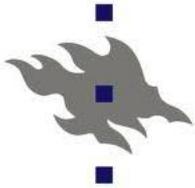


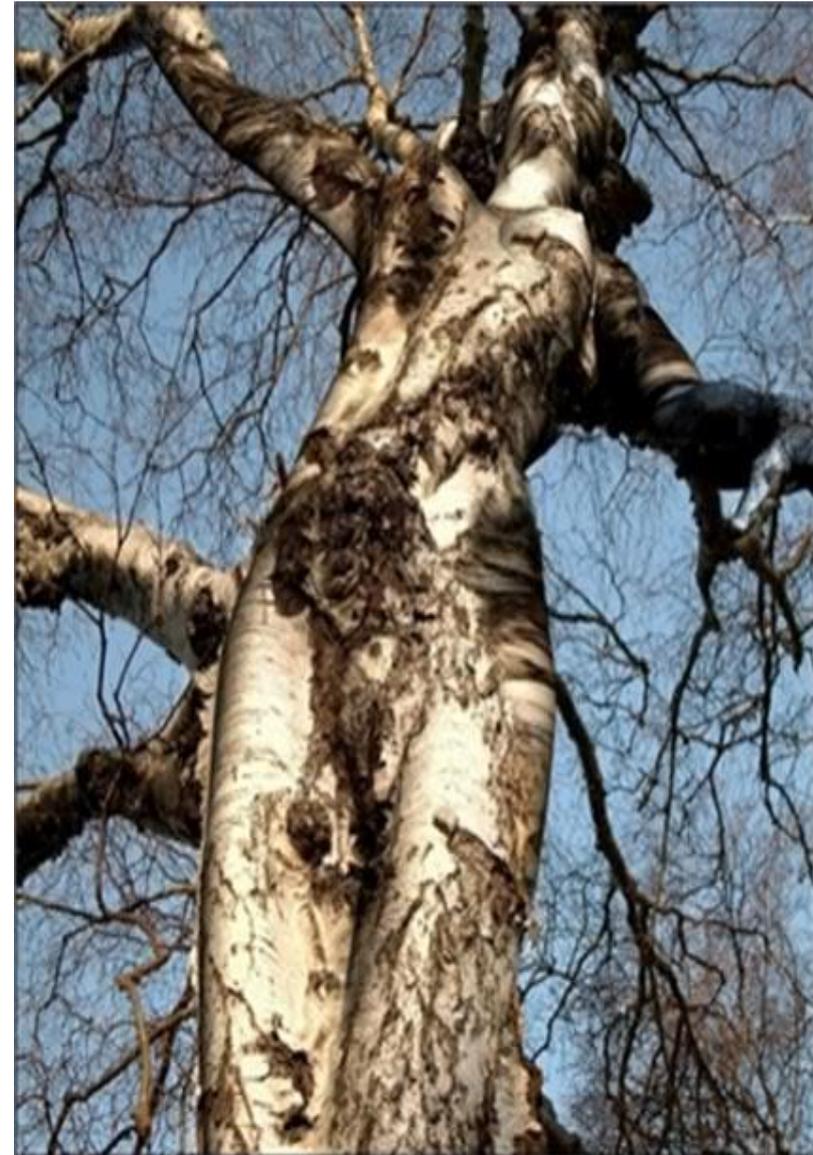
# WE ARE ALL LICHENS:

How symbiosis theory is reconfiguring  
critical biological boundaries

**Scott F. Gilbert**  
**Swarthmore College, USA**  
**University of Helsinki, Finland**



UNIVERSITY OF HELSINKI



## PART 1: THE BODY POLITIC:

A **body politic** is a metaphor wherein a nation is considered to be a corporate entity, a corpus, like the human body.

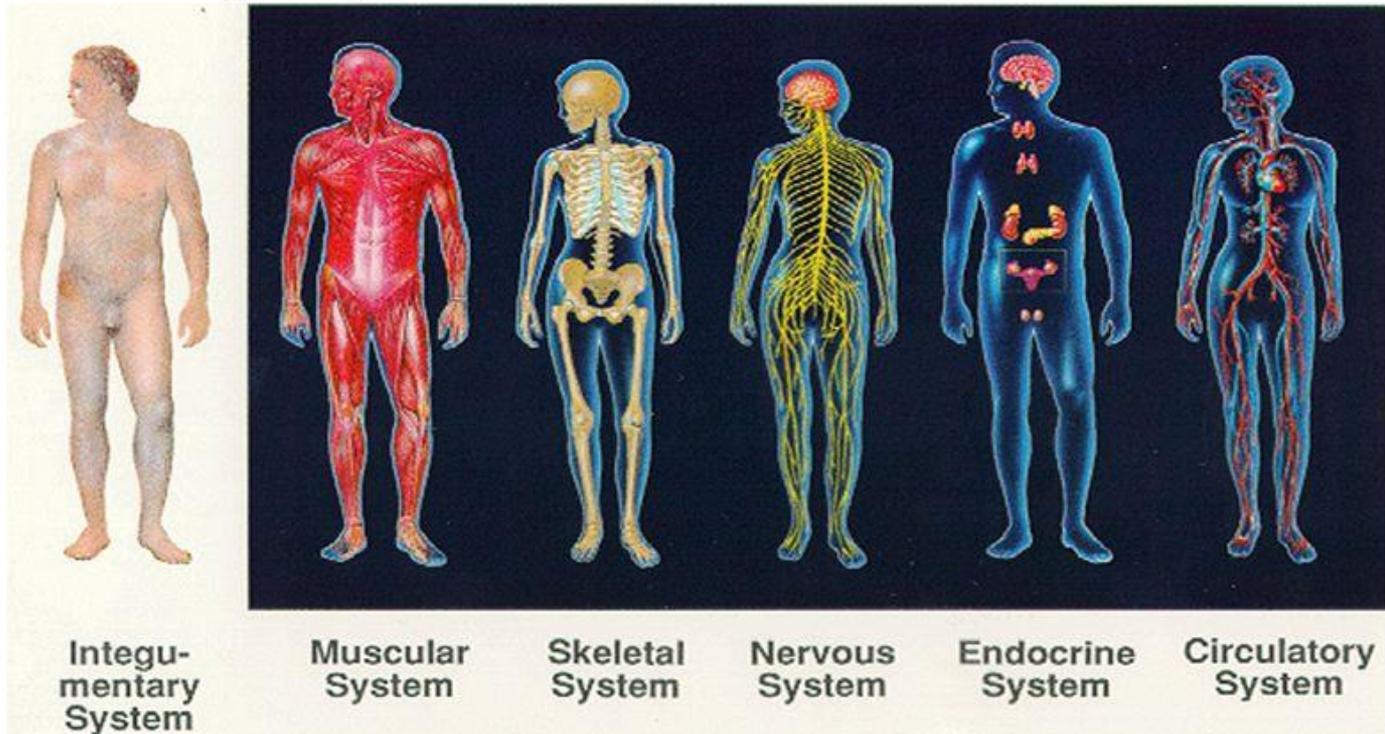
What is true for the body is often true for the polity—and vice versa.



# Example: Division of Labor

## Division of Labour

- **Division of Labor:** organ systems of multicelled body show this compartmentalization of function
  - Help body survive in ways no one tissue can offer



**Emil Durkheim (1859 – 1917):**

**Division of labor** is key to regulating modern societies  
With division of labor, each person contributed to the functioning of the social body by their individual tasks.

Their individual tasks create a value consensus of shared common goals and these help society function in a healthy manner.

These beliefs help create social order through a shared social consensus.



# But what defines the borders of the body?

## Three major types of bodies:

- Body politic defined by **immune system**: Defense  
Boundaries are defended by immune network  
(If I were to put my skin on yours, you'd reject it.)
- Body politic defined by **nervous system**: Culture  
French culture, Western civilization, the American Way  
(If I were to put my brain into you, you'd be me.)
- Body politic defined by **genes**: The tribe or gens  
Finns, French, Germans, Croats, Serbs, Hutu, Tutsi  
(My genes determine who and what I am. I would risk my life for those who share ancestry.)

## **Another extension of body to body politic: The body politic is susceptible to disease**

- 1. Infection.** Body is inherently pure, but susceptible to outside poisons. Communist infiltration. Quarantining Cuba. Disease from active external agents.
- 2. Cancer.** Disease is from part of the body that has escaped regulation: Media, military-industrial complex. “There is a cancer on the presidency.” “We have met the enemy and they are us.” Disease from active internal agents.
- 3. Decrepitude and degeneration:** Disease from old age. The infrastructure is crumbling.

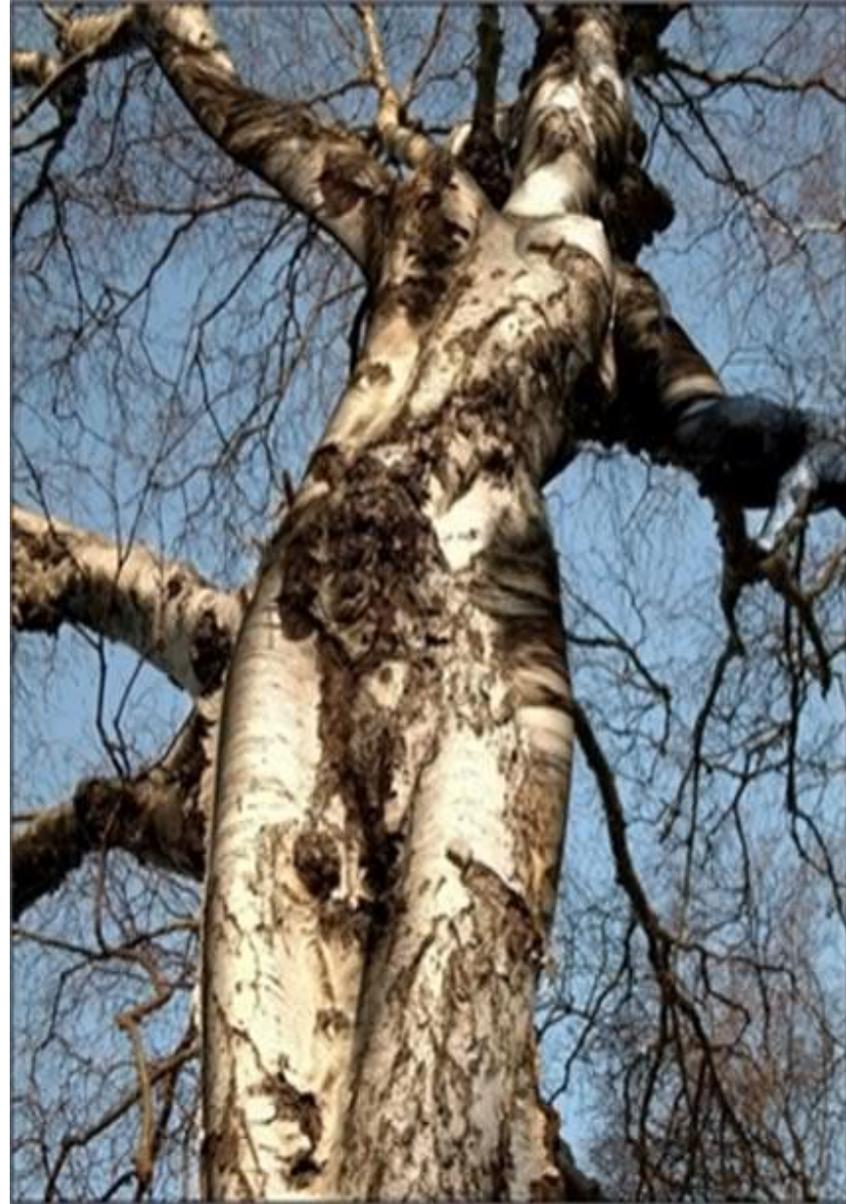
We easily transfer disease from corporal anxieties to political ones.

## **PART 2: OUR NEW BODIES**

How science is deconstructing  
the old notion of individual bodies

and is replacing it with a new  
notion of individuality

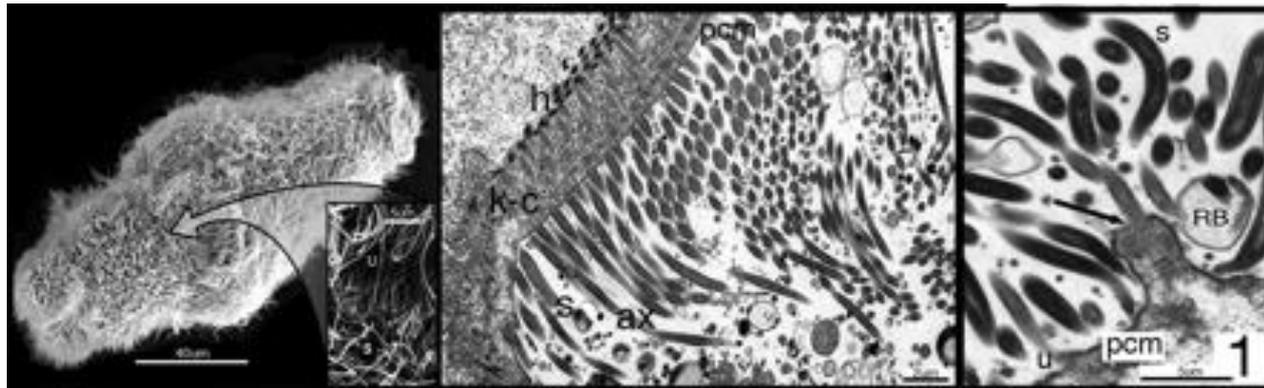
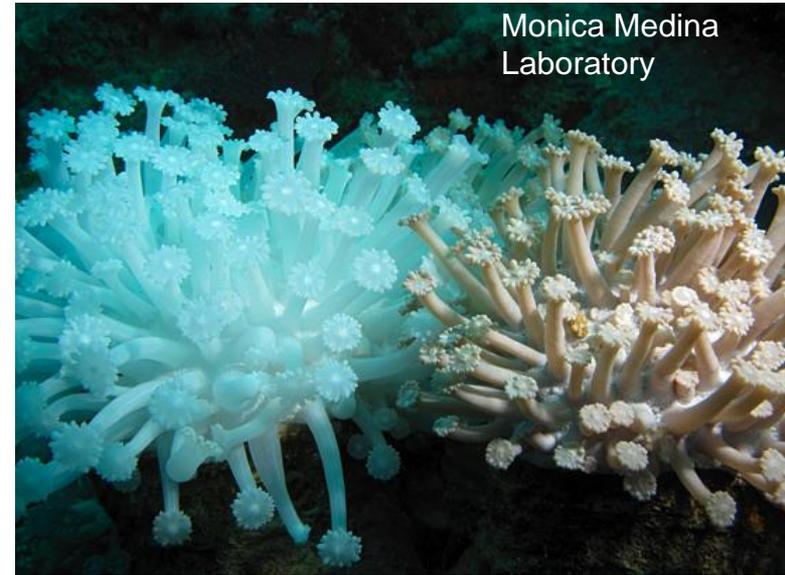
**We've been using a wrong  
view of the body, a "genomcally  
pure" body where each cell is  
genetically similar and shares  
a common embryological history.**



# Characterizing Animal Organismal “Individuality”

- Anatomical Individuality  
Our body has one genome and integrates cells to a common wholeness.
- Physiological Individuality  
Integrated organ systems to a common end.
- Developmental Individuality  
We are the products of the fertilized egg
- Immune Individuality  
Self vs non-self discrimination; rejection of others
- Genetic Individuality  
Genome of each cell from sperm-egg fusion and nearly identical.
- Evolutionary Individuality  
Individuals (organisms or genes) compete in the contest of natural selection.

# “HOLOBIONT”: The animal plus its persistent microbial communities



[Eugene Rosenberg, Ilana Zilber-Rosenberg, et al. 2007. The role of microorganisms in coral health, disease and evolution. \*Nature Rev. Microbiol.\* 5: 355.](#)

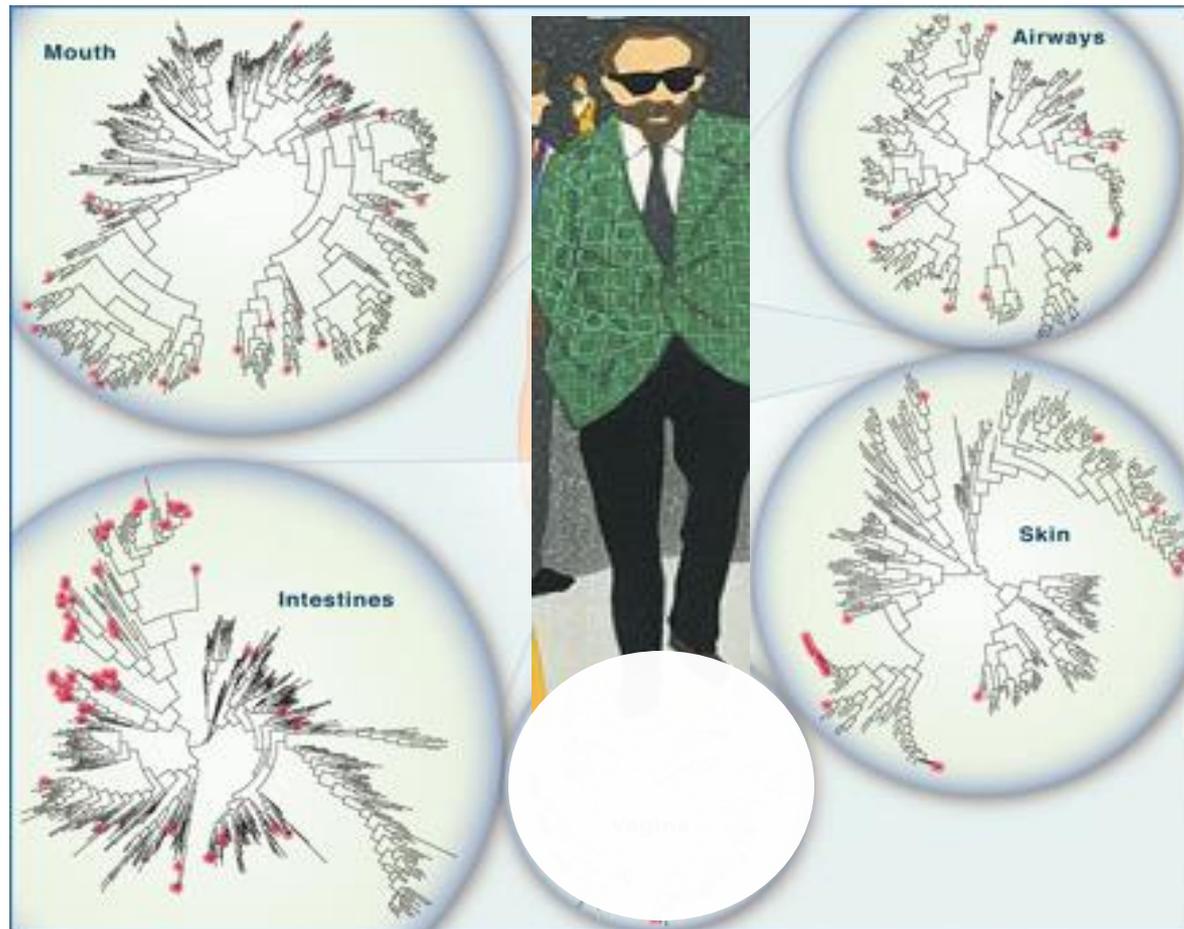
# Anatomical Individuality:

The individual is an organized collective of cells distinct from other members of the species.



# Holobiont Perspective: Humans are Holobionts, not Anatomical Individuals

Over 50% of our cells are prokaryotic, with specific locations  
160 species per person; 1100 species per human species  
“The eleventh organ system” = several ecosystems

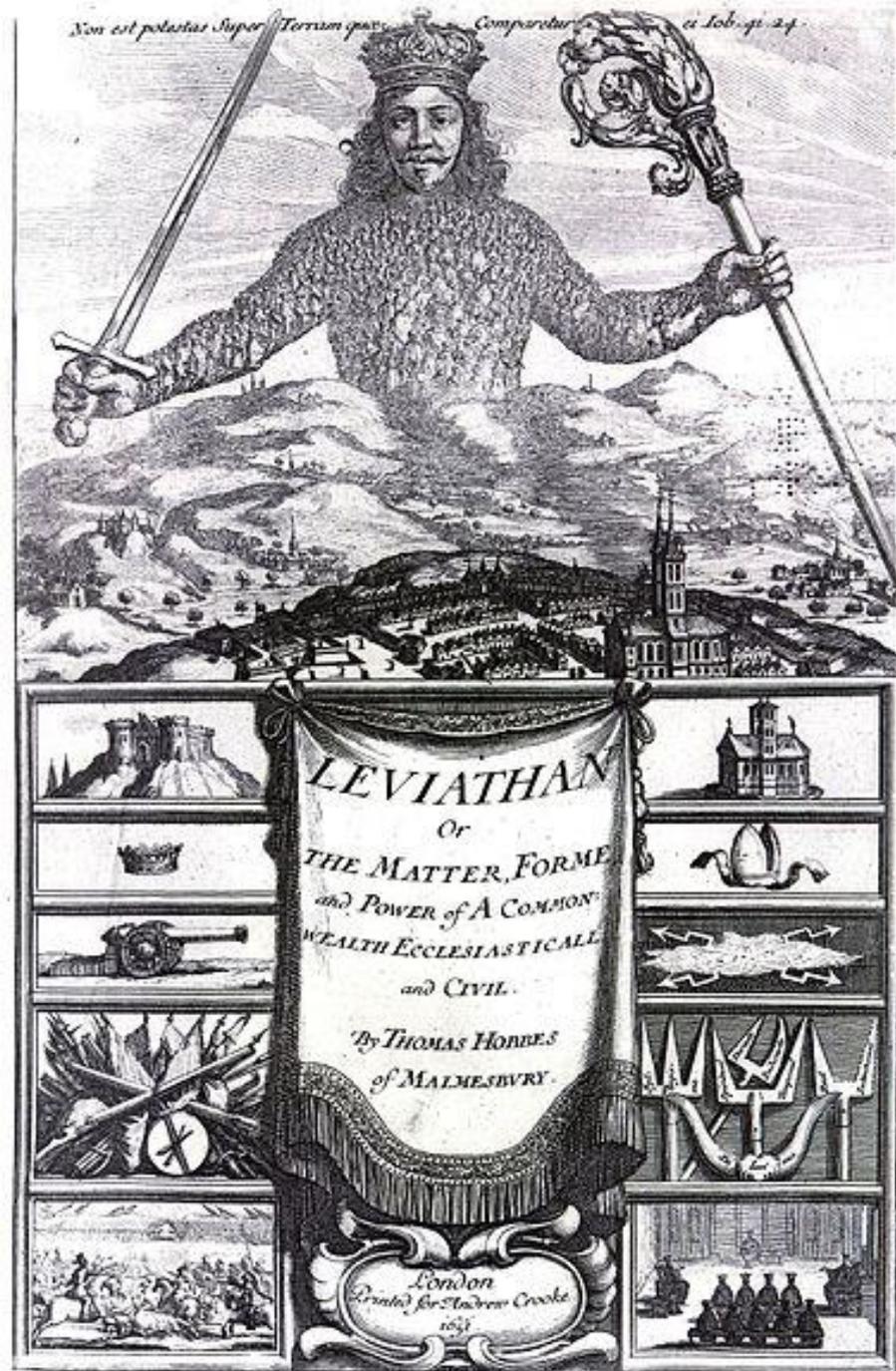


# Physiological Individuality:

Organism is an individual whose component parts cooperate for the benefit of the Whole.

Thomas Hobbes  
Adam Smith

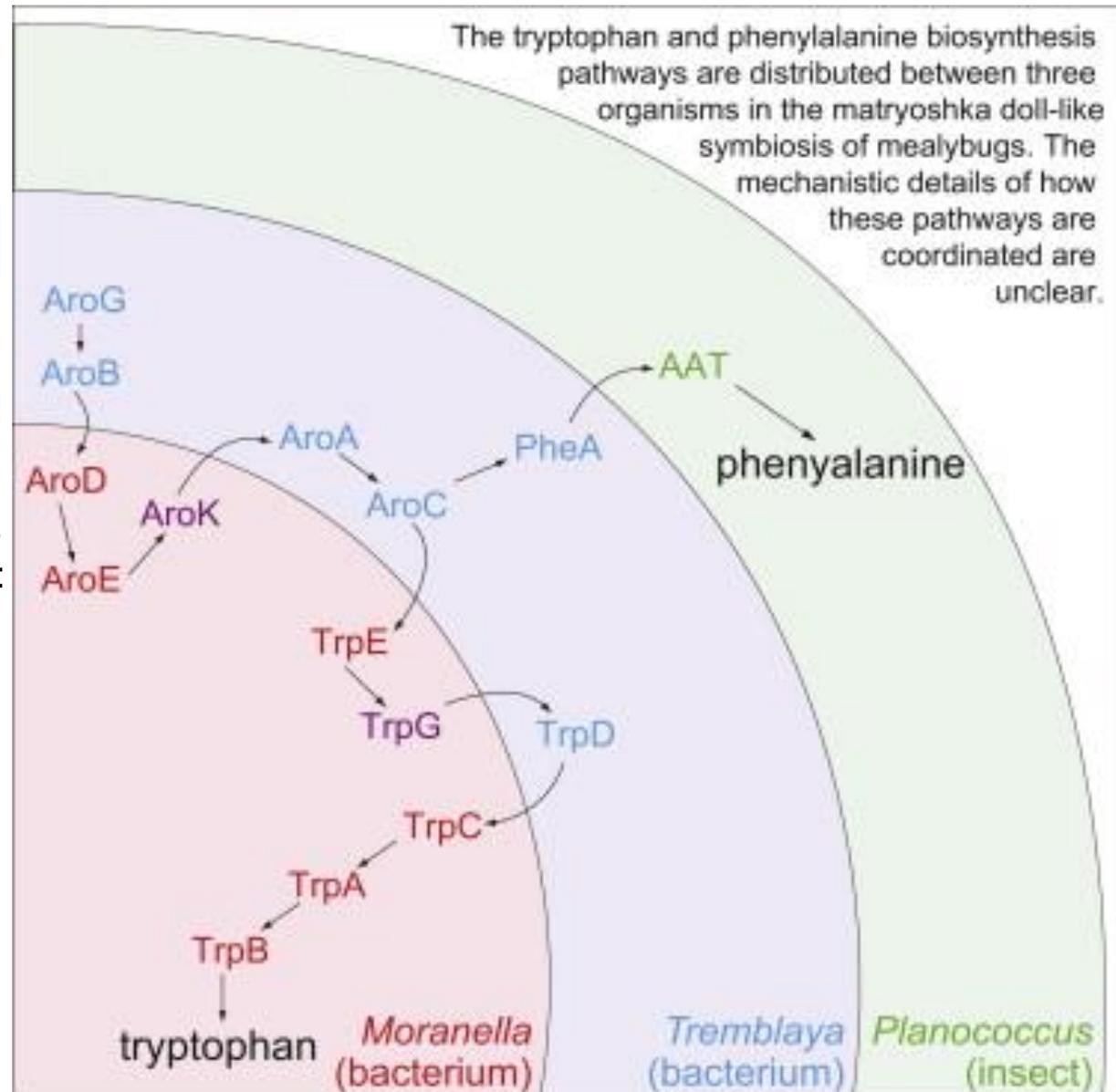
Henri Milne-Edwards  
Rudolf Leukert



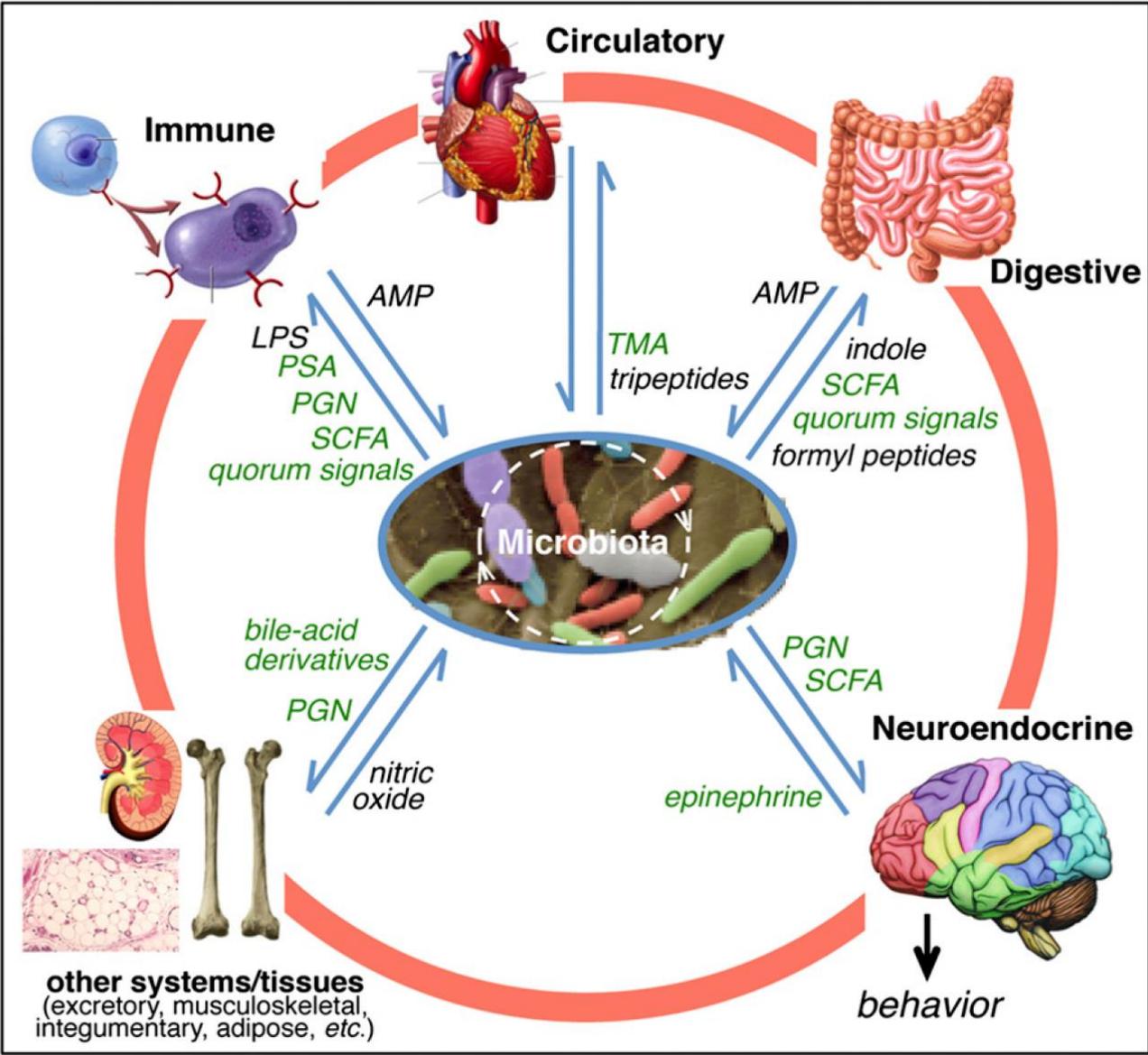
# Holobiont Perspective: Multiple organisms for the common good. Each of us is a team.

McCutcheon JP, von Dohlen CD. 2011. An interdependent patchwork in the nested symbiosis of mealybugs. *Current Biology*. 21: 1366-1372.

Genomic and physiological coordination.

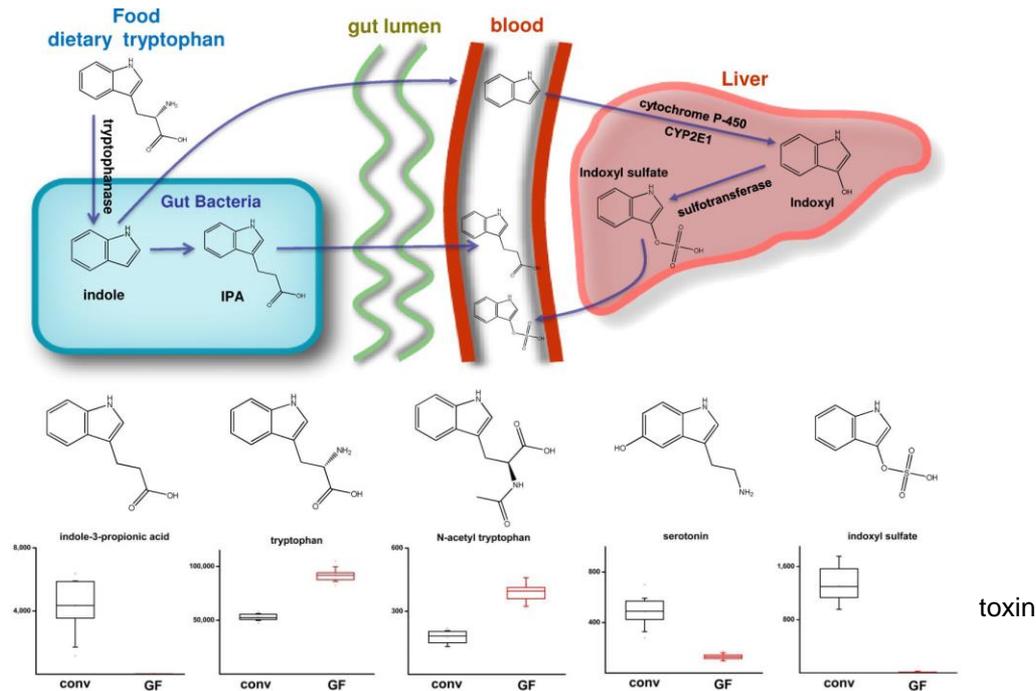


# Microbiome critical to normal physiological homeostasis



# Co-Metabolism Between Microbes and Mammals

As in *Planococcus*, intimate communication between the symbiont microbes and hosts



“As much as one third of an animal’s metabolome—i.e., the diversity of molecules carried in its blood—has a microbial origin; thus, the circulatory system extends the chemical impact of the microbiota throughout the body.

--McFall-Ngai, M. et al. 2013. PNAS 7Feb.

Wickoff, W. R. et a. 2009. PNAS 106: 3698- 3703

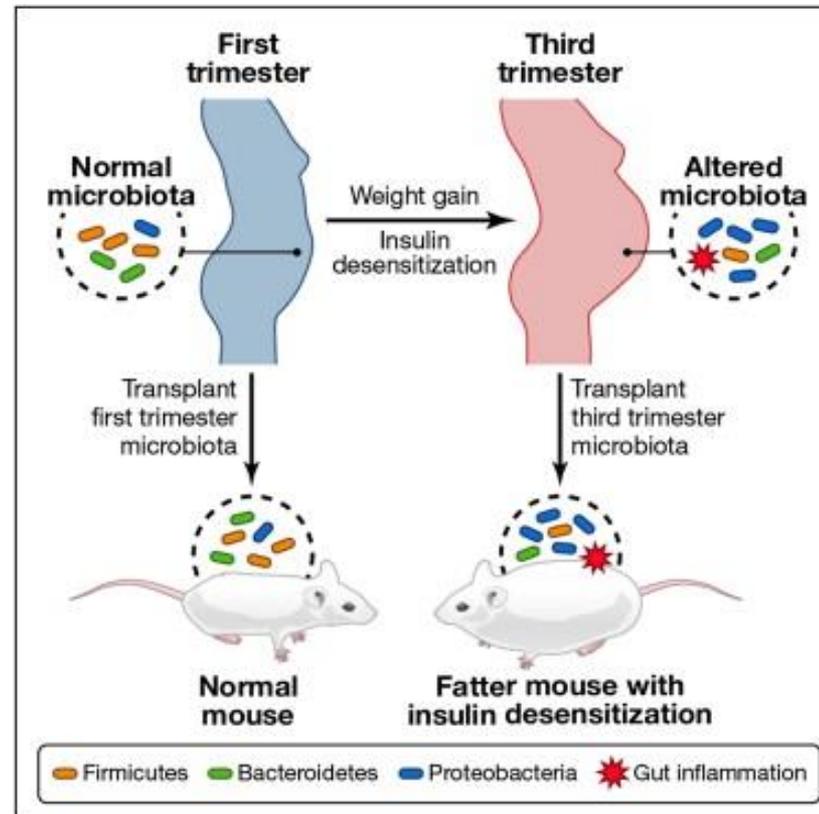
Indigenous bacteria from the gut microbiota regulate host serotonin biosynthesis.

--Yano, J. M. et al. 2015. *Cell* 161: 264 – 276.

# Interactions Between Diet and Microbes: Pregnancy

Women's Physiology Alters Gut Microbiome During Third Trimester, and the Gut Microbiome Produces Insulin Desensitization

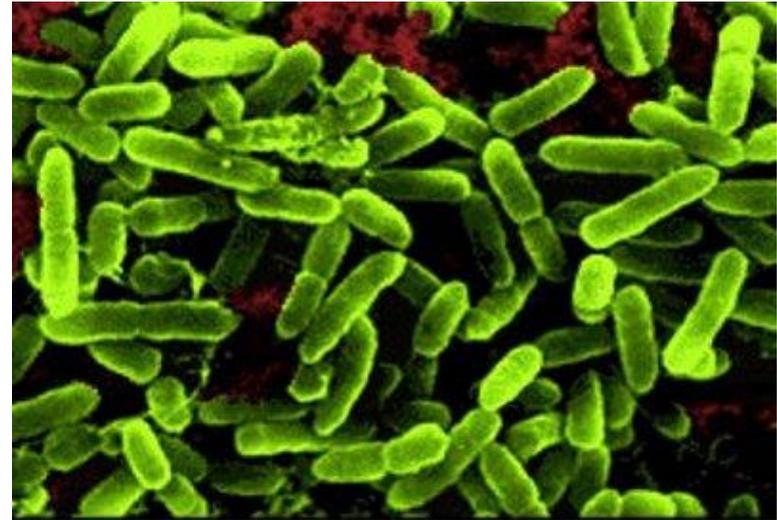
Koren, O. et al 2012.  
*Cell* 150: 470-480



- The composition of the gut microbiota changes dramatically during pregnancy; probably the same species, but more Proteobacteria and Actinobacteria
- Third trimester stool is associated with greater inflammatory cytokine (IFN- $\gamma$ , IL-2, IL-6, and TNF- $\alpha$ ) and energy content
- Third trimester microbiota induce pregnancy-like metabolism in germ-free mice
- Gut microbiota impacts metabolism in pregnancy similarly to metabolic syndrome

Birth: Passing from one symbiotic system to another:

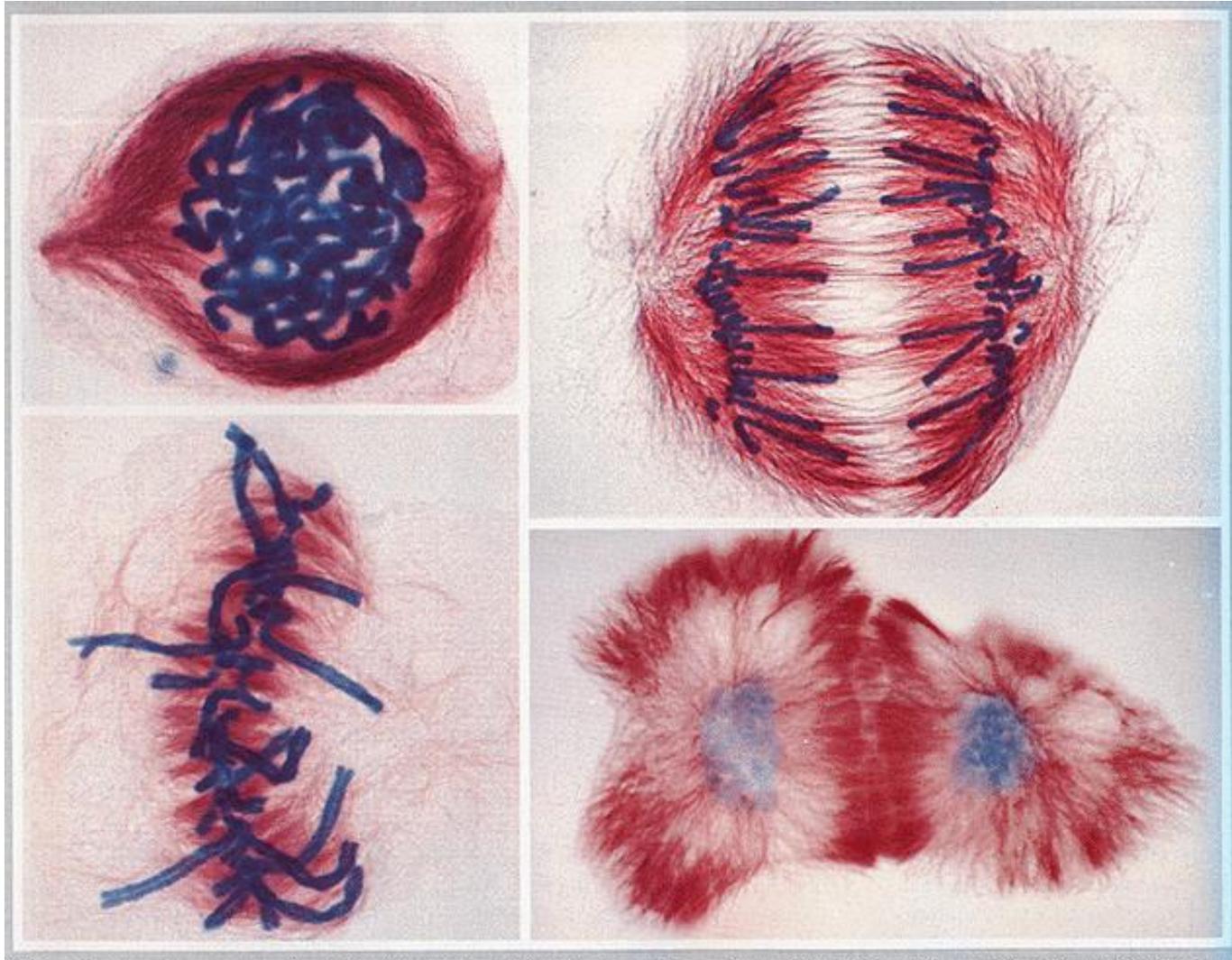
Human Milk Oligosaccharides Promote the Growth of Specific Bacteria, Such as *Bifidobacterium longum* subsp. *infantis*



Natural prebiotics for  
The continuity of communities

## GENETIC INDIVIDUALITY:

All the cells of the body have the same nuclear genome, which are the replicates of the genome established at fertilization.



WHAT IS TAUGHT TO US:

GENETIC PERSONHOOD:

Each of us is a polity that consists of those cells that descend from the fertilized egg. Each of us is a genetically unique individual.

“...revealing what it is that makes you, you.”  
television ad for ancestry.com 2015

## ERROR I

The instructions for development and heredity are all in the fertilized egg.

RAMSEY (1970):

“Genetics teaches that we were from the very beginning what we essentially are in every cell and in every human attribute.”

STANDUP GIRL (2005):

Even more amazingly, intelligence and personality – the way you look and feel – were already in place in your genetics code. At the moment of conception you were essentially and uniquely you.

# Popular Culture Promotes the Fallacy of “Sacred DNA”

## DNA AS SOUL

1. That which is your essence
2. That which determines your behaviors
3. That from which you can be resurrected  
(à la *Jurassic Park*)



(From Christian Business Network website)

Newsweek, May 23, 2005



**SAME DNA. SMALLER CHROMOSOMES.**

THE ALL-NEW MIDSIZE H3. LIVING UP TO THE OFF-ROAD REPUTATION HUMMER MADE FAMOUS.  
COMING SOON. STARTING AT \$29,500. VEHICLE SHOWN \$30,195.\*

**HUMMER**  
LIKE NOTHING ELSE.™

\*MSRP. TAX, TITLE, LICENSE, DEALER FEES AND OPTIONAL EQUIPMENT ARE EXTRA. †3000 REAL 4WD  
© GENERAL MOTORS CORPORATION, 2005

/ 2011



# JEEP COMPASS

It's in the genes...

The new 2011 Jeep. Compass is genetically engineered with legendary Jeep 4x4 capability and iconic beauty but with a size, shape, and red-blooded attitude all its own.



ALL-NEW  
**SPORTAGE**

Own it in 7 days\*

**GENETICALLY MODIFIED.**

\* Armed with completely modified DNA, the Sportage is primed to tackle roads with ease. Born of a commitment to progression, it is the personification of Kia's mantra - **The Power to Surprise™**. Packed with features in a sleek new form, the Sportage will take you from one place to another in style. And with eye-catching LED daytime running lights leading the way, you can be assured of an adventure every time you start the engine.

[www.kia-sportage.com](http://www.kia-sportage.com)

## SYLLOGISM BASED on SACRED DNA:

1. DNA is soul
2. Given: We receive our DNA at fertilization

Therefore:

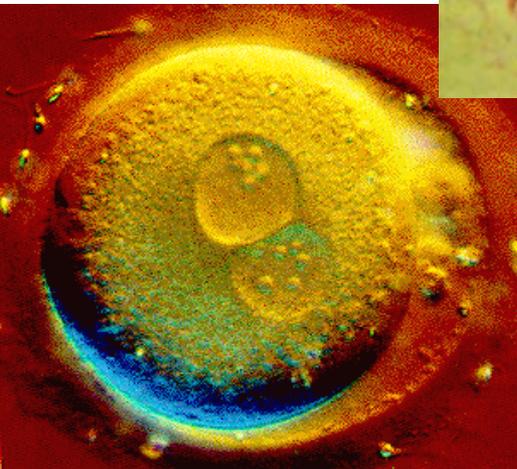
We receive our soul and become individuals  
at fertilization

## FERTILIZATION IS ENSOULMENT

**“Pro-life is scientific. Biologically, life begins at conception. That’s irrefutable from a biological standpoint.”**

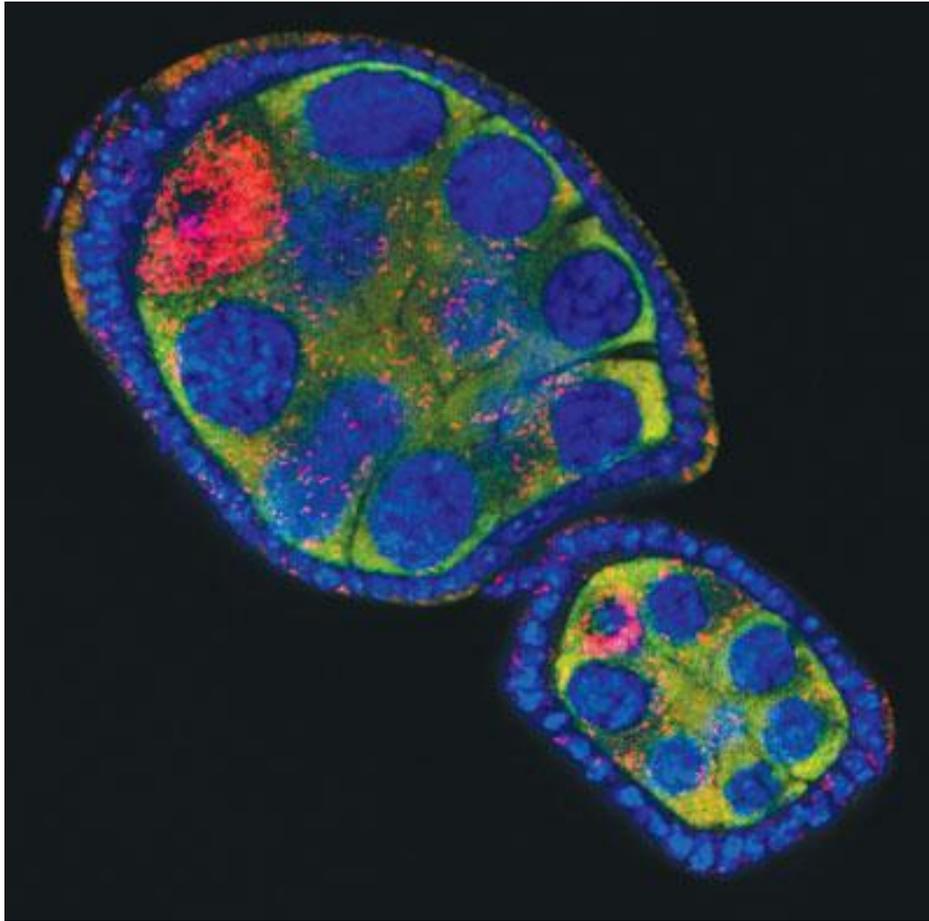


**Governor Michael Huckabee; The Daily Show, 12 Nov. 2012**

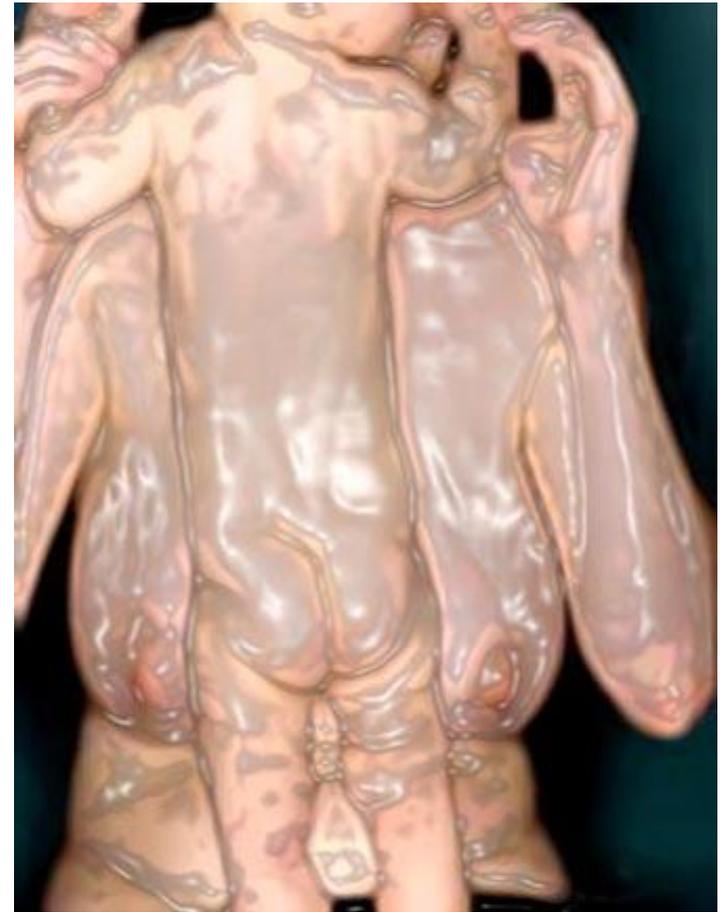


## Holobiont Perspective: We are Not GENETIC Individuals.

Symbionts are part of our epigenetic inheritance. They can be acquired and transmitted either directly or indirectly from one generation to the next.



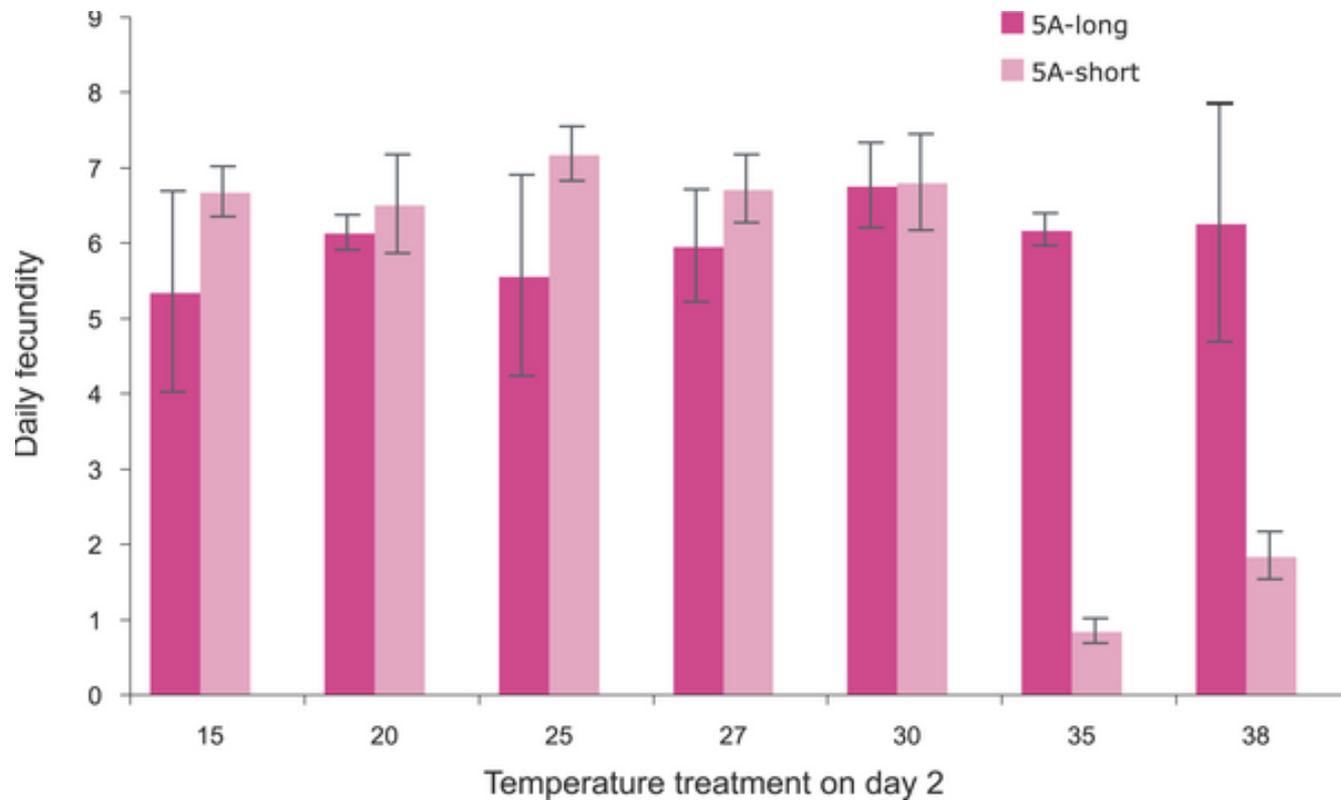
Vertical (direct) transmission of *Wolbachia* bacteria in *Drosophila* oocytes



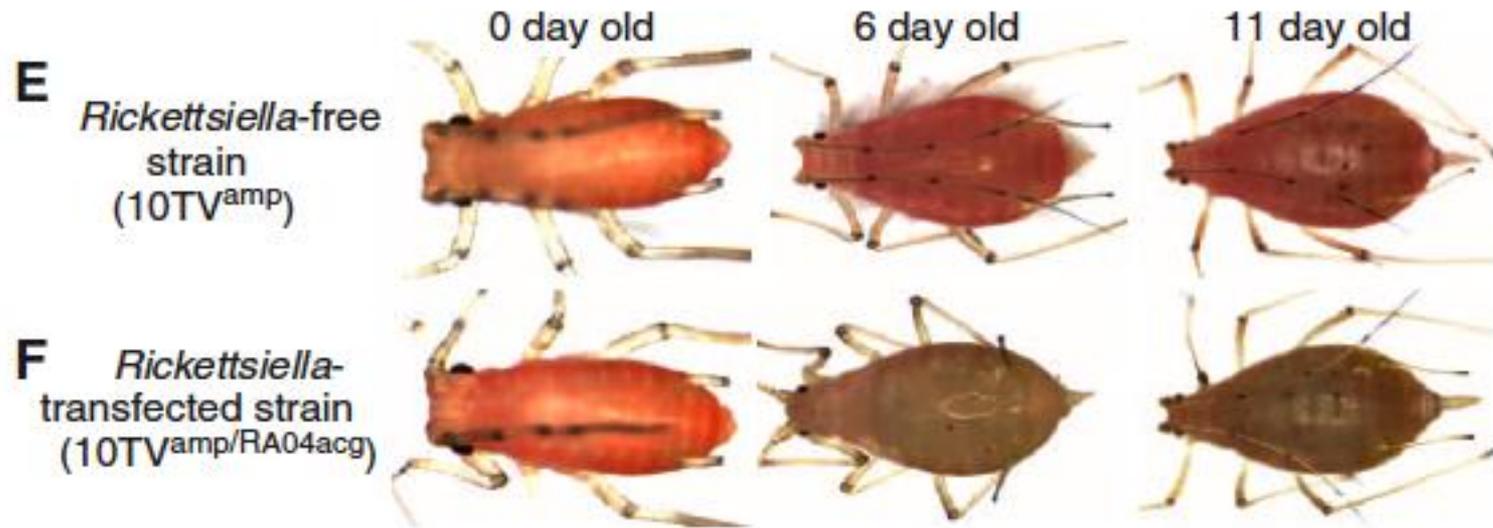
Horizontal (infectious) transmission of *Bacteroides* to human gut (8 million vs 22,000 different genes)

# Temperature and Selection in Pea Aphid Holobiont:

Allelic difference in *Buchnera* symbiont genome effects thermotolerance of holobiont.  
Trade-off between fecundity at lower temperatures and heat tolerance at high temp.



# In Some Strains of Pea Aphids, Color Variation Provided for by *Symbiont* Genotype, Not Host Genes



Without *Rickettsiella*, red aphid newborns become red adults.  
With *Rickettsiella*, red aphid newborns become green adults.

*Rickettsiella* induces synthesis of quinones in aphids

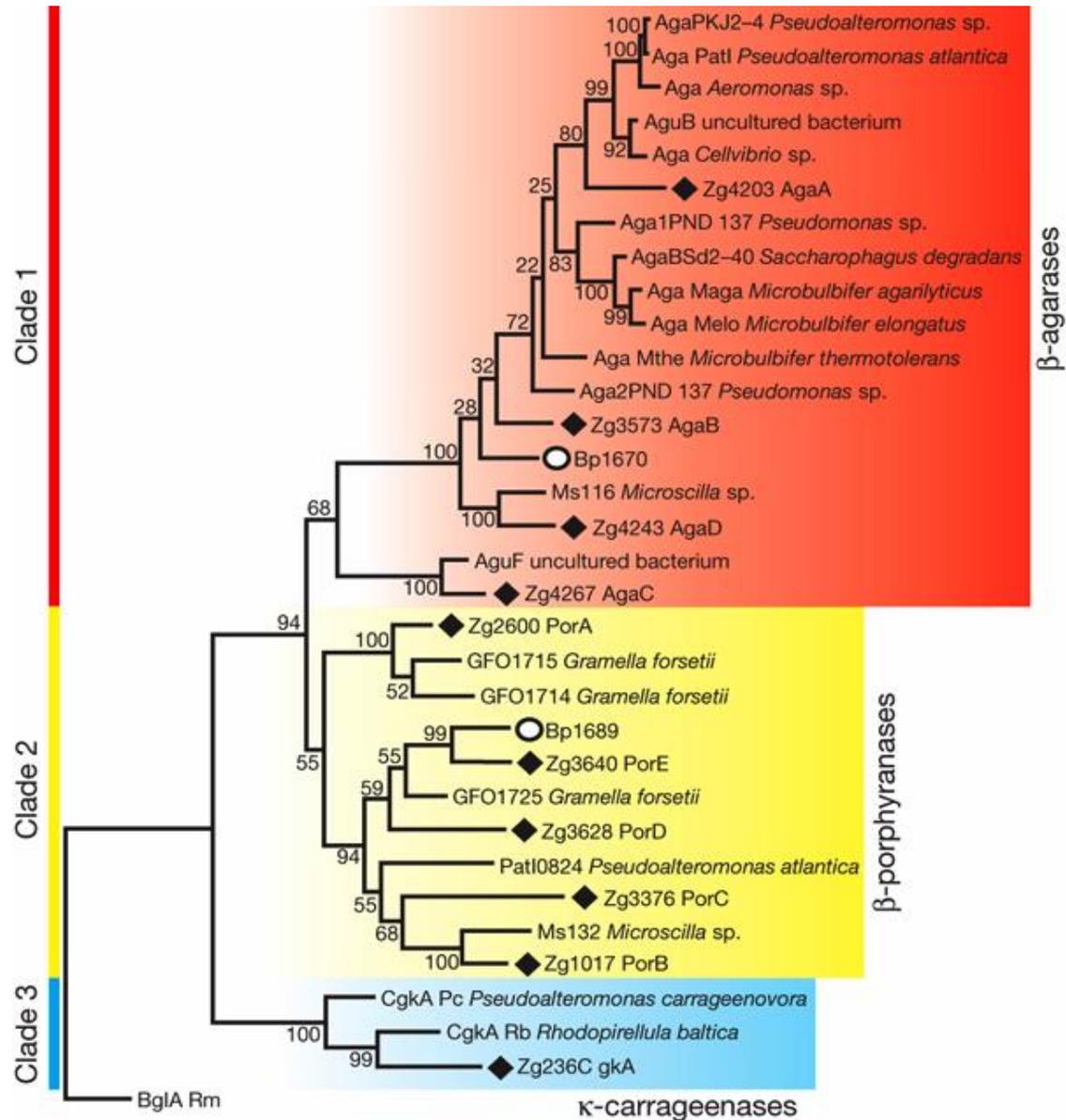
# Humans

Sushi-eating Japanese population contains a different strain of *Bacteroides plebius* than Western populations.

The Japanese strain contains genes whose protein products digest the complex sugars found in seaweed.

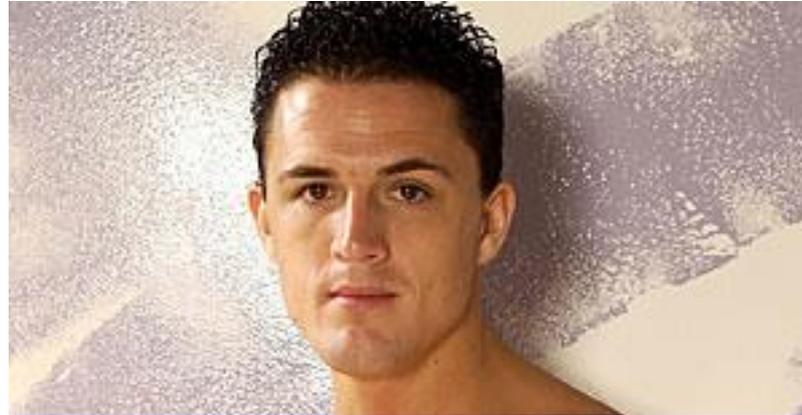
These genes appear to have been laterally transmitted to *B. plebius* from a marine *Bacteroides* species that thrives on red algae.

Hehemann, J.H. et al. 2010. *Nature* 464: 908- 912.



# Immunological Individuality:

Immune system is like an armed defense force, protecting the animal from a microbial onslaught.



# Holobiont Perspective:

Immune system is like a force of bouncers or passport control agents. They know who to let in and who to keep out. They help establish the symbioses.



# Even in mammals, the immune system helps to facilitate symbioses

Peterson, DA *et al* 2007 *Cell Host Microbe* 2: 328

IgA reduces intestinal proinflammatory signaling and bacterial epitope expression, thereby balancing suppression of the oxidative burst with the antibody's negative impact on bacterial fitness. These results underscore the adaptive immune system's critical role in establishing a sustainable host-microbial relationship. Immunoselection of bacterial epitope expression may contribute to the remarkable strain-level diversity in this ecosystem.

Obata, T. *et al* 2010. *Proc. Natl Acad. Sci USA* 107: 7419:.

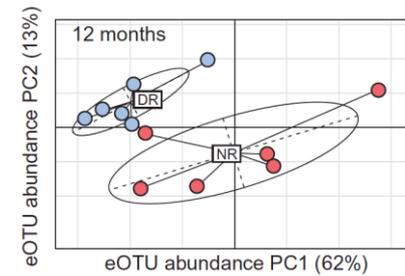
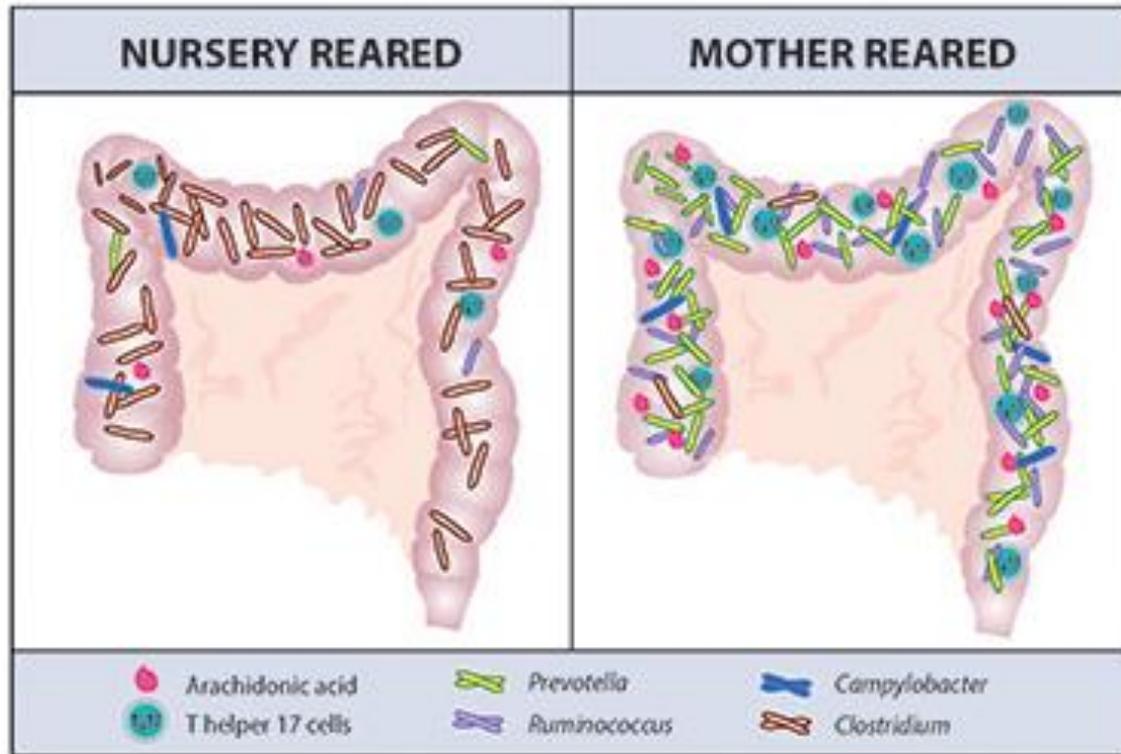
Thus, indigenous opportunistic bacteria uniquely inhabit PPs, leading to PP-DCs-initiated, local antigen-specific Ab production; this may involve the creation of an optimal symbiotic environment on the interior of the PPs.

Round, JD. *Et al.* 2011. *Science* 332: 974.

Toll-like receptors (TLRs) mediate recognition of microbial patterns to eliminate pathogens. By contrast, we demonstrate that the prominent gut commensal *Bacteroides fragilis* activates the TLR pathway to establish host-microbial symbiosis...Therefore, commensal bacteria exploit the TLR pathway to actively suppress immunity. We propose that the immune system can discriminate between pathogens and the microbiota through recognition of symbiotic bacterial molecules in a process that engenders commensal colonization.

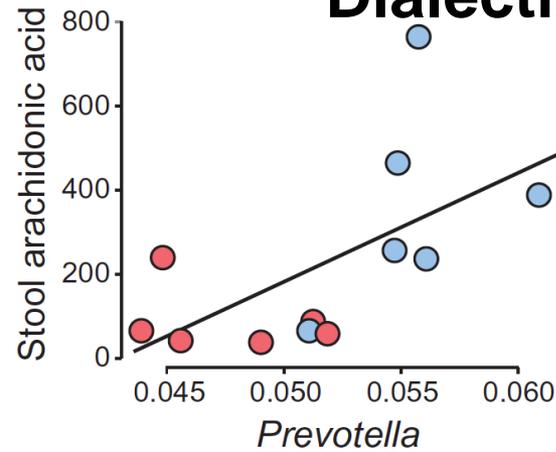
# Breast-fed and bottle-fed infant rhesus macaques develop distinct gut microbiotas and immune systems

Amir Ardeshir,<sup>1\*</sup> Nicole R. Narayan,<sup>1,2\*</sup> Gema Méndez-Lagares,<sup>1,2\*</sup> Ding Lu,<sup>1,2</sup> Marcus Rauch,<sup>3</sup> Yong Huang,<sup>4</sup> Koen K. A. Van Rompay,<sup>1</sup> Susan V. Lynch,<sup>3</sup> Dennis J. Hartigan-O'Connor<sup>1,2,5†</sup>

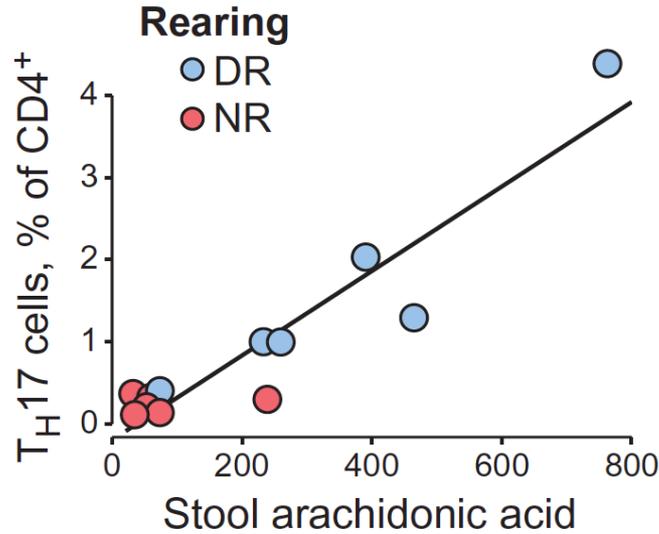


# Dialectic between microbes and immune system

1. Bacteria promoted by breast milk make arachidonic acid

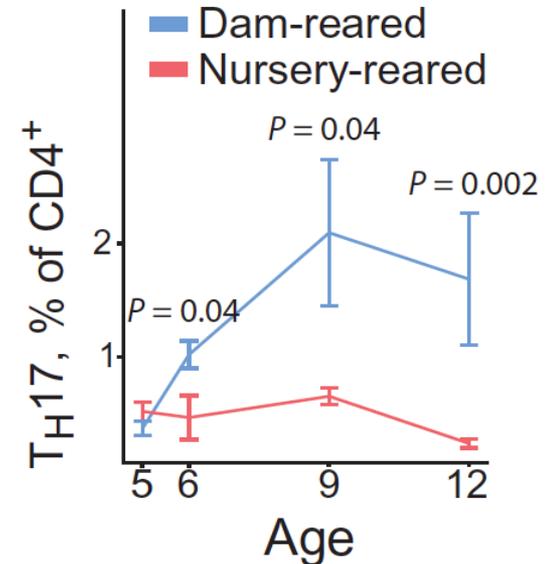


2. Arachidonic acid induces  $T_H17$  cells



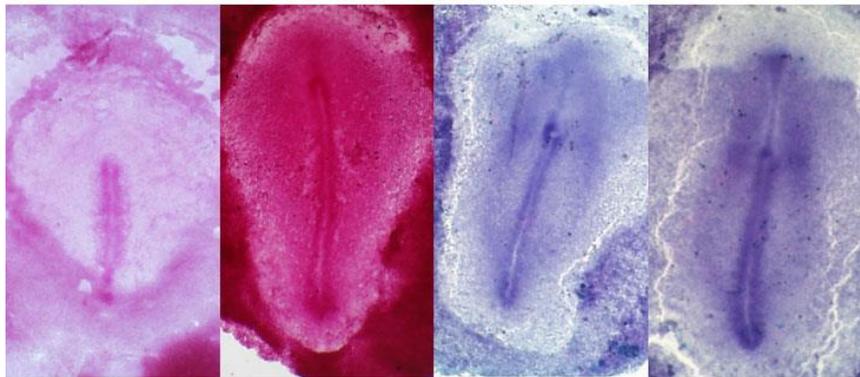
3. Breast-fed macaques have more  $T_H17$  cells than formula-fed macaques

$T_H17$  cells produce IL-17, IL-22, which induce gut cells to make proteins against *Candida*, *Salmonella*, *Staphylococcus*. Important against opportunistic infections.



# Developmental Individuality

An individual is the organism from ovum to ovum, as progeny of the zygote.



3

4

5

6



7

8-

8

9



10

11

12

13



14

15+

16+

17

# Holobiont Perspective:

Animals are symbiopoietic, not autopoietic, organisms. We use instructions from the environment and from other species (symbionts)

Where are the boundaries of this fetus?



# Poster Organisms for Developmental Symbiosis

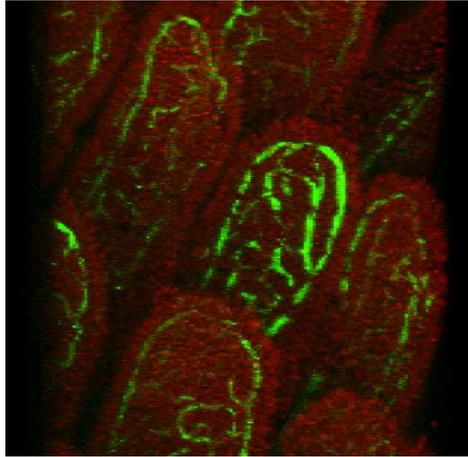
The light organ of *Euprymna* isn't made until the bacterial symbionts (only *Vibrio fischeri*) attach and enter the ventral surface



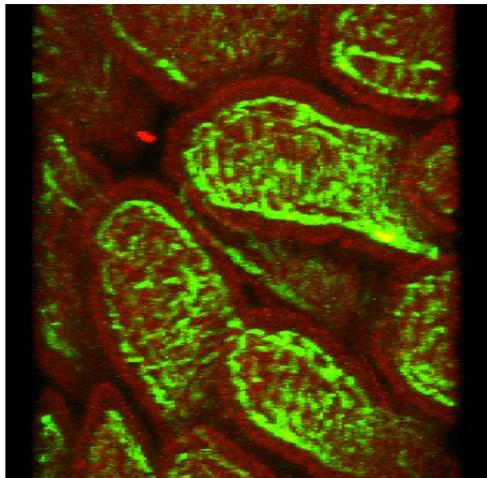
Tim Myashiro lab



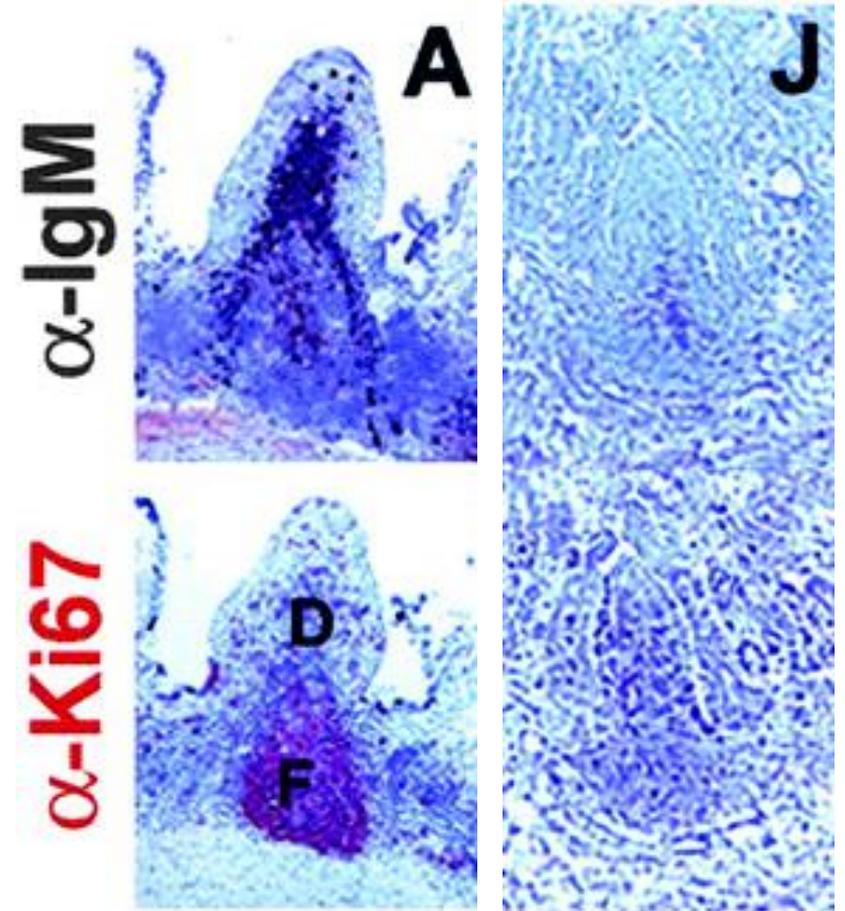
Orchid seeds are so small and lacking in carbon resources that they need fungal hyphae to germinate



Intestinal vessels **without** microbes

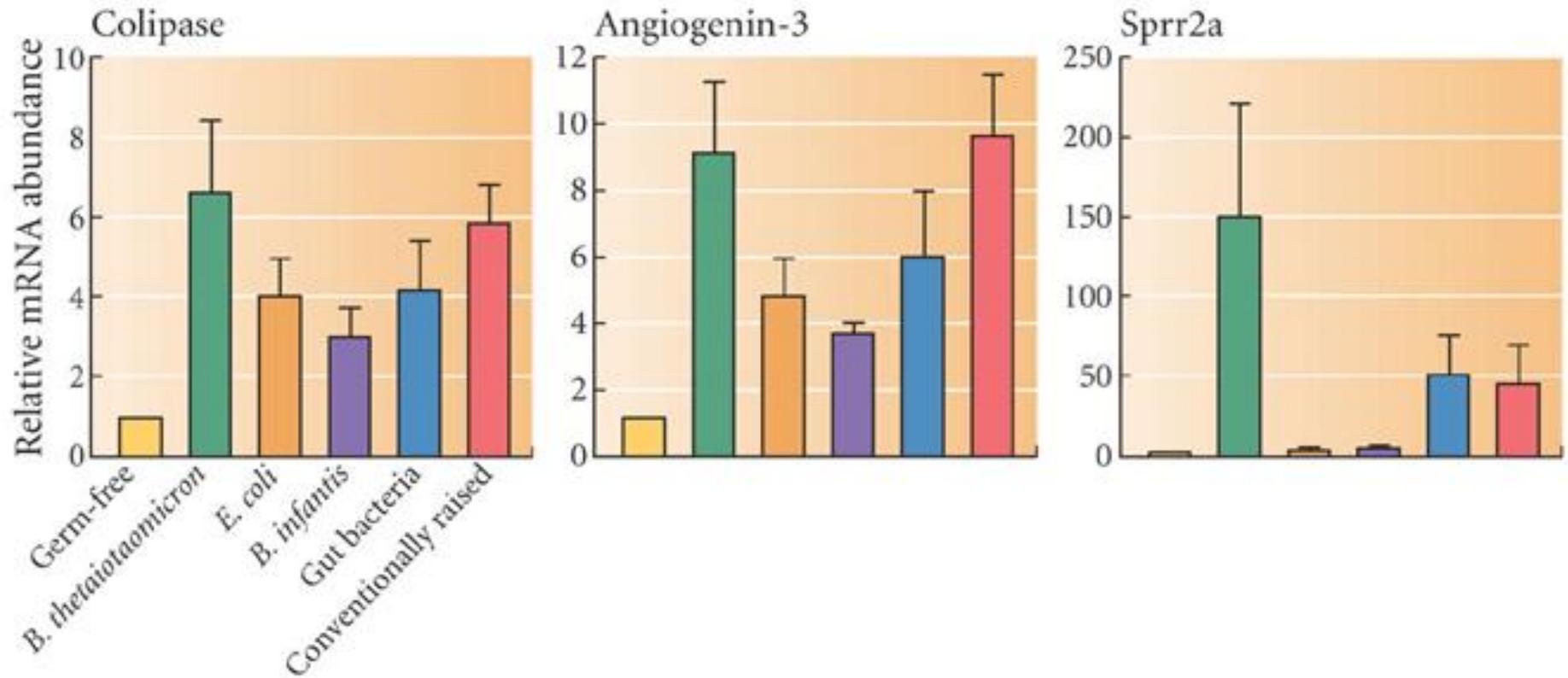


Intestinal vessels **with** microbes



Follicle and Dome of gut lymphoid tissue with gut microbes without gut microbes

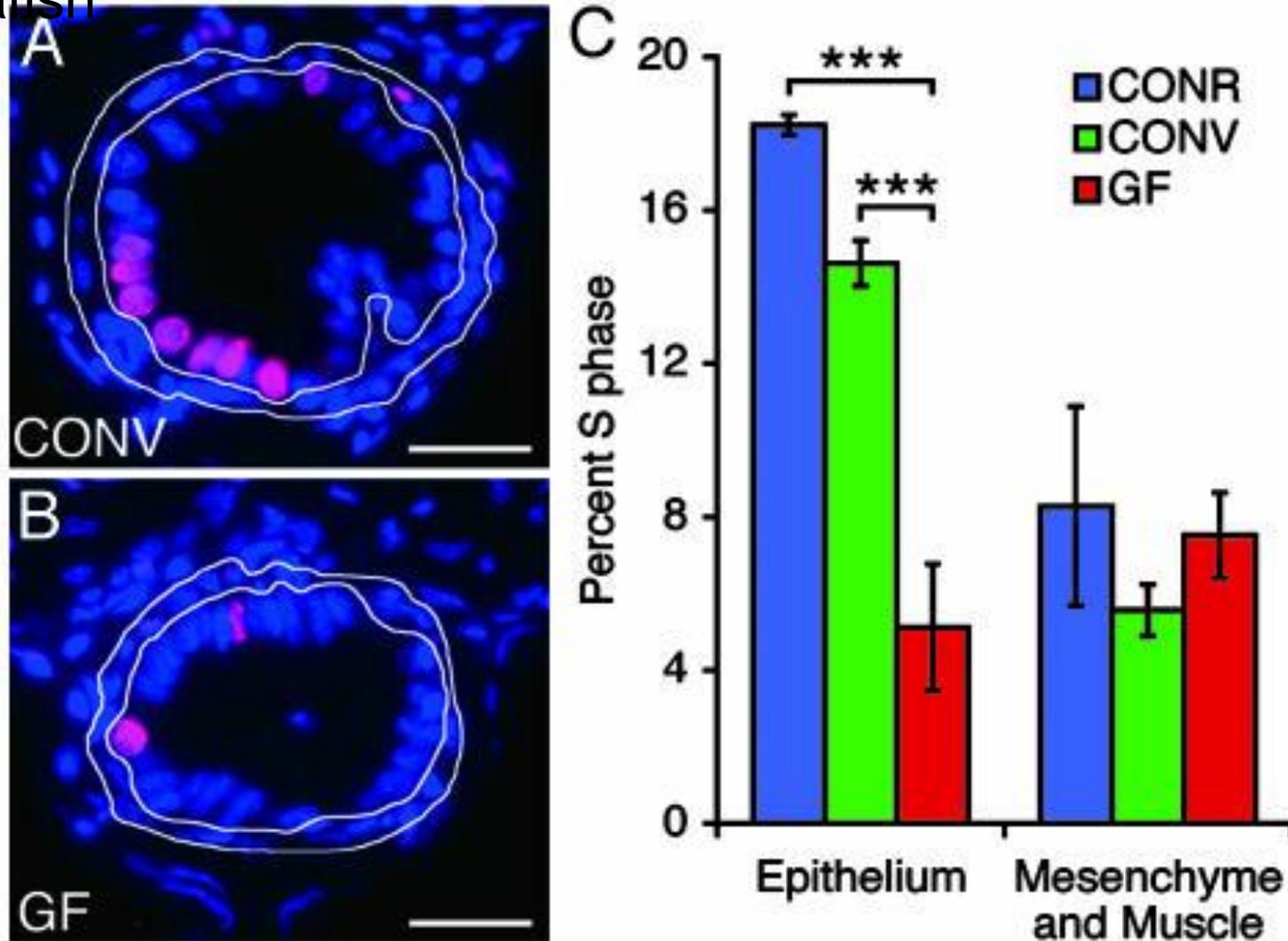
# Induction of Murine mRNAs by Associated Gut Microbes



>100 bacterial species in the individual human gut

“outsourcing” developmental phenomena

# Microbial Symbionts Boost Epithelial Cell Formation in Zebrafish



A, B. 6d conventional (A) and germ-free (B) intestine stained for cells (blue) and dividing cells (magenta). Mesenchyme and muscles outlined in white  
Rawls et al. 2004. *PNAS* 101: 4596 – 4601. (Symbionts work through beta-catenin stabilization

# Normal Gut Microbiota Modulates Normal Brain Development and Behavior

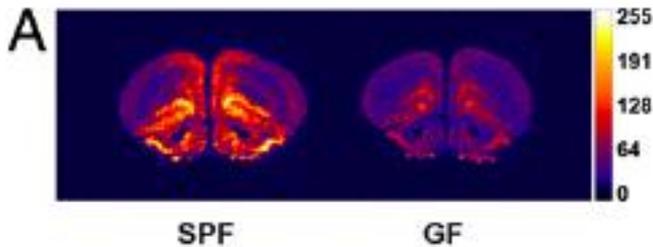
“The microbiota-gut-brain axis”

-Cryan and O’ Mahony 2011; McLean et al 2012

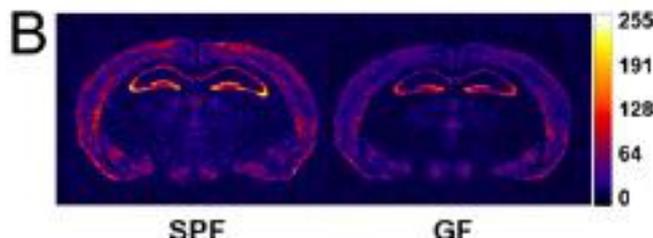
Germ-free mice have increased motor activity than colonized mice

- Germ-free mice had elevated dopamine, norepinephrine, and serotonin in striatum.
- Germ-free mice have lowered NGF1-A and BDNF (“plasticity”) gene expression
- Germ-free mice had lower amounts of synaptophysin (synaptic vesicle maturation) in the striatum

“...during evolution, the colonization of gut microbiota has become integrated into the programming of brain development, affecting motor control and anxiety-like behavior.”



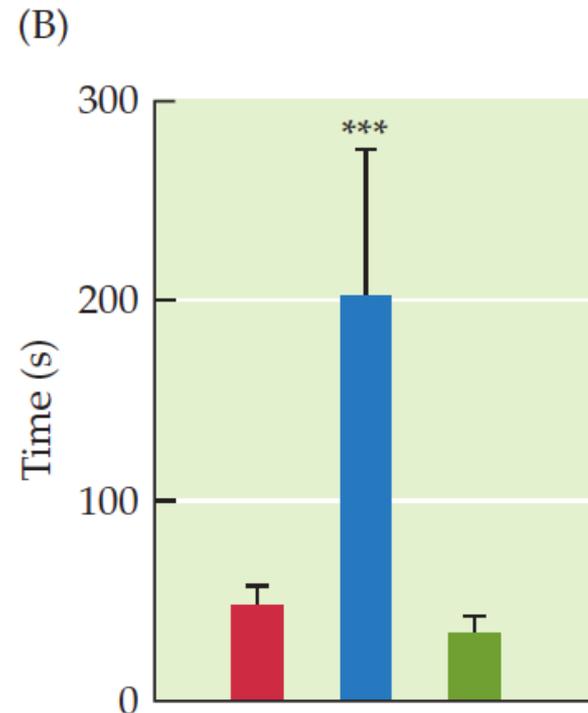
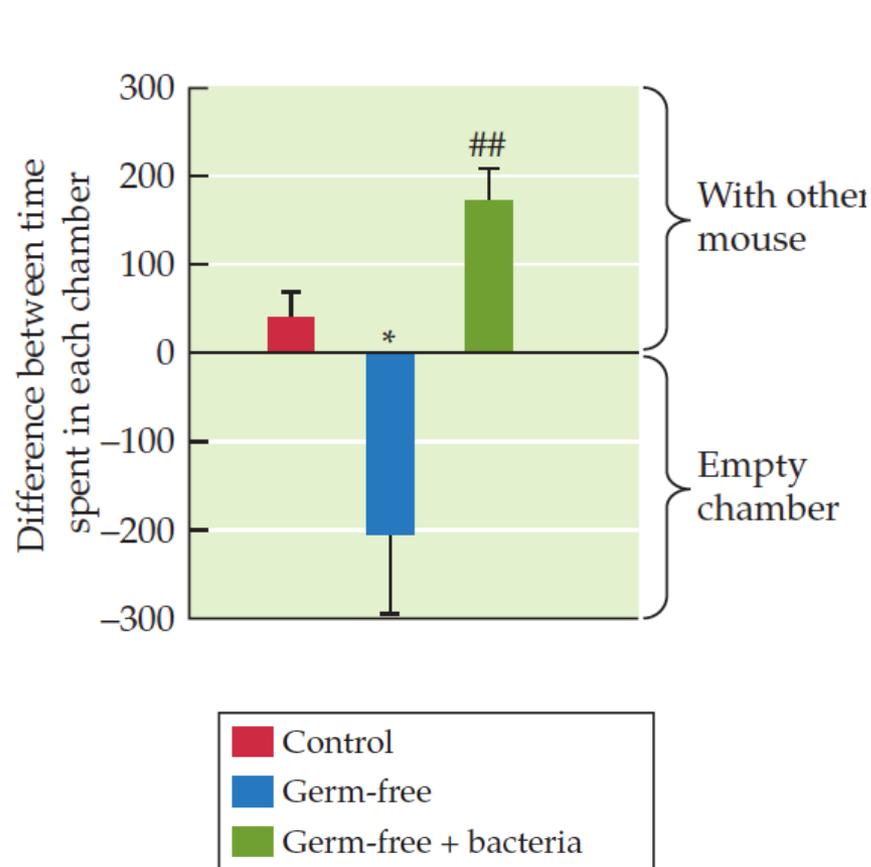
NGF1-A



BDNF

# Germ-free mice have autism-like behavioral symptoms

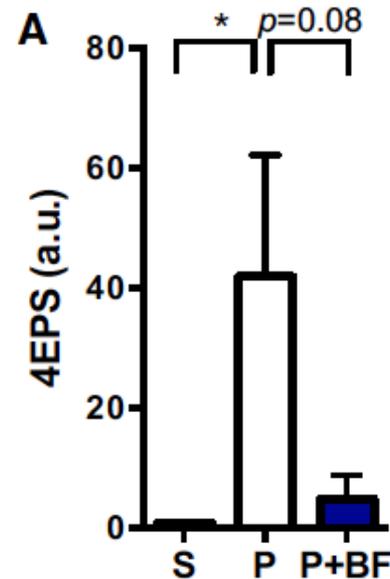
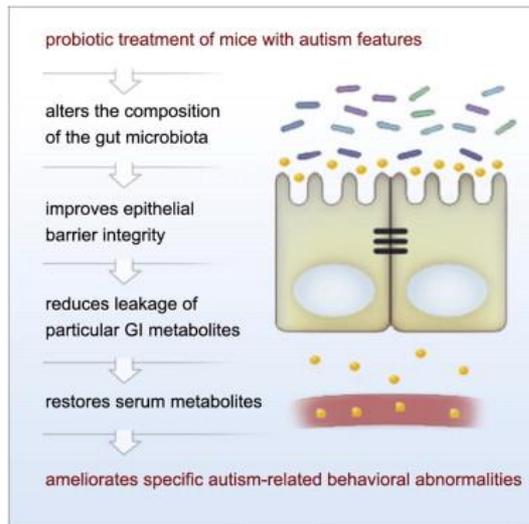
Desbonnet, L., G. Clarke, F. Shanahan, T. G. Dinan and J. F. Cryan.  
2014. Microbiota is essential for social development in the mouse. *Mol. Psychiatry* 19: 146–148.



Effects of germ-free (GF) rearing and germ-free bacterial consortium (GFC) on social behaviors in male mice. (A) Measuring sociality by the difference between times spent in chambers with and without other mice. Germ-free mice had social avoidance. \*,  $p < 0.05$  versus controls; ##,  $p < 0.001$  versus germ-free mice. (B) Time spent in repetitive self-grooming. Both autistic-like behaviors could be relieved by adding microbes later in life.

# *Bacteroides fragilis* corrects intestinal epithelial defects in and metabolic leakage in a mouse model of autism

Hsiao, E. Y. et al 2013. Microbiota modulate behavioral and physiological abnormalities associated with neurodevelopmental disorders. *Cell* 155: 1451-1463.



Ethylphenylsulfate levels are extremely high in germ-free mice and can also be removed when epithelial integrity is restored by the addition of *Bacteroides fragilis* ( $p < 0.05$ )

# Current Holobiont Evolution

*“In short, I believe that most evolutionary novelty arose, and still arises, directly from symbiosis.”*



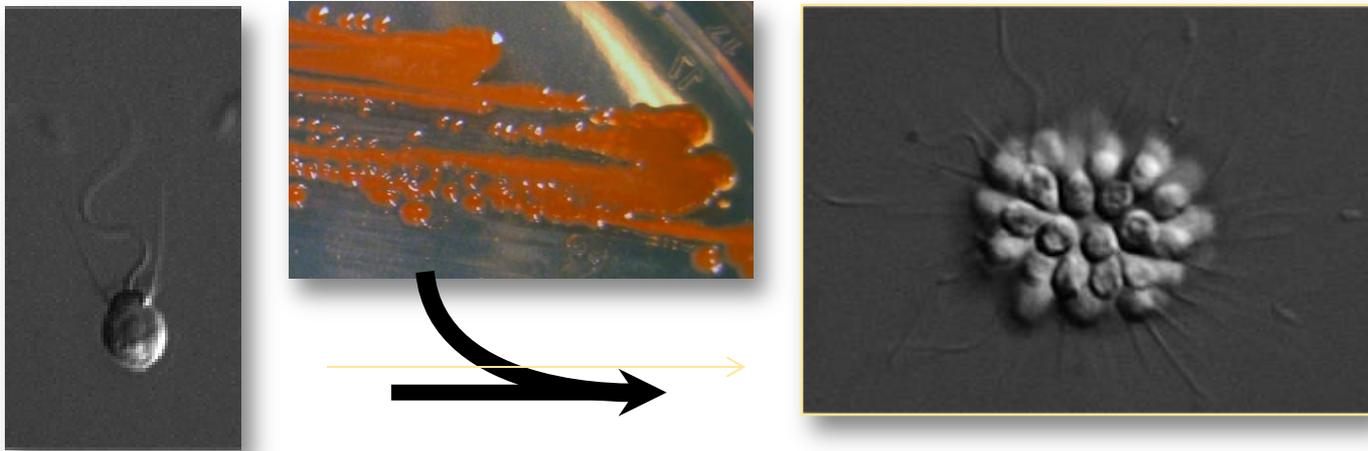
*“Life did not take over the globe by combat, but by networking.”*

*-Lynn Margulis, Symbiotic Planet, 1998.*

## **Mechanisms of speciation:**

- A. Genetic variation through symbionts
- B. Reproductive isolation through symbionts
  1. Selective mating preferences
  2. Cytoplasmic incompatibility

# *Algoriphagus machipongonensis* Induces *S. rosetta* multicellularity



co-isolated natural prey of *S. rosetta* choanoflagellate

Bacteroidetes phylum

found in marine environments, animal gut, soil

# No Biological “Individuality” for Animals

- Anatomical Individuality  
Nine out of every ten of “our” cells is microbial.
- Physiological Individuality  
Joined metabolic pathways; collective purpose, defense.
- Developmental Individuality  
Gut microbes help build gut, immune system; light organ;  
prevent ovarian cell death
- Immune Individuality  
Microbes help build immune system, expand lymphocyte  
repertoire; microbes “become” self. Bouncer, not army.
- Genetic Individuality  
Genome evolved with those of symbionts; over 100  
different genomes; many with phenotypic outcomes
- Evolutionary Individuality  
Symbionts can provide selectable variation, isolation

So, We Are TEAMS

## PART 2: OUR NEW BODIES

How science is deconstructing  
the old notion of individual bodies

and is replacing it with a new  
notion of individuality

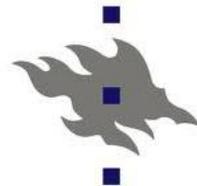
**We've been using a wrong  
view of the body, a "genomically  
pure" body where each cell is  
genetically similar and shares  
a common embryological history.**



# The NEW Body Politic:

**TEAM** Scott F. Gilbert  
Swarthmore College, USA  
University of Helsinki, Finland

What does it mean if we  
are multispecies teams?



UNIVERSITY OF HELSINKI



# 1. For Biology: The evolution, physiology, and development of holobionts

- How do symbionts enter the body and what provides the specificity for permitting their entry?
- What signals are symbionts using to help form capillaries, lymphoid tissues, gut tissues, etc.
- How are the microbial symbionts organized within the body and how do they use existing developmental cues (such as Hox genes) to cluster?
- How do cells make bacteria-containing cells, bacteriocytes, and form organs, bacteriomes.
- What is the evo-devo of holobionts? How do the parts form the whole.

## 2. For social sciences:

What does it mean to have a chimeric body?

For instance: immigration policy

***Gasterbeiten*** if the model is of a monogenomic animal.

**Lawful Permanent Residents** if the model is of an animal with porous boundaries.

**Full citizens of the holobiont.** The symbionts help build the animal and benefit

### 3. Philosophy:

What if life is an amalgam of

**“Becoming with the other” ....**

and **“the battle of each against all.”**

#### “Making the Team”

- Competition to become the team.  
(Particular combinations as in *The Boys in the Boat*)
- Cooperation within the team to compete against other teams.
- Integration of teams into networks (leagues/ecosystems) that are stable, cooperative structures that might compete with other leagues or ecosystems.

# **New view of health: Partnership /domestication**

Easier to alter bacterial genome than human genome

Food, fuels, fibers, and medical treatments from microbes

## **MICROBIOME**

# *A unified initiative to harness Earth's microbiomes*

Transition from description to causality and engineering

SCIENCE sciencemag.org 30 OCTOBER 2015 • VOL 350 ISSUE 6260

“Harnessing” is the metaphor now widely used

# FOR HEALTH: Are certain microbes essential for preventing Diabetes, Asthma, Autoimmune Diseases, even Dietary Diseases?

## Diet and Microbes Co-metabolism in Disease States: Gut Microbiomes of Malawian Twins Discordant for Kwashiorkor

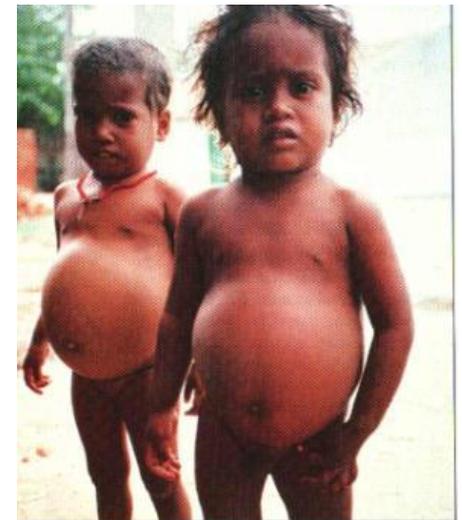
*Smith et al 2013. Science 548 – 554.*

MZ twins discordant for Kwashiorkor had discordant microbiomes.

Combination of Kwashikor gut microbes + Malawian diet caused weight loss in GF mice, along with changes in metabolism.

When both twins were given RUTF (peanut-based Ready-to-Use Therapeutic Food), microbiomes changed to functional, and Kwashiorkor symptoms vanished.

“Microbe-host **cometabolism** as a function of microbiota and host diet”



Kwashiorkor: severe acute malnutrition, edema, wasting, skin rashes, anorexia

# SYMBIOSIS IS THE EVOLUTIONARY STRATEGY THAT SUPPORTS LIFE ON EARTH:



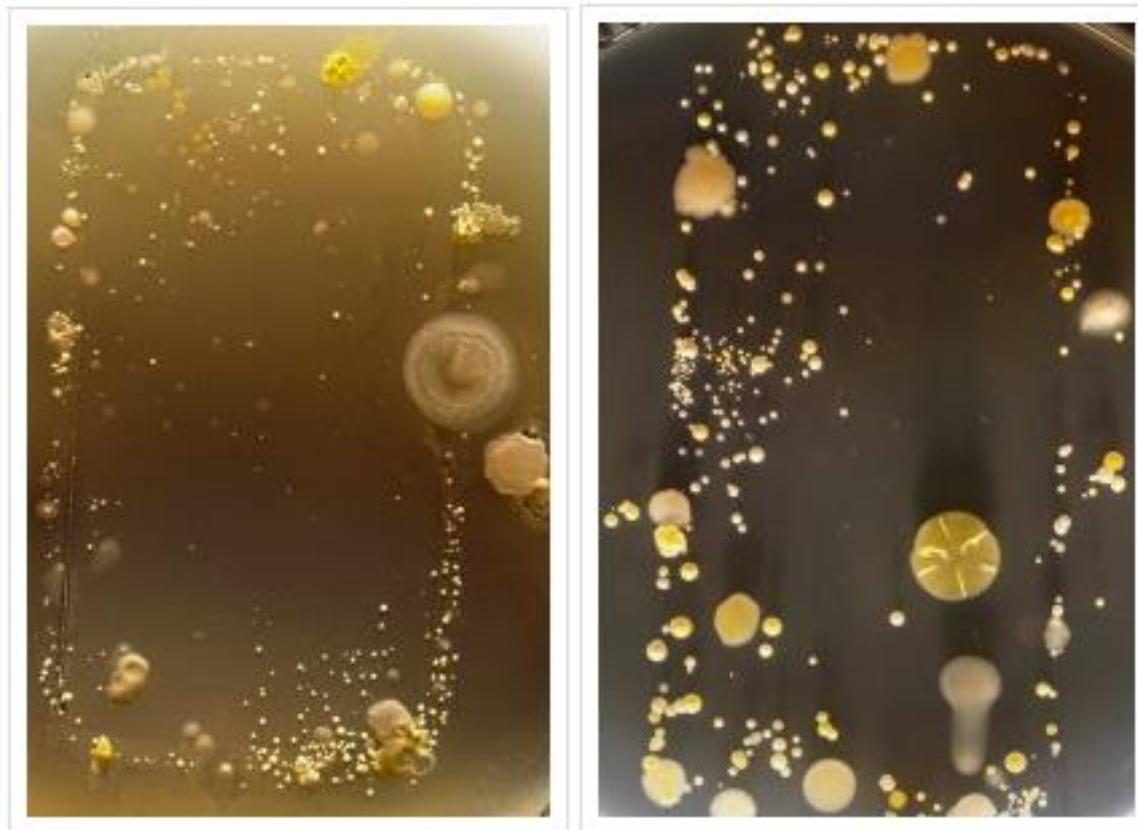
1. Rhizobacteria/Legumes for nitrogen fixation
1. Mycorrhizal interaction with plant roots and seeds
3. Endophytic fungal protection against desiccation, etc.
4. Coral reefs and tidal seagrass ecosystems sustain oceanic biodiversity

And within these big symbioses are the smaller symbiotic webs we call “organisms,” and the products of ancient symbioses we call “cells,” and the products of other ancient symbioses we call “genomes.”

# The Boundaries of the Human: Symbiont and Cyborg

Forensic analysis of the microbiome of phones and shoes

Simon Lax, et al **Microbiome** 20153:21 DOI: 10.1186/s40168-015-0082-9



Simon Park's  
BioArt of  
Cell Phones

Dirtier than  
Toilet seats

# We Are All Lichens:

How symbiosis theory is  
reconfiguring  
critical biological boundaries

**TEAM** F. Gilbert

Swarthmore College, USA

University of Helsinki, Finland

