

The Economist

The Catholic church's unholy mess
Paul Ryan: the man with the plan
Generation Xhausted
China, victim of the Olympics?
On the origin of specie

AUGUST 18TH - 24TH 2012

Economist.com

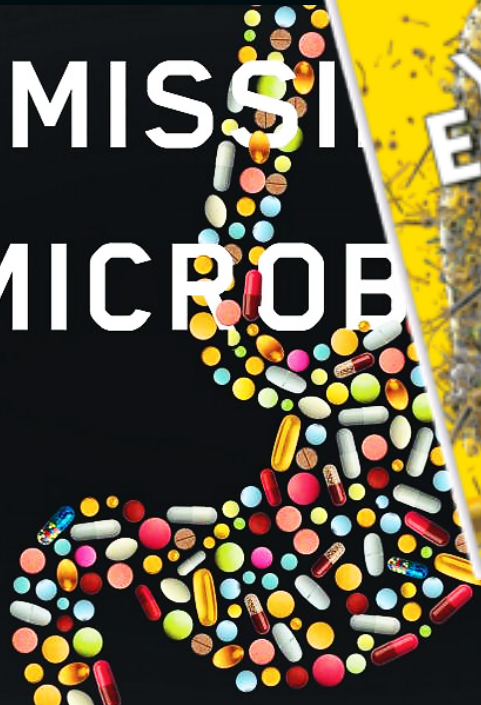
Microbes maketh man



The Human Microbiome



MISSISSIPPI MICROB



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NHGRI/NIH
SLA: June 13, 2018

Topics for this talk

- ✓ **What is the human microbiome?**
- ✓ **NIH Human Microbiome Project**
- ✓ **Recent advances in human microbiome research**
- ✓ **US gov't-wide microbiome research**

What are microbes?

- ▶ often used to mean bacteria
- ▶ broader meaning: microscopic lifeforms
- ▶ many kinds (bacteria, archaea, viruses, bacteriophage, fungi, protozoa)
- ▶ in nature, key principles: don't live alone, interact as communities



Humanity's war against infectious disease

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





~1400 human pathogenic microbes

vs.

~1 trillion 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

The Human Microbiome

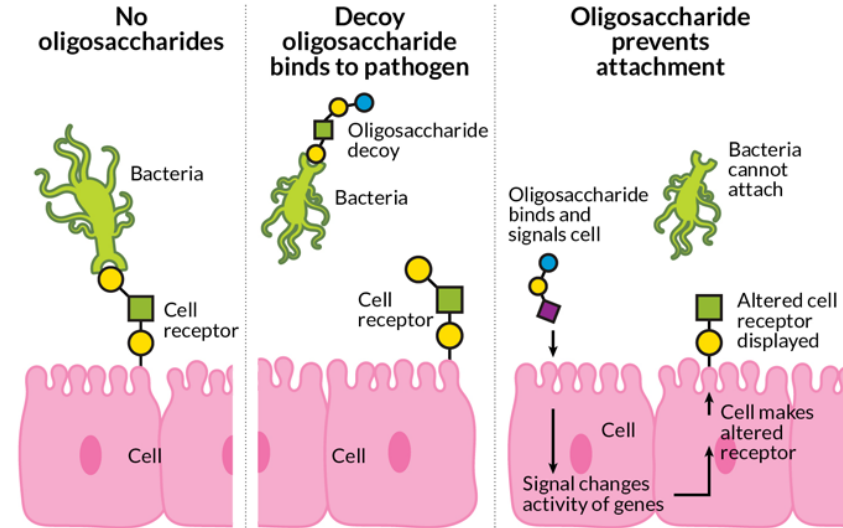
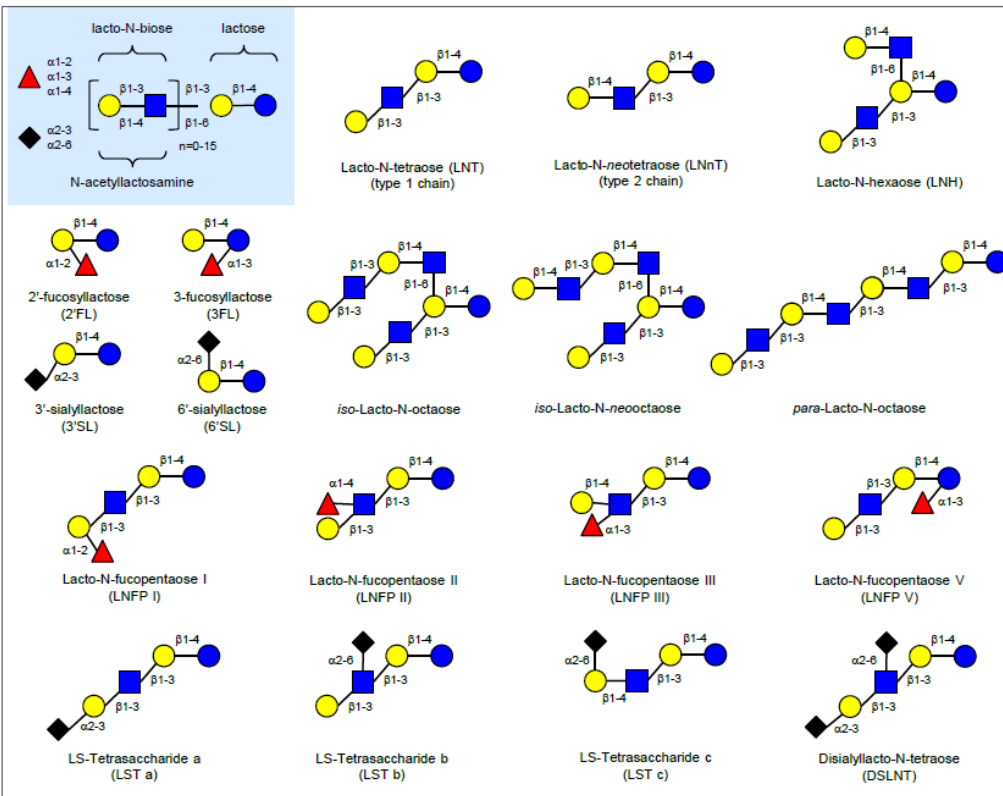
1. **Thousands of microbial species***, possessing millions of genes, live with humans.

Human milk oligosaccharides (HMOs)*:

- 1) microbial food for the developing microbiome
- 2) protects against invading pathogens

100s of different kinds of HMOs

HMOs as molecular decoys



[Breastmilk: (per 100 mls) protein = 2.5 g, fat = 5 g and *HMOs = 0.5 g]

Co-development of microbiome/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.

Microbiome becomes more 'adult-like' over first 1-2-3 years of life.

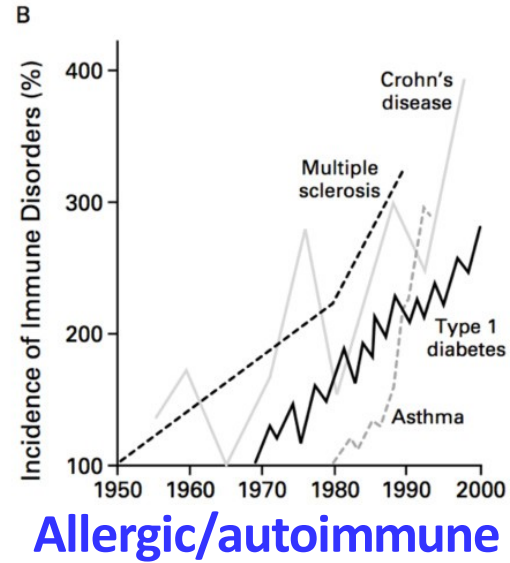
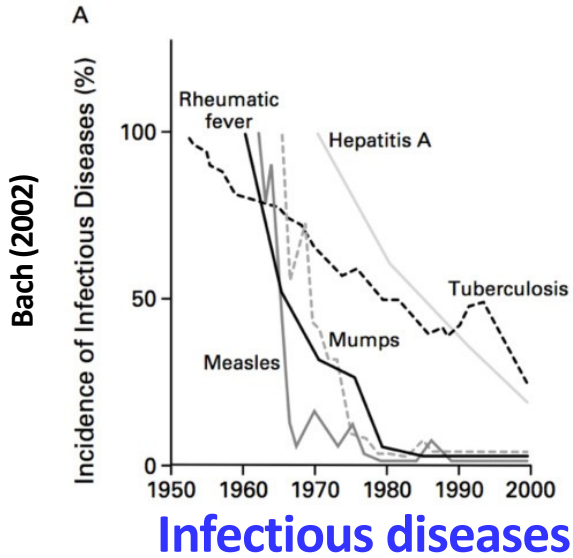
Microbiota and host *interact* to regulate human health.

- ✓ Digests the 'indigestibles'
(ex. plant material, host cells, mucous)
- ✓ 'Educates' the immune system to recognize self from nonself,
- ✓ Produces energy substrates for host cells (ex. SCFAs such as acetate),
- ✓ Detoxifies/activates drugs,
- ✓ Produces beneficial compounds (ex. vitamin B and K, antimicrobials)
- ✓ Communicates with the brain



Rationale for Human Microbiome Project

Changes in the microbiome and appearance of 'modern' diseases?



Ten-year (FY2007-2016) Human Microbiome Project

\$215M community resource program



HMP program goals

- 1) *Develop research resources:*
e.g. reference datasets,
clinical & analytical methods,
statistical & computational
tools and pipelines
- 2) *Rapidly release resources:*
e.g. public repositories &
community databases, HMP
Data Analysis Coordination
Center (DACC), GitHub &
meetings/webinars
- 3) *Build research community*

NIH Human Microbiome Project

\$215M community resource

HMP resources developed in both phases

1) Sequence and other 'omic reference datasets of microbiome and host

- 16S rRNA & metagenome sequences from five major body regions of 300 adult men and women [*>2,000 metagenomes (10 TB) of sequence data. ~20-30 TB total for Phase One and Two.*]
- Human genome sequences from subjects
- Multi-omic profiles (e.g. transcript, protein, metabolite) from hosts and microbiomes

2) Computational, statistical tools & pipelines for multi-omic data analyses

- Sequence analysis, including meta-transcriptomic analysis
- Composition, metabolic pathway, network analysis
- Meta-proteomic analysis
- Meta-metabolomic analysis
- Cloud-based analyses

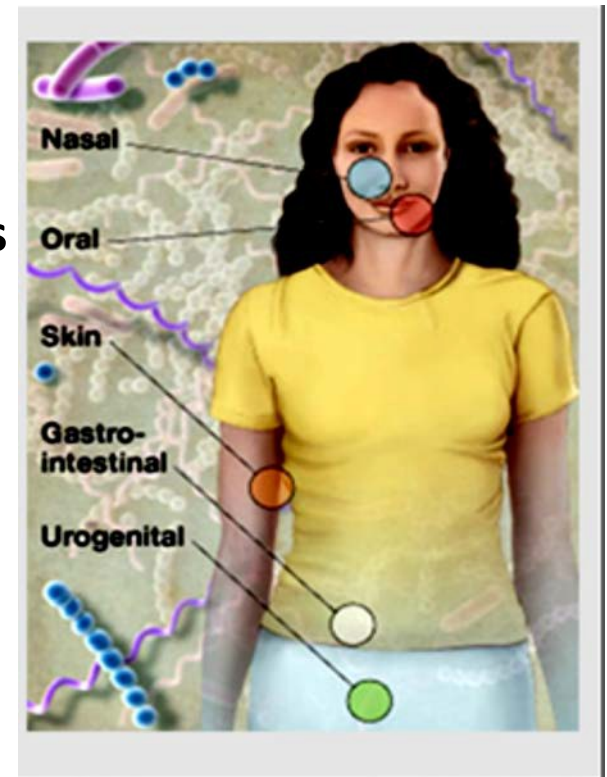
3) Analytical protocols for microbiome sample analysis

4) Clinical protocols for collection/storage of samples

- Skin
- Oral
- GI tract
- Urogenital tract (both vagina and penis)
- Nares

5) IRB protocols for clinical studies of microbiome

6) Identification/evaluation of ethical issues



HMP Data Analysis and Coordination Center (www.hmpdacc.org)

NIH Human Microbiome Project



Characterization of the microbiomes of healthy human subjects at five major body sites, using 16S and metagenomic shotgun sequencing.

Enter HMP1



Characterization of microbiome and human host from three cohorts of microbiome-associated conditions, using multiple 'omics technologies.

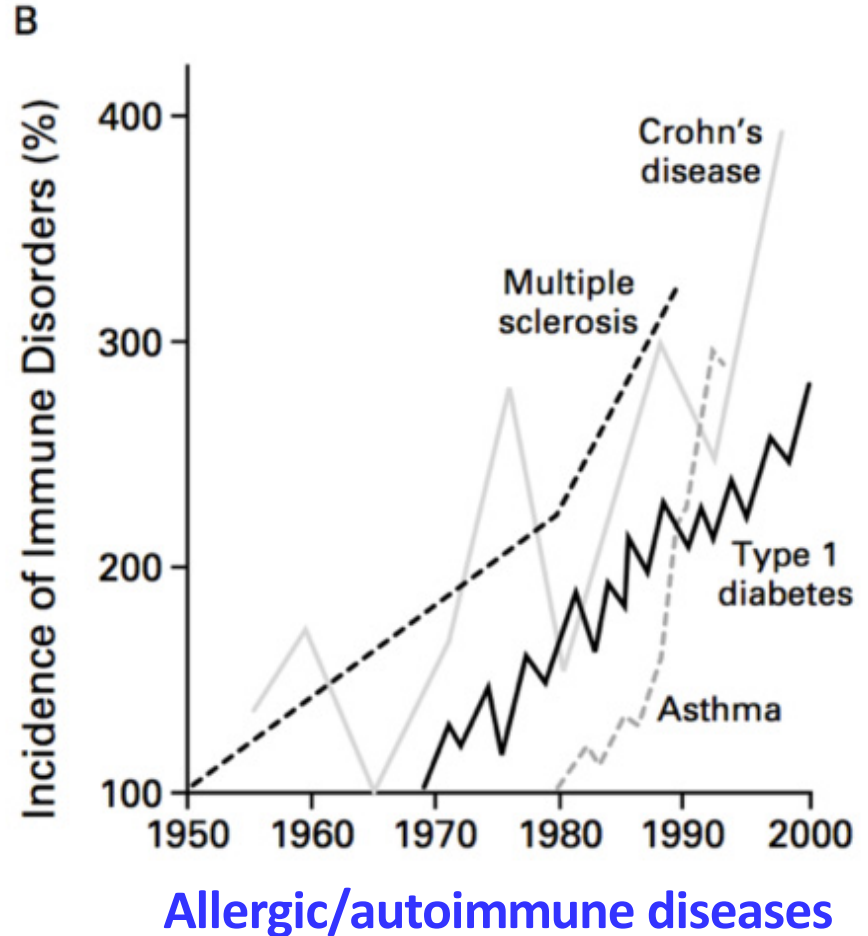
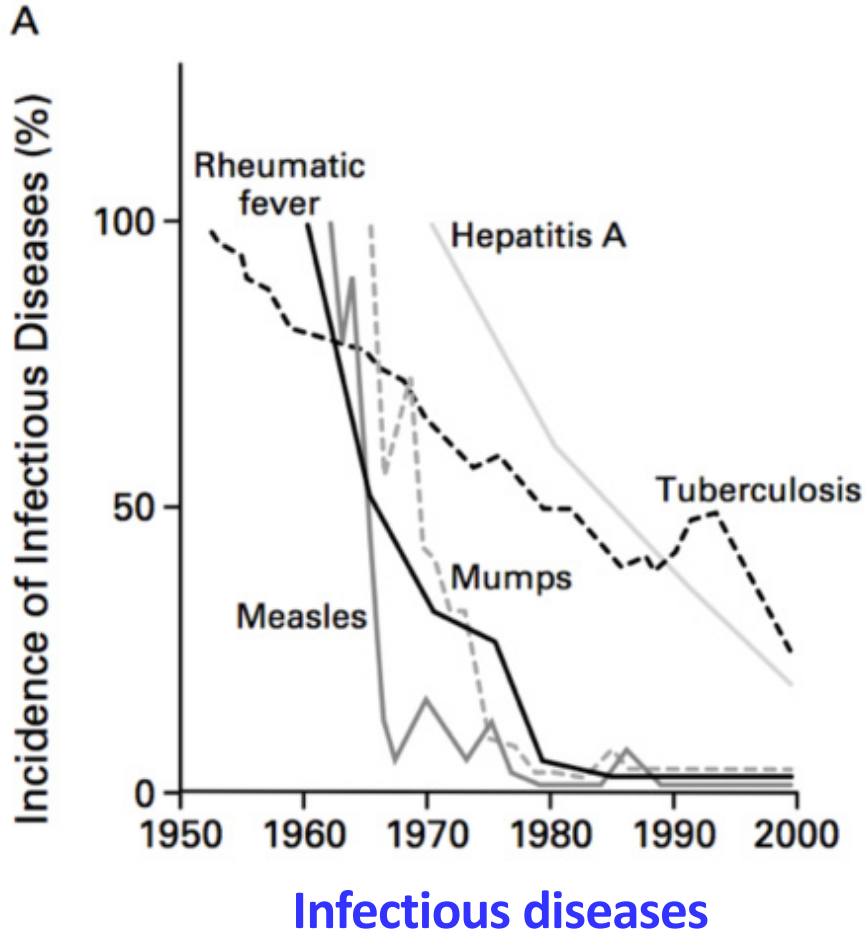
Enter iHMP

2018

- ✓ **iHMP Nature collection**
 - 3 flagship papers
 - 35 companion papers
- ✓ **HMP DACC:**
 - **multi-omic datasets**
 - **associated tools**
 - **pipelines**

All primary and derived datasets, tools, and analytical pipelines

Are changes in the microbiome related to appearance of modern diseases?



Increase in immune disorders over last ~ 75 yrs

Possible factors which may be impacting the microbiome

Contemporary practices:

sanitation

clean water

bathing

antibiotic use

caesarean birth

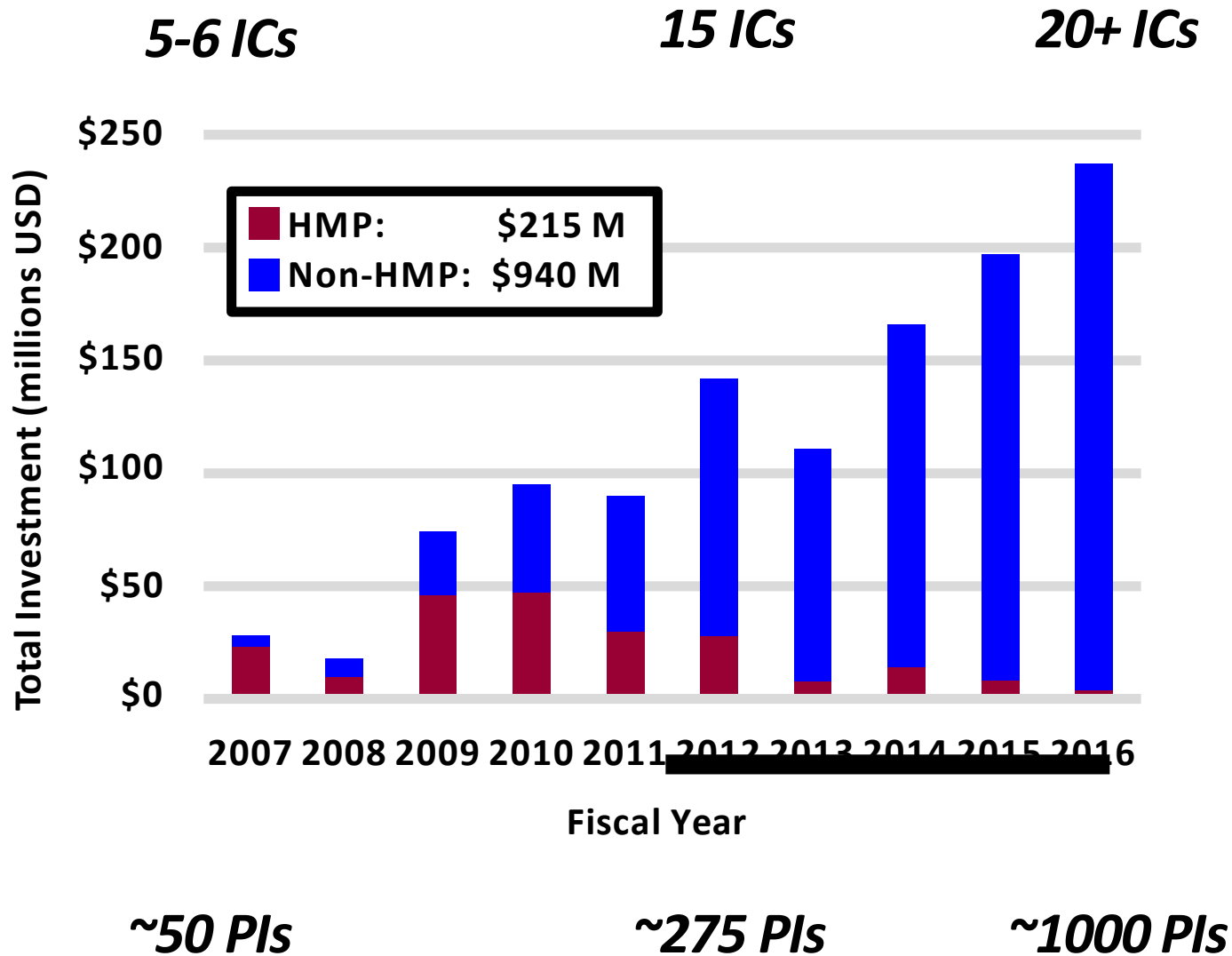
formula feeding

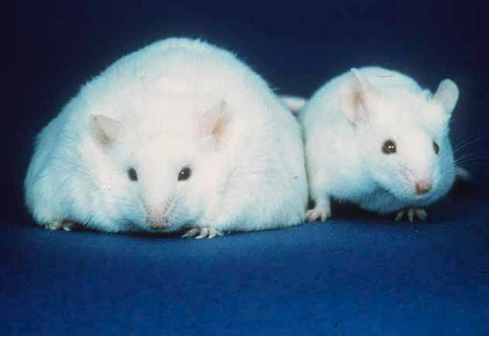
Hg amalgams

processed foods (low fiber/high sugar)

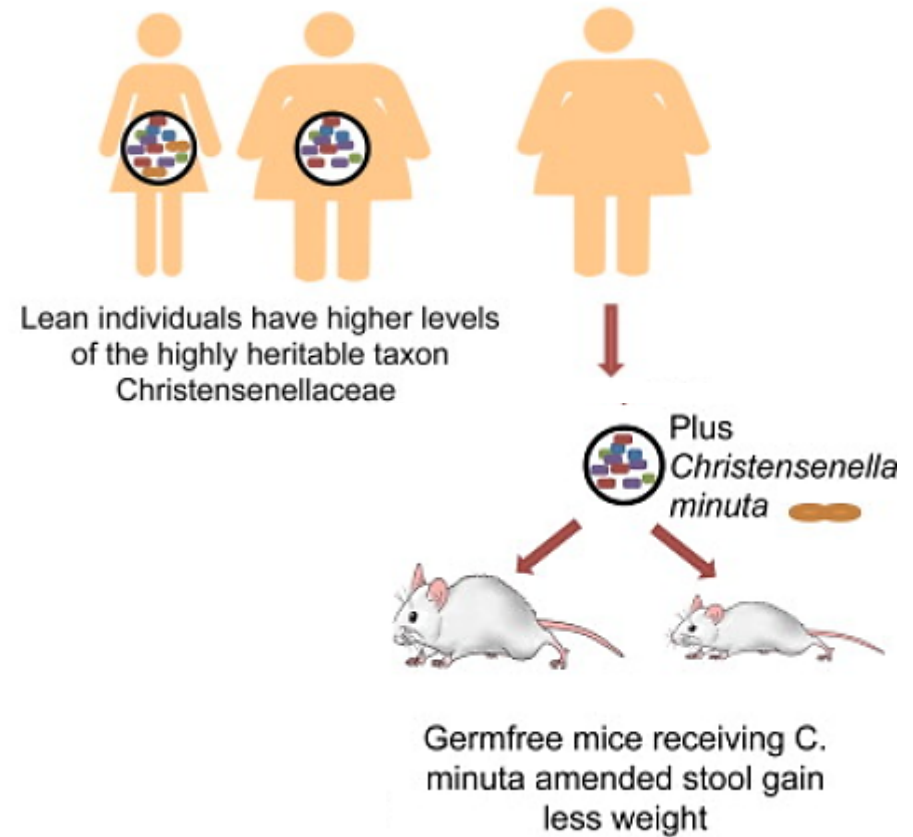
etc.

Expansion of human microbiome research at NIH over FY2007-2016



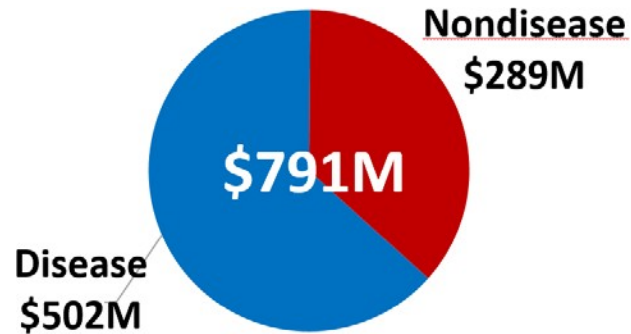


Q: Do our gut microbiota regulate our phenotype?



Proof-of-principle: Gut microbiota can regulate host phenotype, in this case – obesity.

Microbiome(s) and disease(s)



100+ classes of disease over FY12-16

GI tract: irritable bowel disease (IBD), ulcerative colitis, Crohn's disease, GERD, necrotizing enterocolitis (NEC) obesity, metabolic syndrome, type 1 and type 2 diabetes

Heart: cardiovascular diseases

Brain/mental: multiple sclerosis, epilepsy, Alzheimer's, autism, psychiatric disorders



Cancers: Hodgkins' lymphoma, liver, gastric esophageal, colorectal, cervical

Lungs: asthma, cystic fibrosis

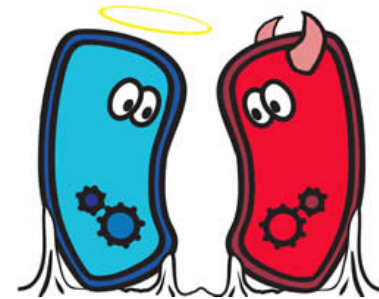
Skin: eczema, psoriasis, acne, rheumatoid arthritis

Vagina: bacterial vaginosis, preterm birth

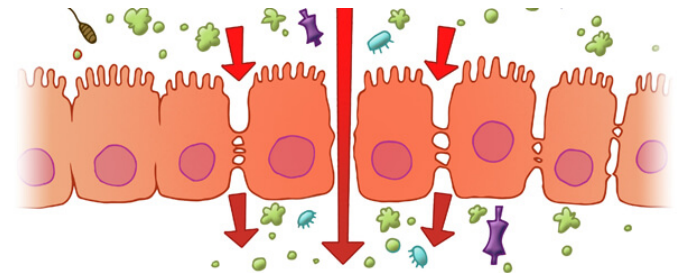
Liver: non-alcoholic liver disease (NAFLD), alcoholic steatosis

Dysbiosis?

Commensal microbes becomes pathogenic
(‘pathobiont’, ex. IBD)



Translocation of commensal microbes
(ex. lupus)

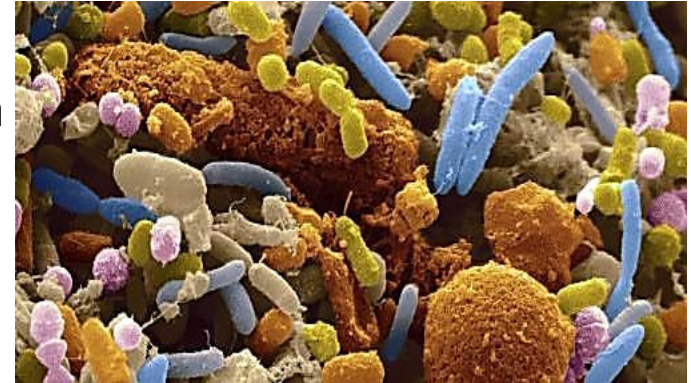


At least three general *mechanisms* by which microbes can cause disease, each of which will inform specific interventions.

Developing microbiome-based treatments

Microbiome-based therapeutic interventions

- Fecal microbiota transplantation
- Microbiome-derived microbial consortia
- Live biotherapeutic products
- Bacteriophage therapy
- Pharmacobiotics

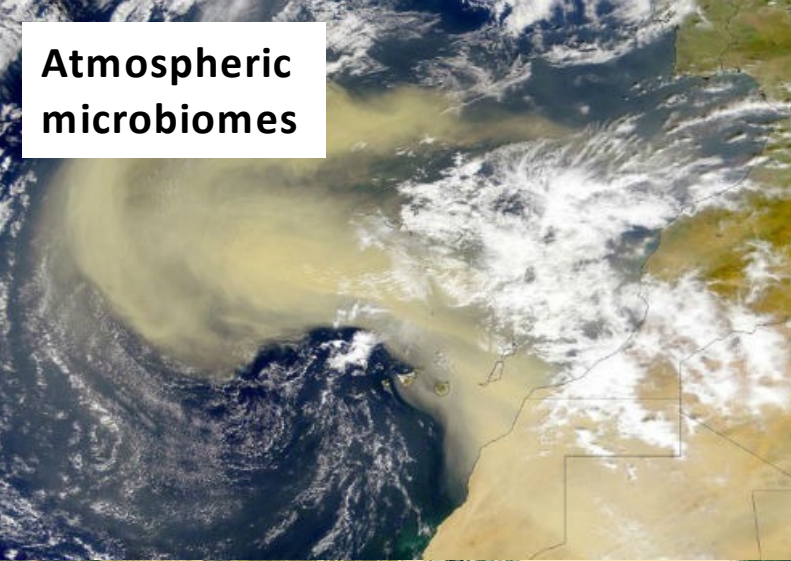


Microbiome as a source of new pharmaceuticals



Mined HMP metagenomic data to discover and develop new and novel antibiotics

**Atmospheric
microbiomes**



**Warfighter
microbiomes**



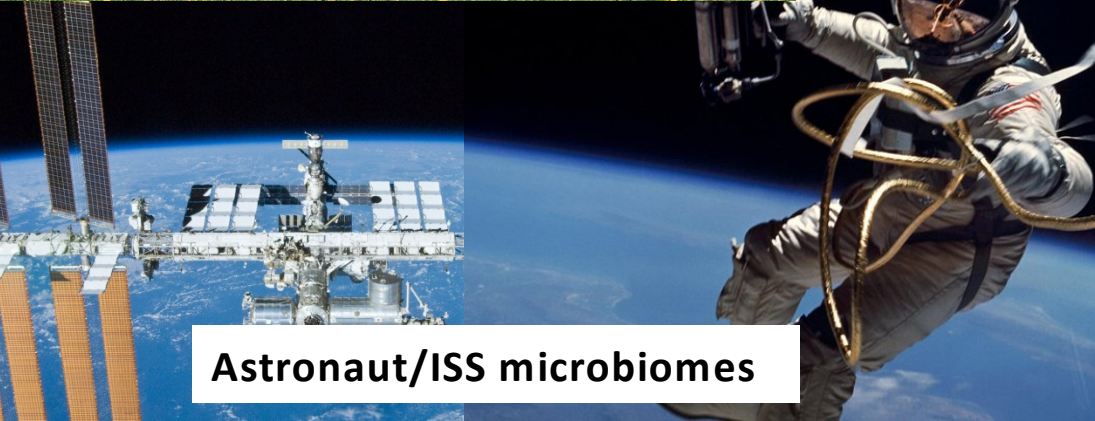
**Coral reef & oceanic
microbiomes**



**Soil & plant
microbiomes**



Livestock/poultry microbiomes



Astronaut/ISS microbiomes



**Hospital & built
environment
microbiomes**

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



2016: The National Microbiome Initiative



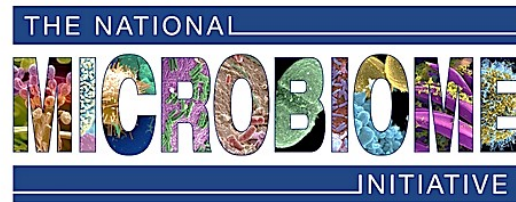
HOME - BLOG

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.



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

16-agency Microbiome Interagency Working Group (MIWG) Federal strategic plan released FY18

Initiatives recently launched or to be launched (e.g. DOD, USDA, NIST)



MIWG

Summary

The human microbiome

- 1000s of microbial species, millions of microbial genes
- Microbiome made up of bacteria, viruses, fungi
- Metabolically diverse, active, mutable 'microbial organ(s)'

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How good of the
benefits of faecal transplants and other things you would rather not know before breakfast

Questions?

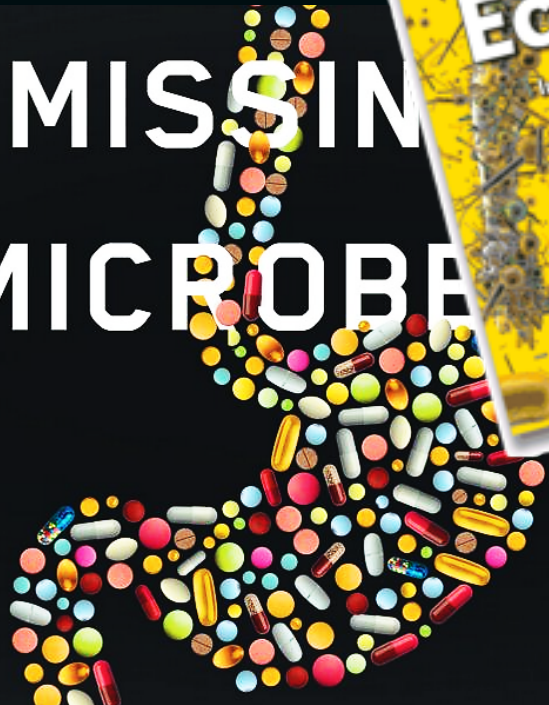


THE SECRET LIVES OF

Germs

WHY BASKETBALL WON'T LEAVE PHIL MICKELSON ALONE BY SAM JOHNSON
LEARN FROM OUR MICROBIOME. BY MICHAEL POLLAN

MISSING MICROBES



Nature

THE INTERNATIONAL WEEKLY JOURNAL OF SCIENCE

Body microbes outnumber our own cells ten to one - it's time we got to know our fellow travellers
PAGES 194, 207 & 208

THE HUMAN MICROBIOME

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