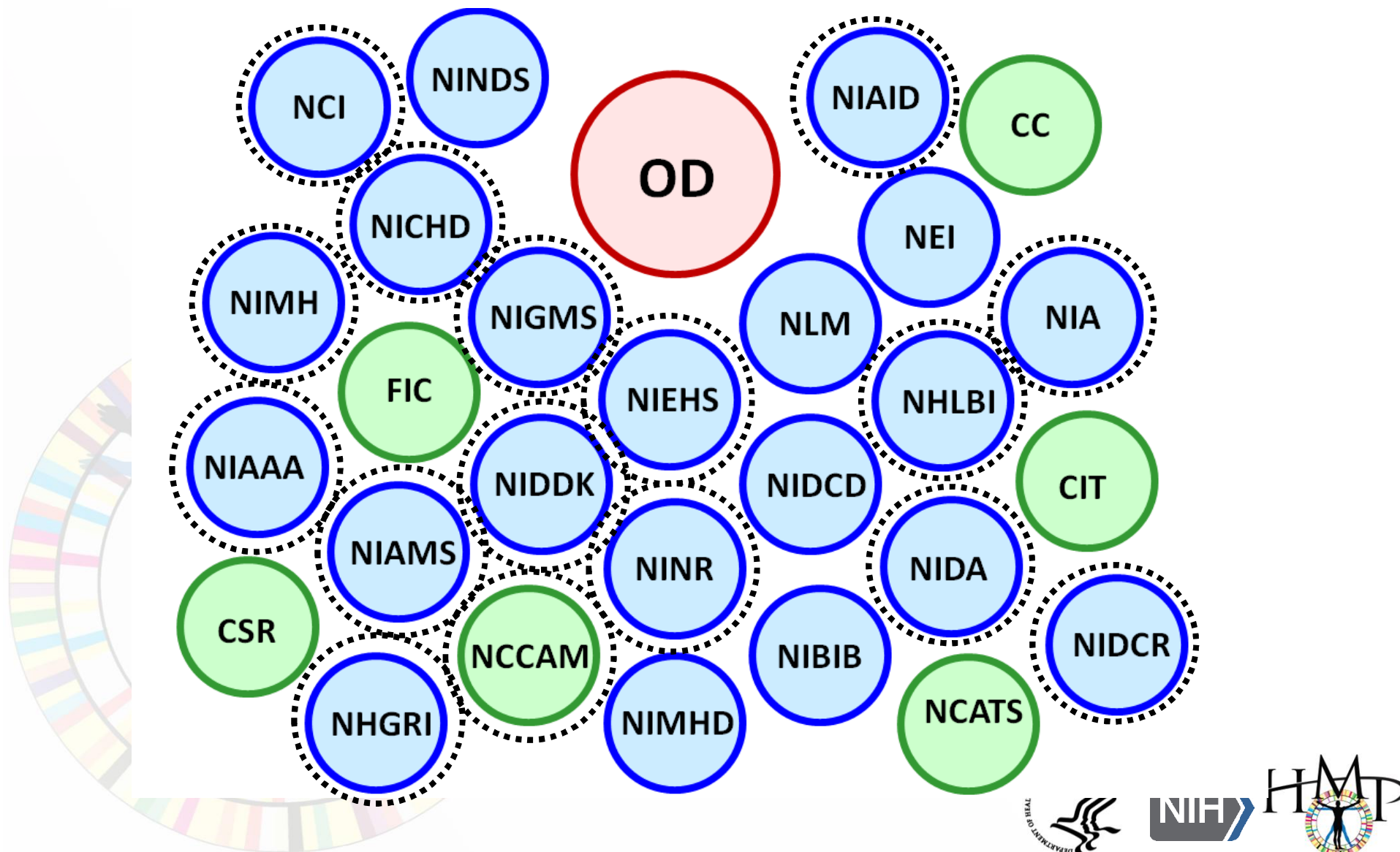
Microbiome research beyond the HMP

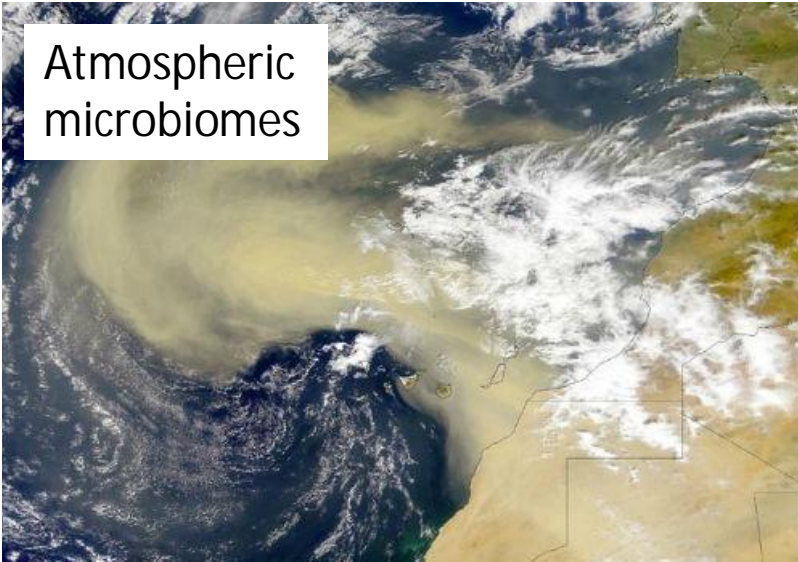


NIH consists of

27 Institutes, Centers and Offices (ICOs)

2012-2013: approx. \$100-150M/yr invested in the human microbiome





Atmospheric microbiomes



Warfighter microbiomes

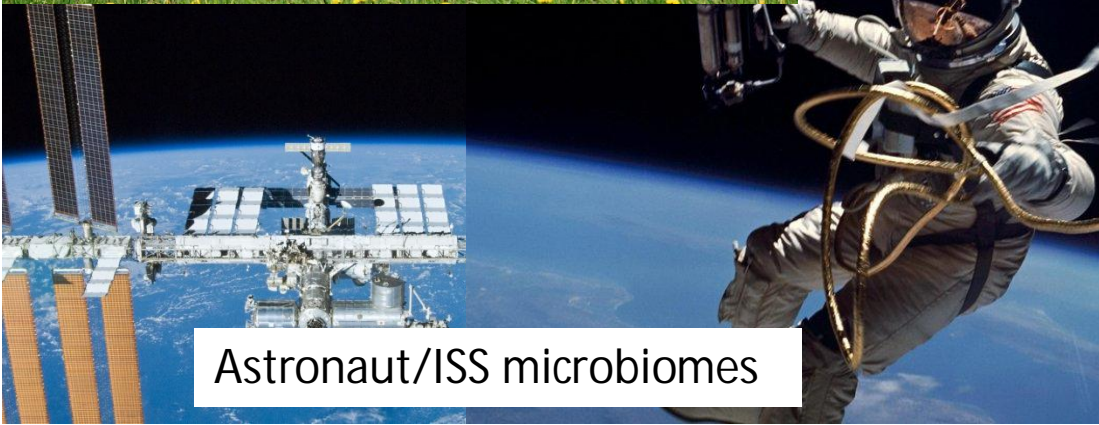


Livestock/poultry microbiomes



Soil & plant microbiomes

Coral reef & oceanic microbiomes



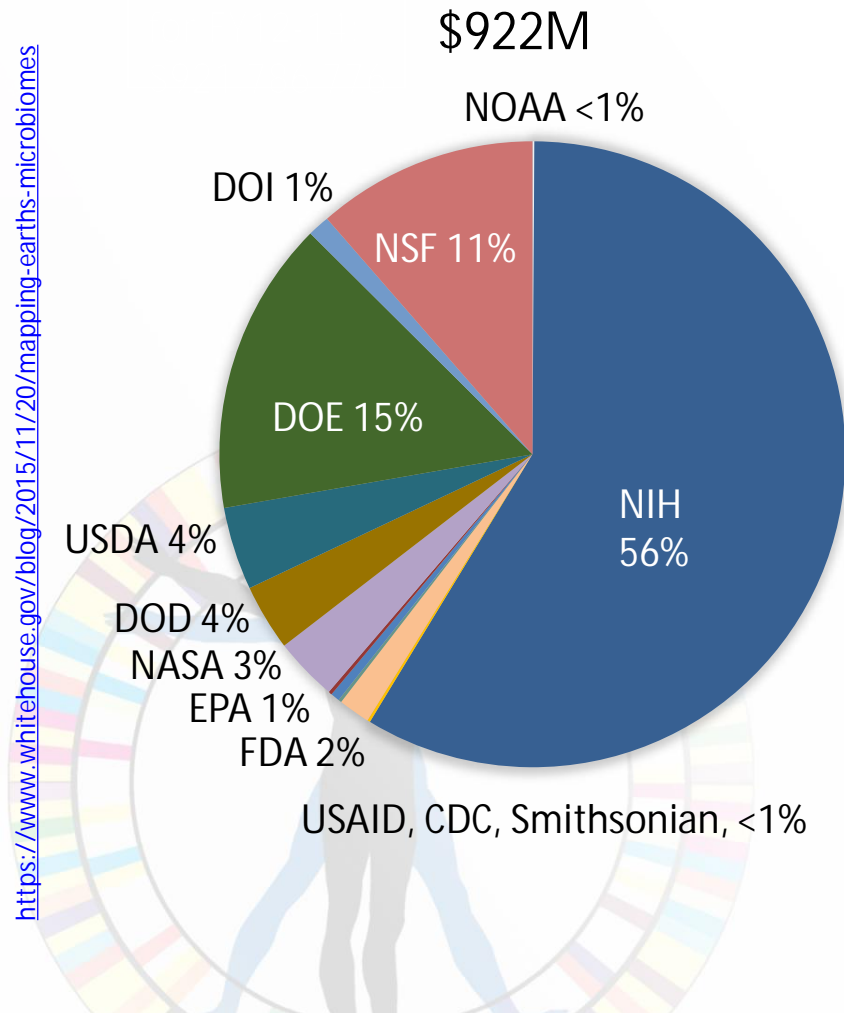
Astronaut/ISS microbiomes



Hospital & built environment microbiomes

FastTrack Action Committee – Mapping the Microbiome (FTAC-MM)

<https://www.whitehouse.gov/blog/2015/11/20/mapping-earths-microbiomes>



FTAC-MM:

- ✓ OSTP charter
- ✓ FY12-14 data call
- ✓ microbiome 'writ large'
- ✓ 6 Departments (16 agencies), 4 Independent Agencies, 1 quasi-governmental entity

Data call results:

- ✓ \$922M over FY12-14
- ✓ NIH comprised 56% of this total
- ✓ NSF and DOE comprised an additional 26% of this total

Nature Microbiology paper:

<http://dx.doi.org/10.1038/nmicrobiol.2015.15>



Microbiome research comes of age: The National Microbiome Initiative



The screenshot shows the top of a White House blog page. At the top left, it says "the WHITE HOUSE PRESIDENT BARACK OBAMA". On the right, there are links for "Contact Us" and "Get Email Updates". Below this is a navigation bar with icons for "BRIEFING ROOM", "ISSUES", "THE ADMINISTRATION", "PARTICIPATE", and "1600 PENN". There is also a search icon. The main content area starts with "HOME · BLOG" and a large heading "Announcing the National Microbiome Initiative". Below the heading is the date and author: "MAY 13, 2016 AT 6:00 AM ET BY JO HANDELSMAN". There are social media icons for Twitter, Facebook, and Email. A summary paragraph follows: "Summary: The new National Microbiome Initiative aims to advance microbiome science in ways that will benefit individuals, communities, and the planet." At the bottom is a large graphic with the text "THE NATIONAL MICROBIOME INITIATIVE". The word "MICROBIOME" is the largest and is filled with various images of microbes and nature. The words "THE NATIONAL" and "INITIATIVE" are in smaller blue boxes above and below "MICROBIOME" respectively.

the WHITE HOUSE PRESIDENT BARACK OBAMA

Contact Us Get Email Updates

BRIEFING ROOM ISSUES THE ADMINISTRATION PARTICIPATE 1600 PENN

HOME · BLOG

Announcing the National Microbiome Initiative

MAY 13, 2016 AT 6:00 AM ET BY JO HANDELSMAN

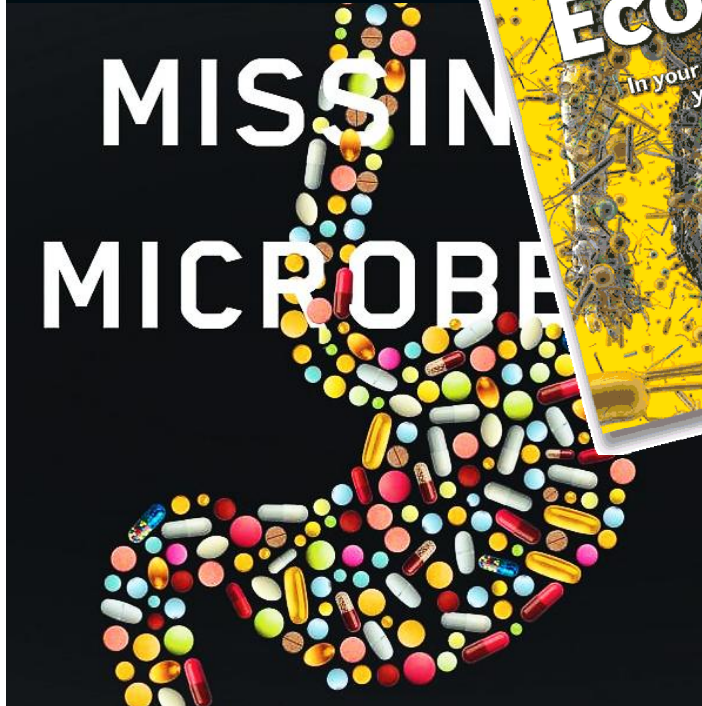
Summary: The new National Microbiome Initiative aims to advance microbiome science in ways that will benefit individuals, communities, and the planet.

THE NATIONAL
MICROBIOME
INITIATIVE

<https://www.whitehouse.gov/blog/2016/05/13/announcing-national-microbiome-initiative>



Questions?



lita.proctor@nih.gov