
Microbiome

What is microbiome?

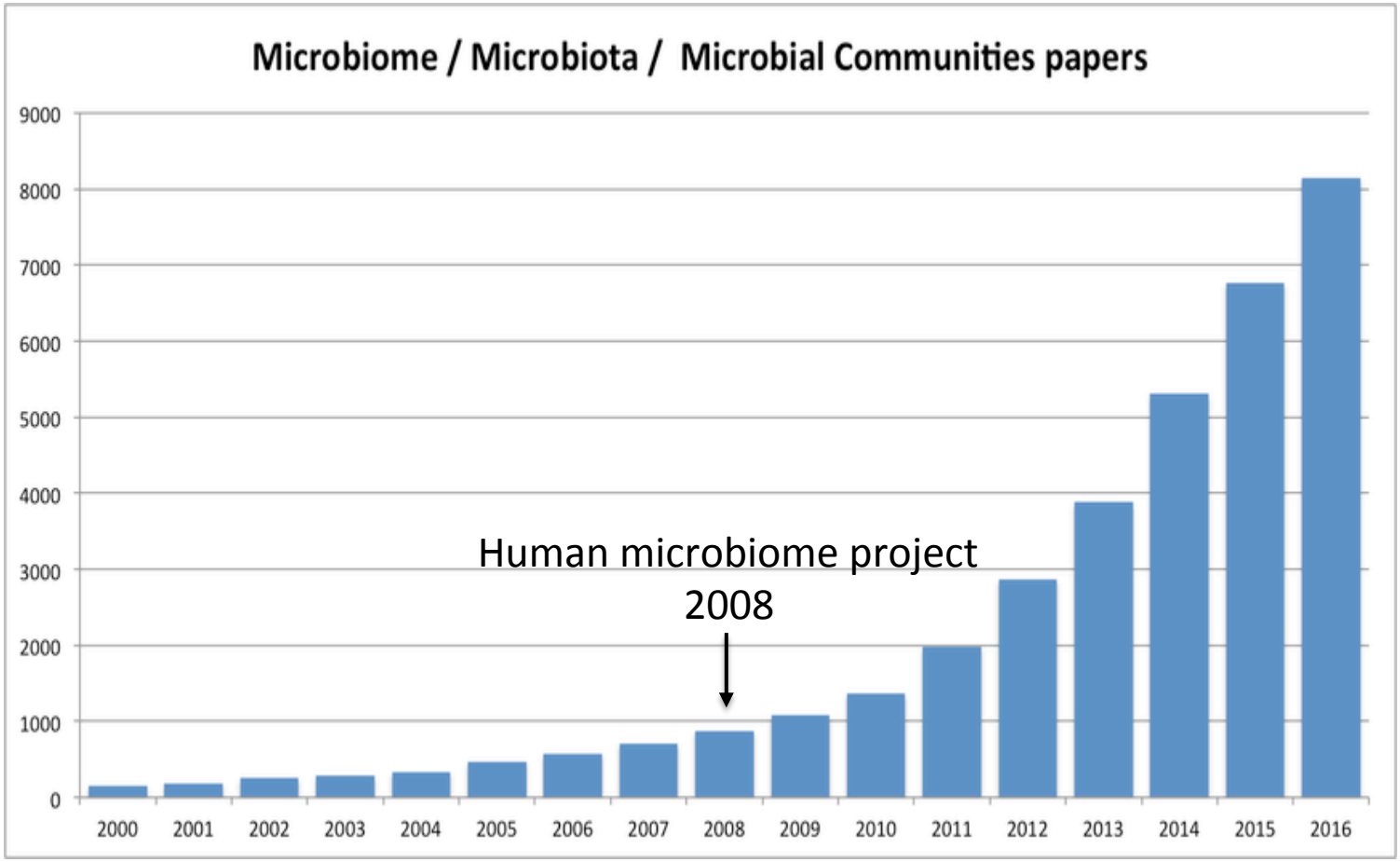
All microbes at particular location

- Human microbiome?

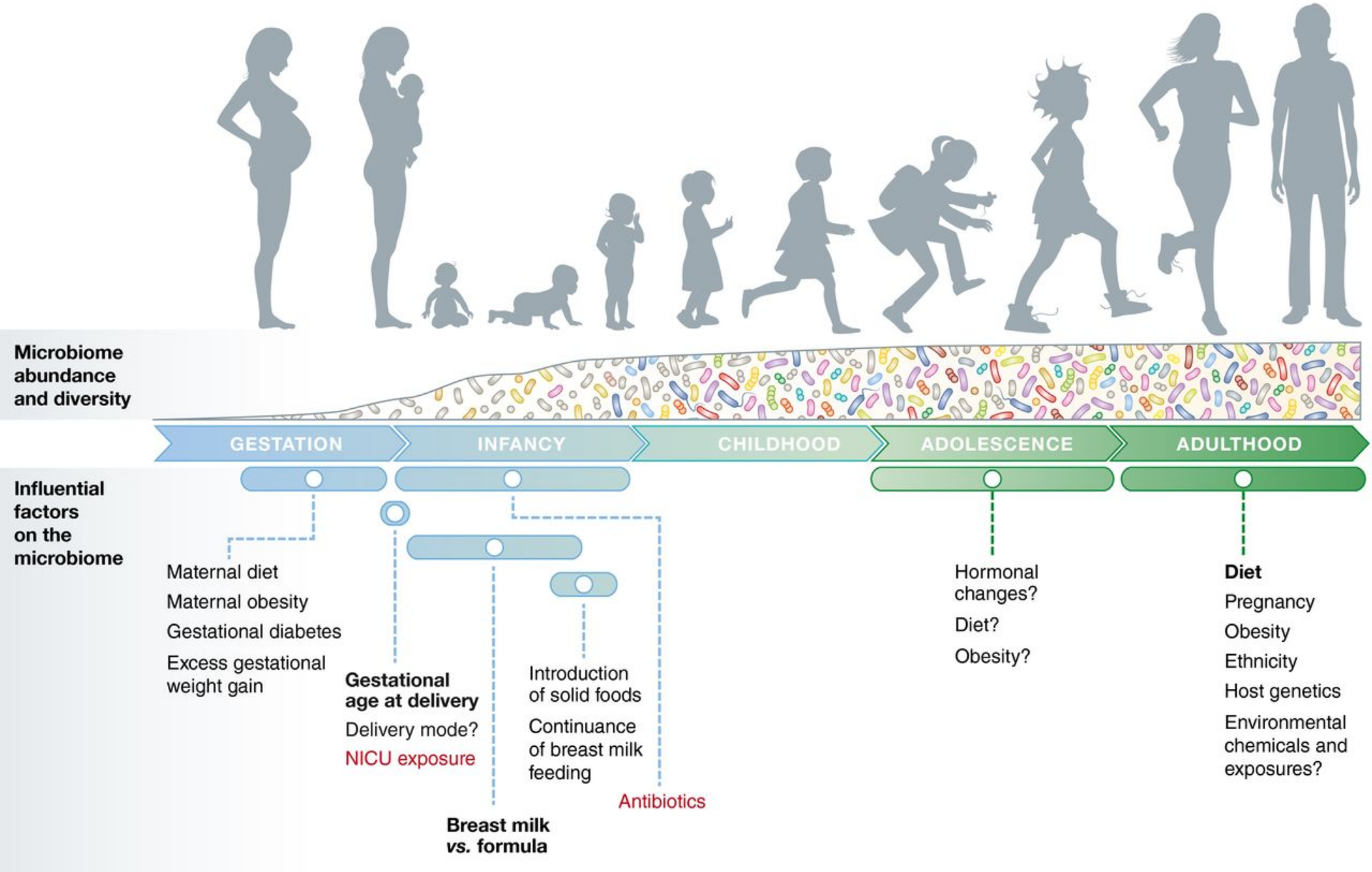
Groups of microbes that lives in and on human body

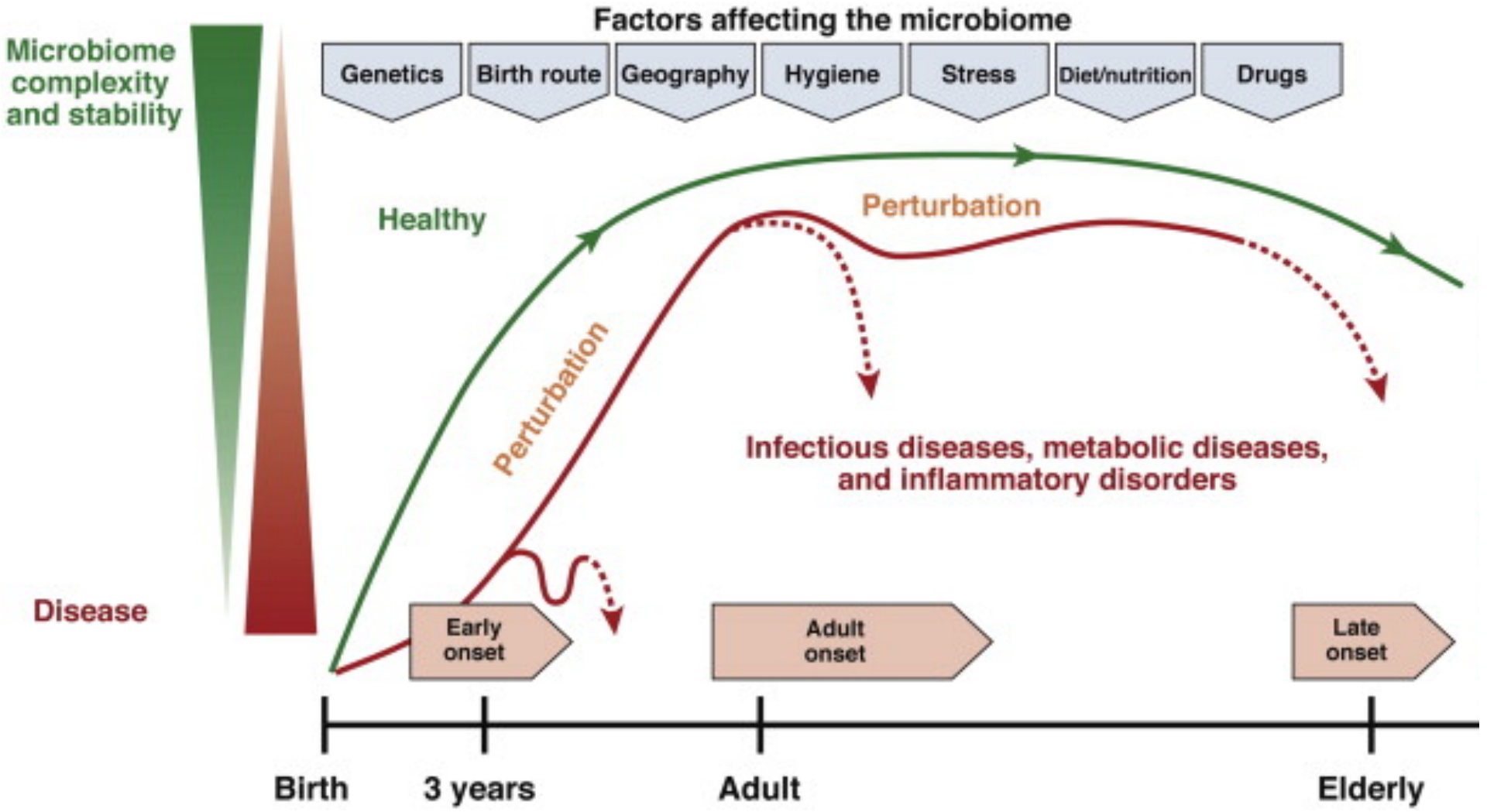
  - Includes bacteria, viruses, fungy and archea
  - Most of ”our” microbes are not harmful and are helping us in many physiological processess.

Number of publications



Microbiome development





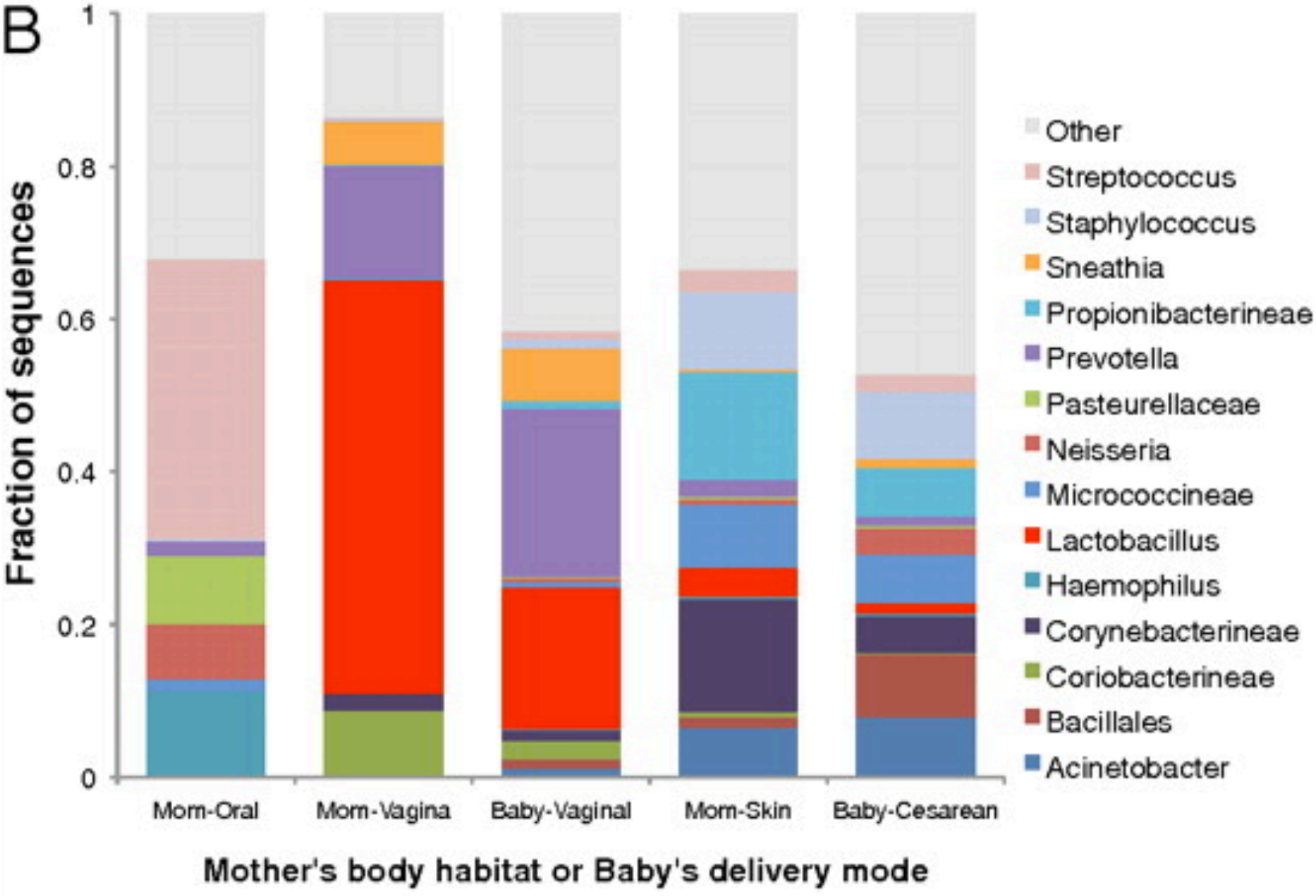
Healthy microbiome

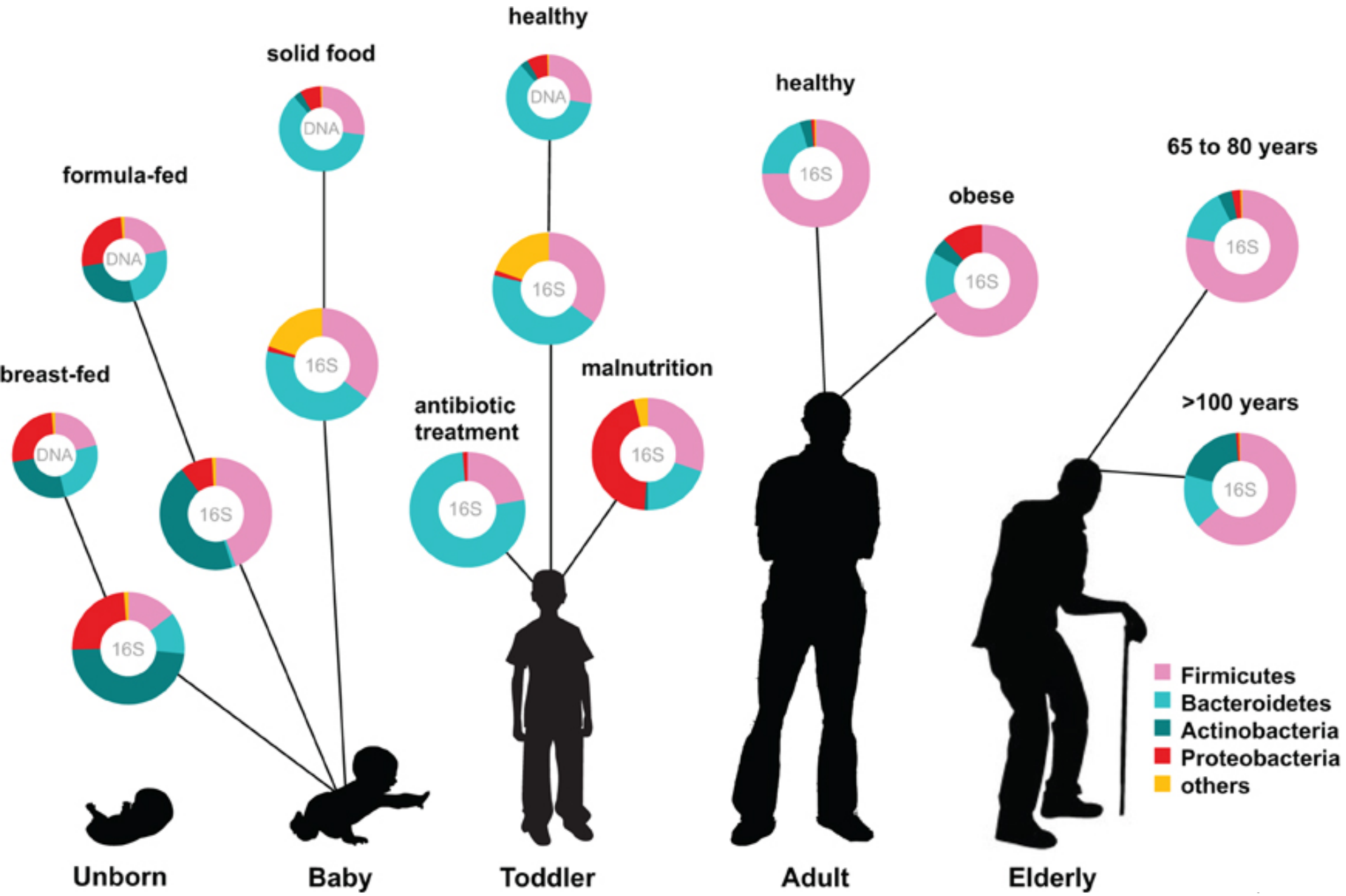
- protects from pathogens
- Stimulate immune respose
- Provides nutrients, energy, vitamines, some fatty acids

Diseased microbime

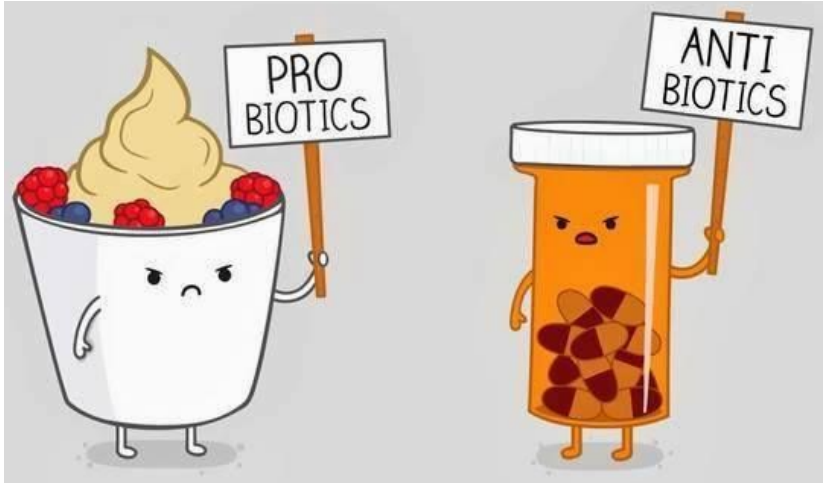
- Induces inflammation (local & sistemic)
- Oxidative stress
- Number of Gramm – bacs
- Opportunistic infections
- Change in metabolite production

How does delivery method affects baby's microbiome




healthy
solid food
DNA
DNA
formula-fed
DNA
16S
breast-fed
DNA
16S
16S
antibiotic
treatment
16S
malnutrition
16S
healthy
16S
obese
16S
65 to 80 years
16S
>100 years
16S
Firmicutes
Bacteroidetes
Actinobacteria
Proteobacteria
others
Unborn
Baby
Toddler
Adult
Elderly

Influence on gut microbiome:



- **Diet** – diverse food types
- **Antibiotics** – agents that can distroy patogenic microbes or stop their growth and replication without harming host
- **Probiotics** – live microorganizams when administered beneficial effects
- **Prebiotics** – undigestible food components that have positive, physiologyical effect on host by stimulating growth and activity of some comensal bacteria
- **Simbiotics** – products that contain pre_ and probiotics

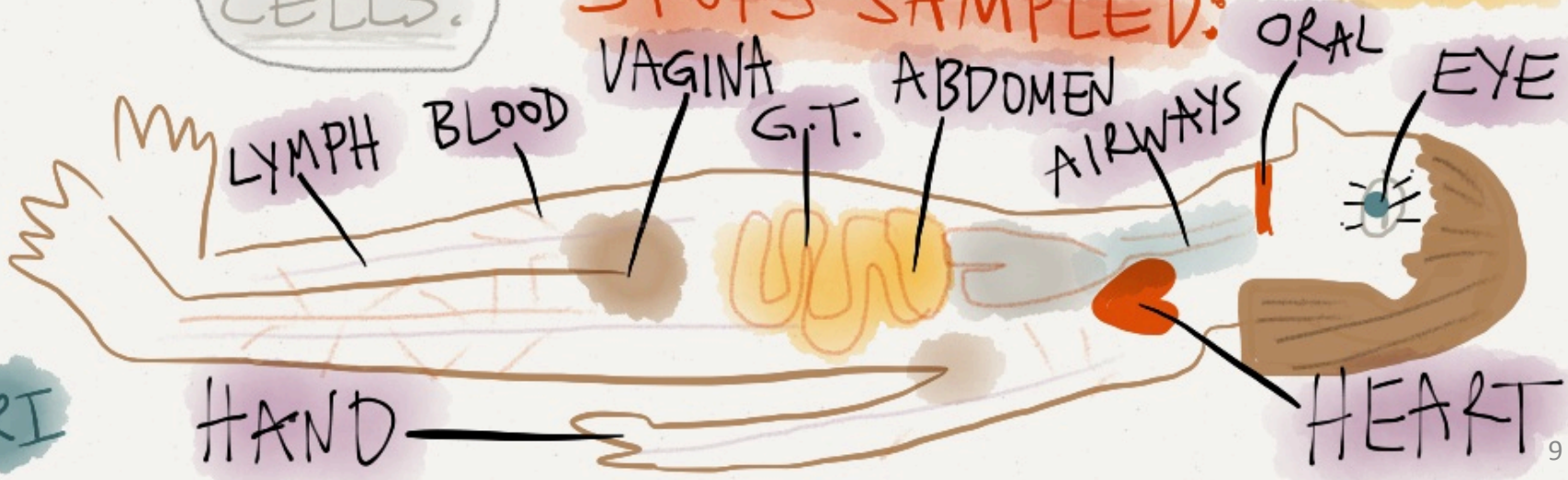
THE HUMAN MICROBIOME PROJECT

CONTAINS **10** TIMES **MORE** MICROBIAL CELLS THAN HUMAN CELLS.

MICROORGANISMS, THEIR GENOMES & ENVIRONMENTAL INTER ACTIONS

250 HEALTHY PEOPLE

SPOTS SAMPLED:



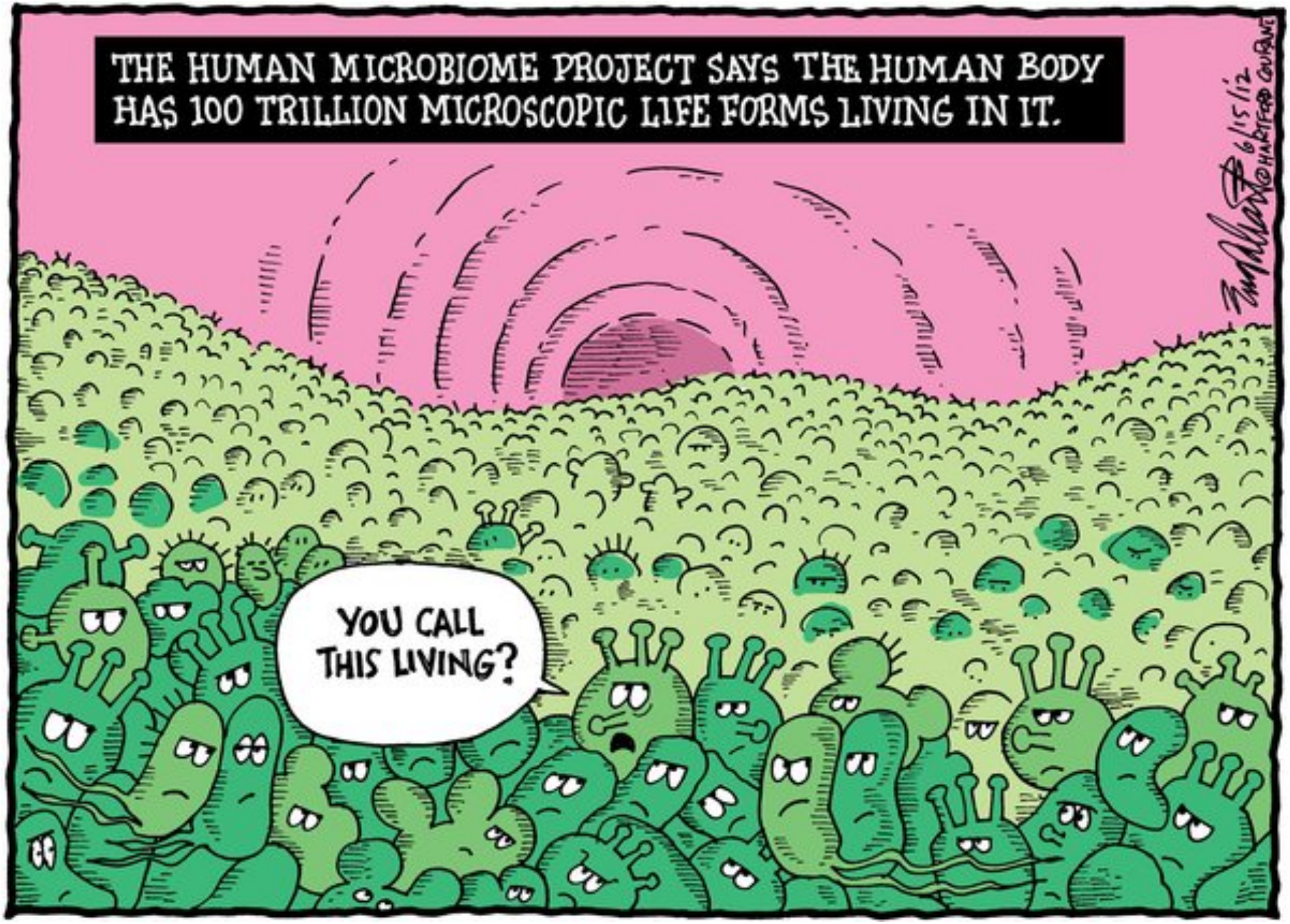
PRI

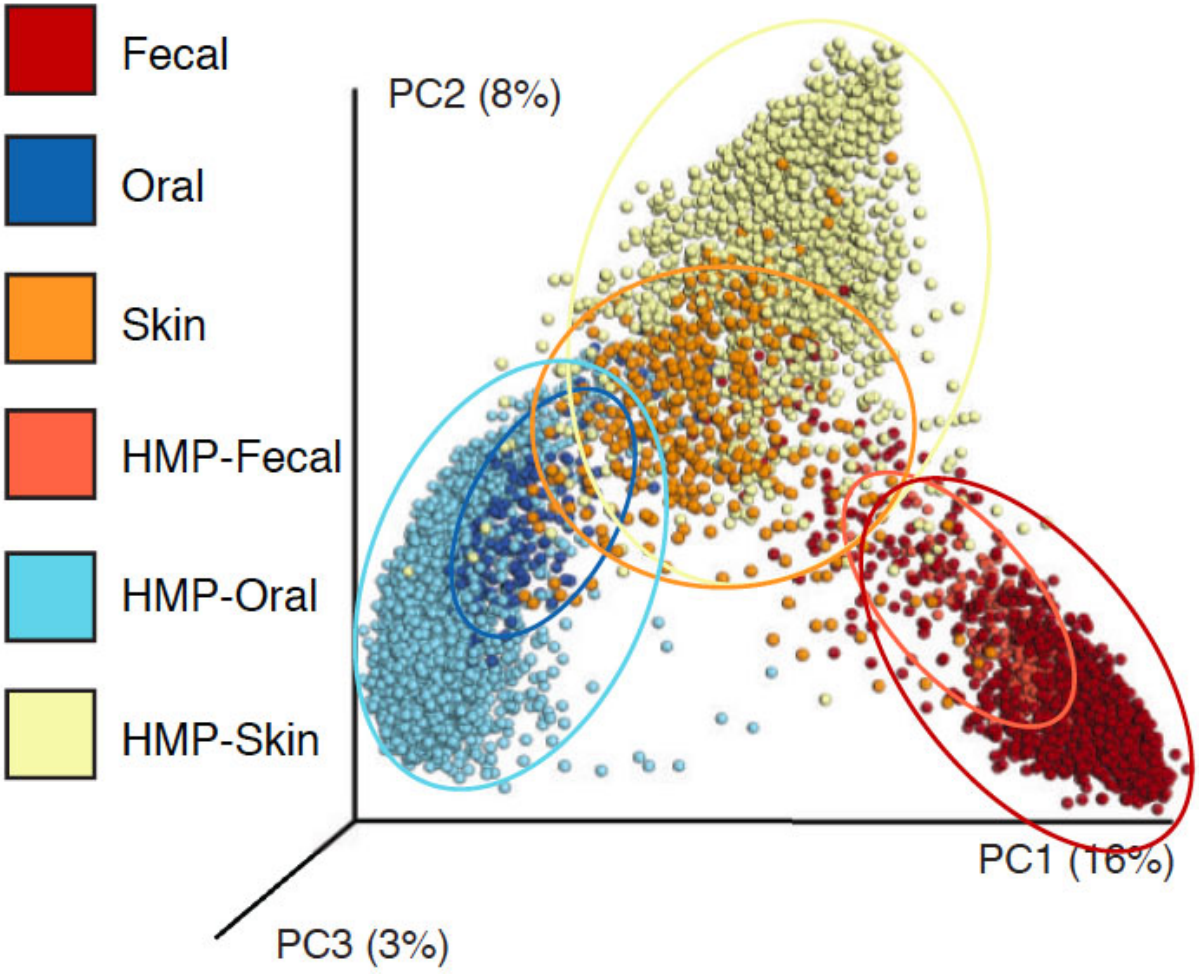
Human microbiome project (HMP1)

- From 2008 to 2012.
- 200 scientist from 80 institutions
- DNA sequencing of 16S RNA was used to identify bacteria
- Microbes were collected at 10 body locations
- WHY?
  - To better understnd role of microbes in human physiology and pathology

Human microbiome project (HMP1)

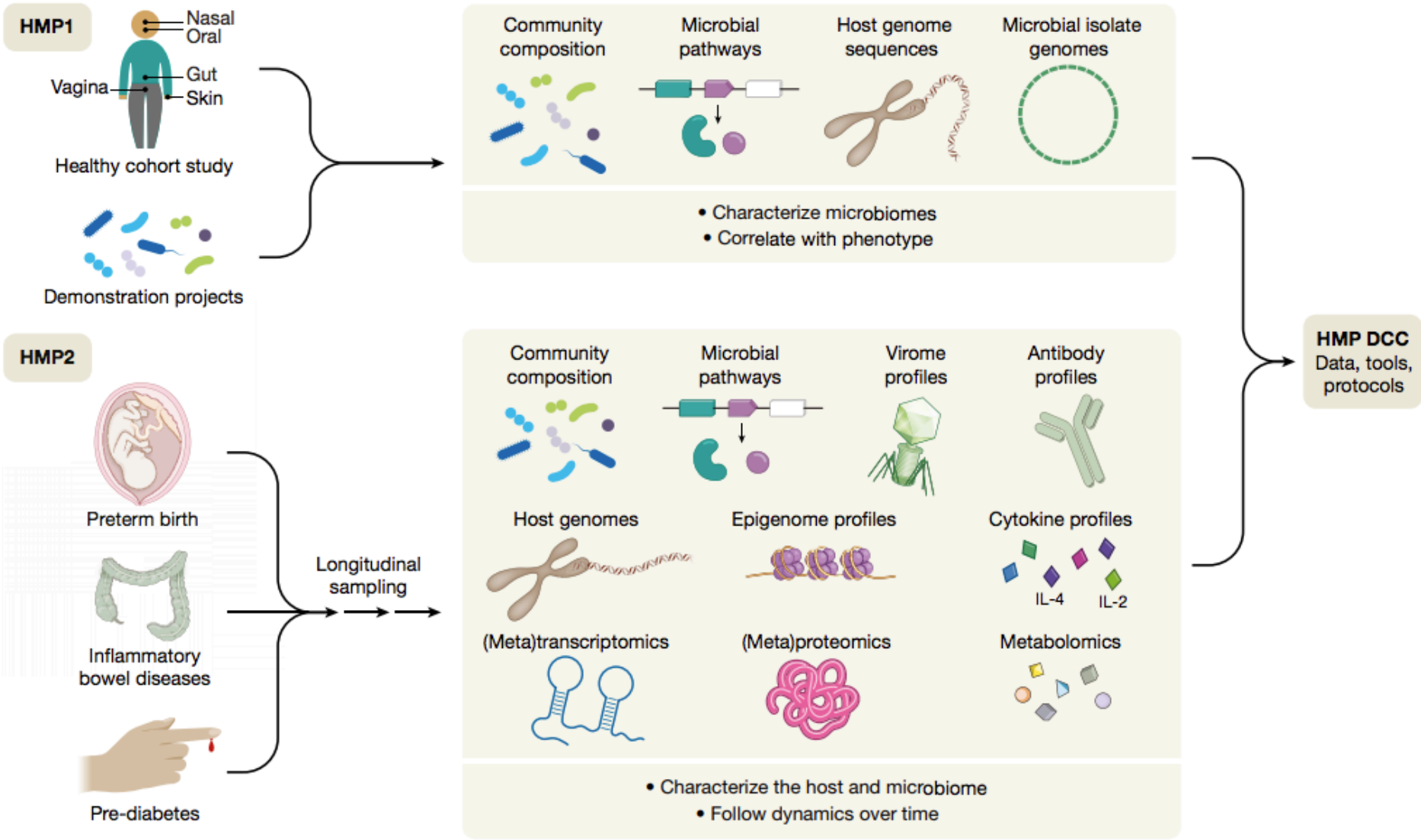
- We have 10 X more bacs then our own cells
- 10^{14} bacs
- 500–1000 kinds of bacteria in the gut
- 500–1000 kinds of bactiria on skin
- 1%–3% of body weight belongs to bacteria
- Microbial genom is 150 X bigger then human

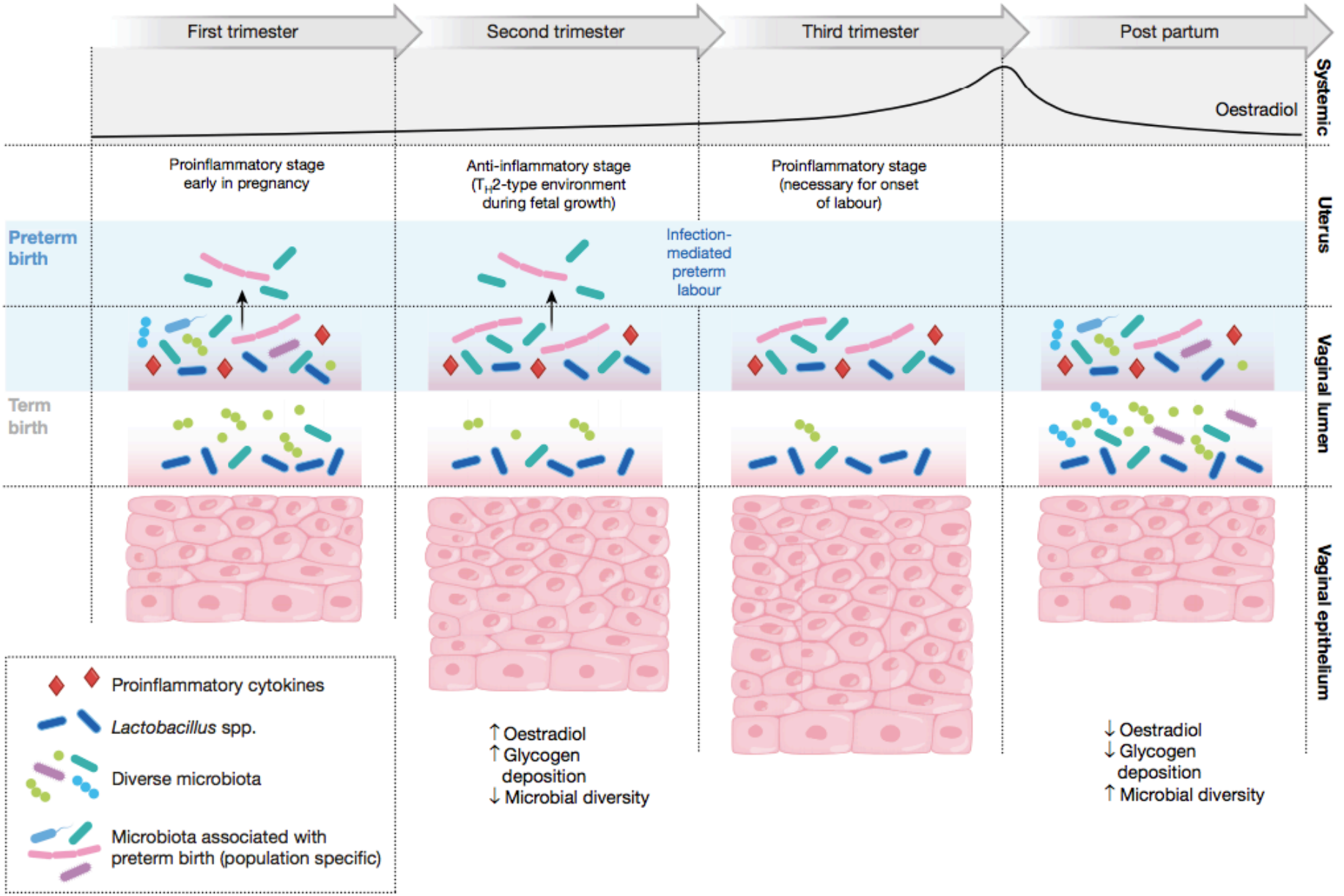

THE HUMAN MICROBIOME PROJECT SAYS THE HUMAN BODY HAS 100 TRILLION MICROSCOPIC LIFE FORMS LIVING IN IT.
YOU CALL THIS LIVING?



Each part of the human body is home to a different community of microbes, according to research conducted by the American Gut Project and the NIH Human Microbiome Project.

HMP 2 (2013–2019)




First trimester
Second trimester
Third trimester
Post partum
Systemic
Oestradiol
Proinflammatory stage early in pregnancy
Anti-inflammatory stage (T_H2-type environment during fetal growth)
Proinflammatory stage (necessary for onset of labour)
Uterus
Preterm birth
Infection-mediated preterm labour
Vaginal lumen
Term birth
Vaginal epithelium
Proinflammatory cytokines
Lactobacillus spp.
Diverse microbiota
Microbiota associated with preterm birth (population specific)
↑ Oestradiol
↑ Glycogen deposition
↓ Microbial diversity
↓ Oestradiol
↓ Glycogen deposition
↑ Microbial diversity

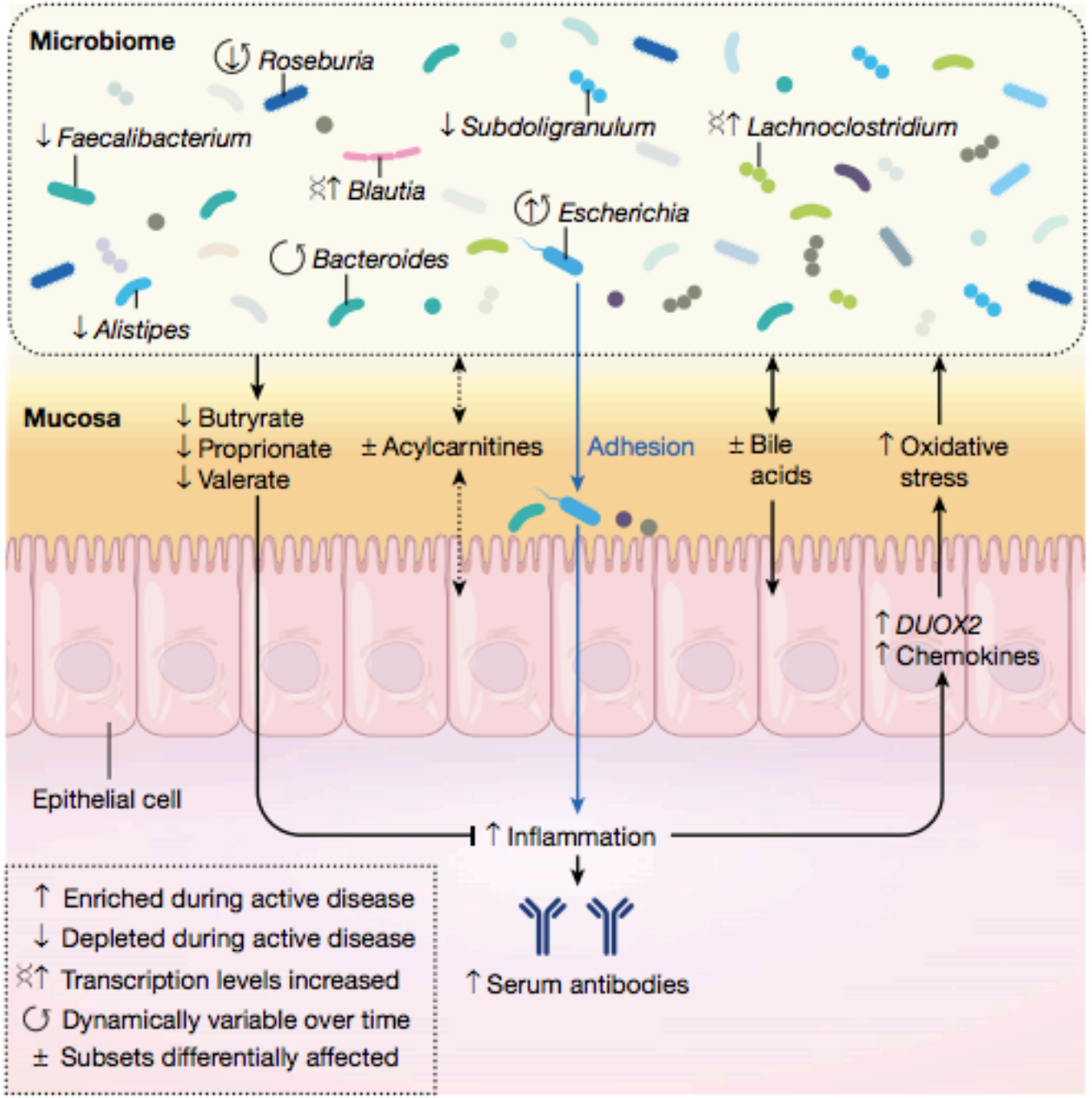


Fig. 3 | Host–microbiome dynamics in IBD. The IBDMDB followed

Why to study human microbiome 1?

Change in composition of comensal microorganisms (due to diet, antibiotic use etc) leads to change in microbial homeostasis = **disbiosis**

Link with inflammatory bowl disease, Crohn's disease, but also with rheumatoid arthritis, multiple sclerosis, diabetes, asthma etc.

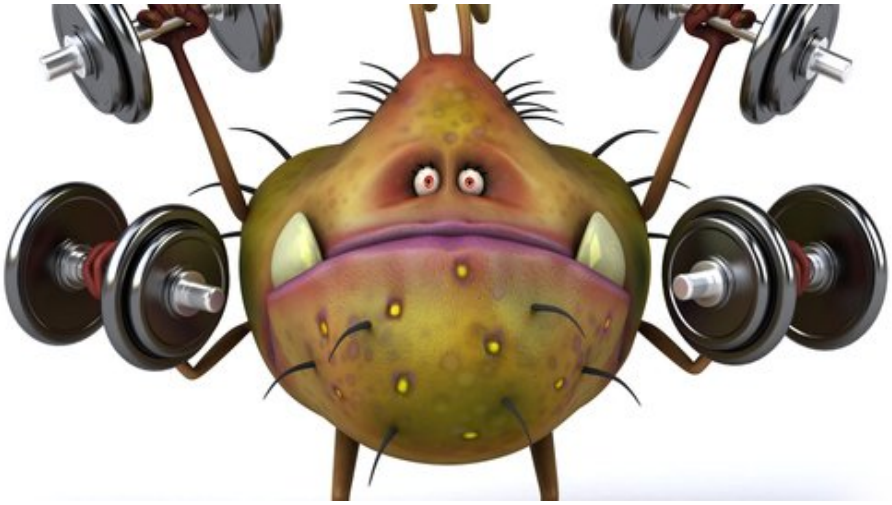
Microbiome & disease

- **Many healthy conditions are under influence of microorganisms like**: acne, diarhorea, asthma/ alergies, autoimmune d., cancer, caries, depression, atopic dermatitis, gastric ulcer, atherosclerosis, IBD etc.
- **Microbiome and obesity** – Bacteroides and Firmicutes? (Nature 2006) - doi:10.1038/4441022a
- **Melamine poisoing** & Klebsiella (2008, China)
- **Fecal bacteriotherapy (FMT)**:
  - For complicated Clostridium difficile infectiones
  - Colitis, irritabile colon, opstipation
  - Some neurological conditions (MS, PD)

- **Antibiotics are changing our microbiome balance**!

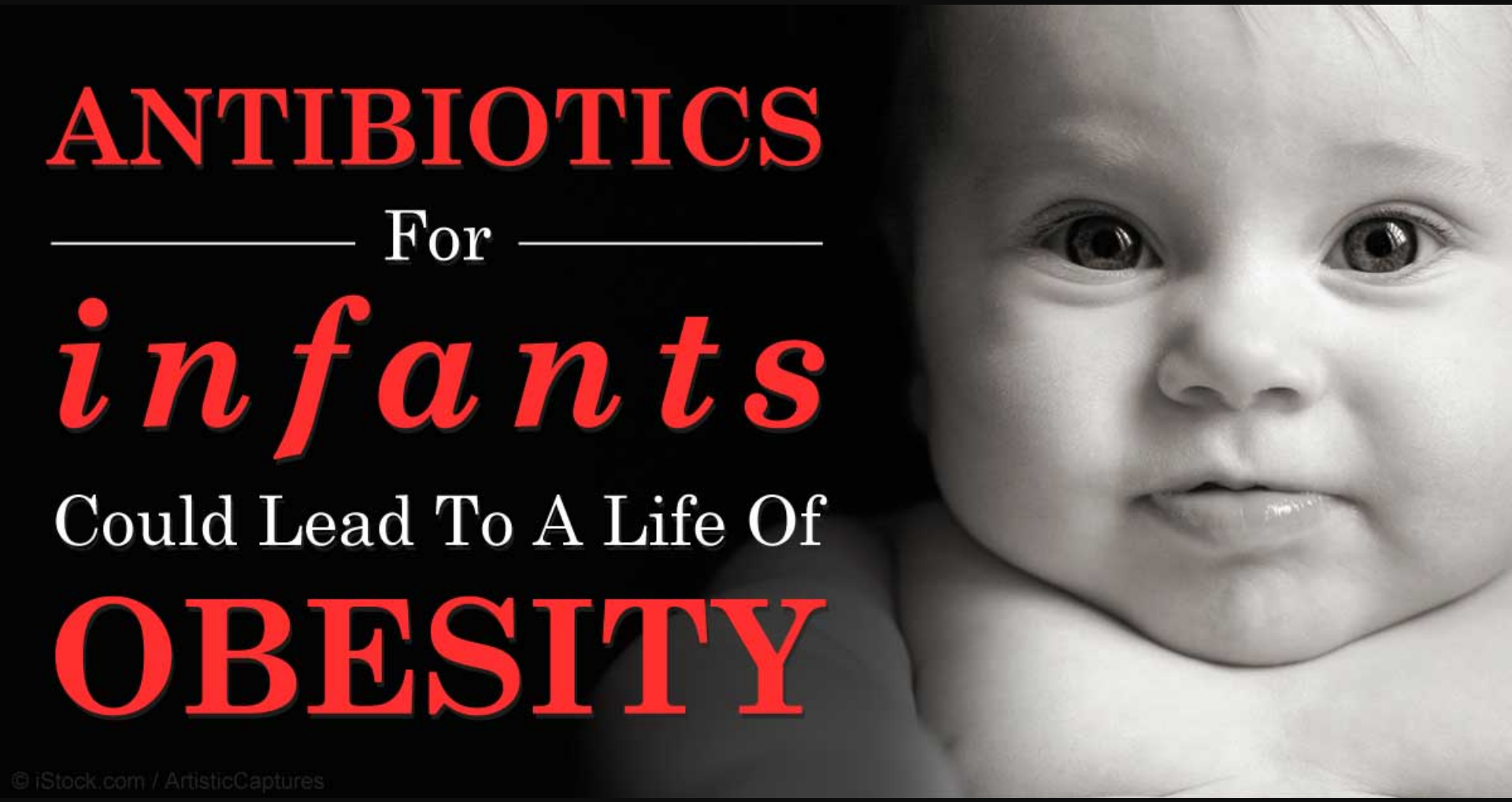
ARE GUT BUGS MAKING YOU FAT?

Microbiome consumes energy



It is estimated that metabolic activity of microbes consumes 16% of energy produced

”Altered micobiome burns fewer calories” Study links change in gut microbiome with lower basal metabolism) DOI:10.1016/j.ebiom.2015.10.018


ANTIBIOTICS
For
infants
Could Lead To A Life Of
OBESITY
© iStock.com / ArtisticCaptures

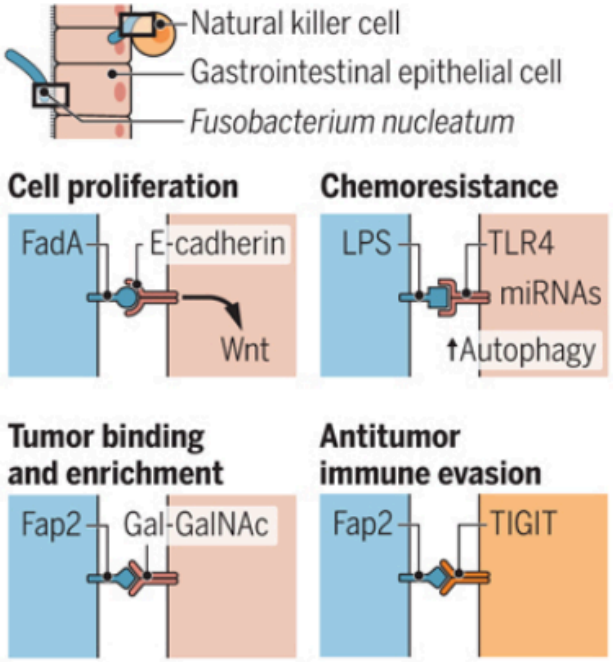

Are we that what we eat?

Why to study human microbiome 2?

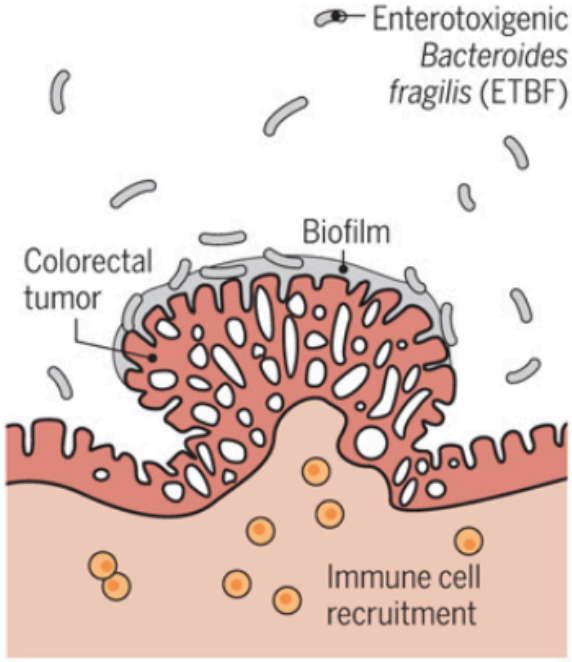
Change in composition of comensal microorganisms (due to diet, antibiotic use etc) leads to change in microbial homeostasis = **disbiosis**

Link with cancers, Alzheimer disease…

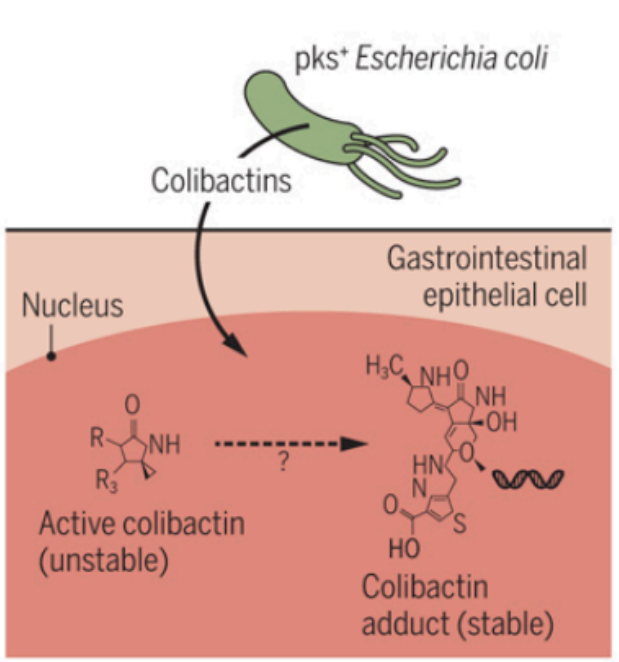
Bugs and colon cancer



F. nucleatum expresses adhesins and lipopolysaccharide (LPS), which can have multiple influences on cell behavior.

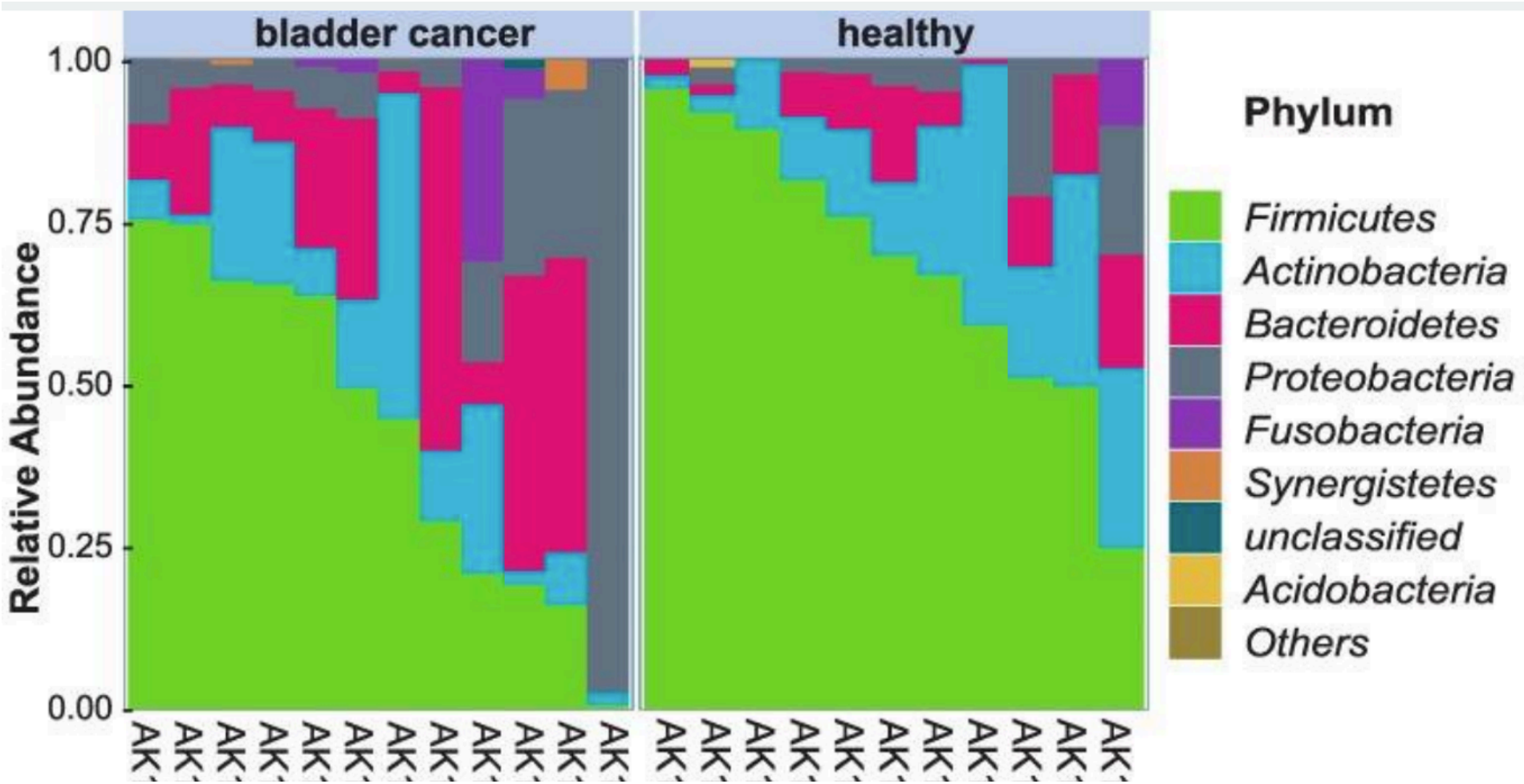


ETBF coats tumors and recruits other bacteria to create a biofilm. ETBF also recruits immune cells and promotes inflammation.

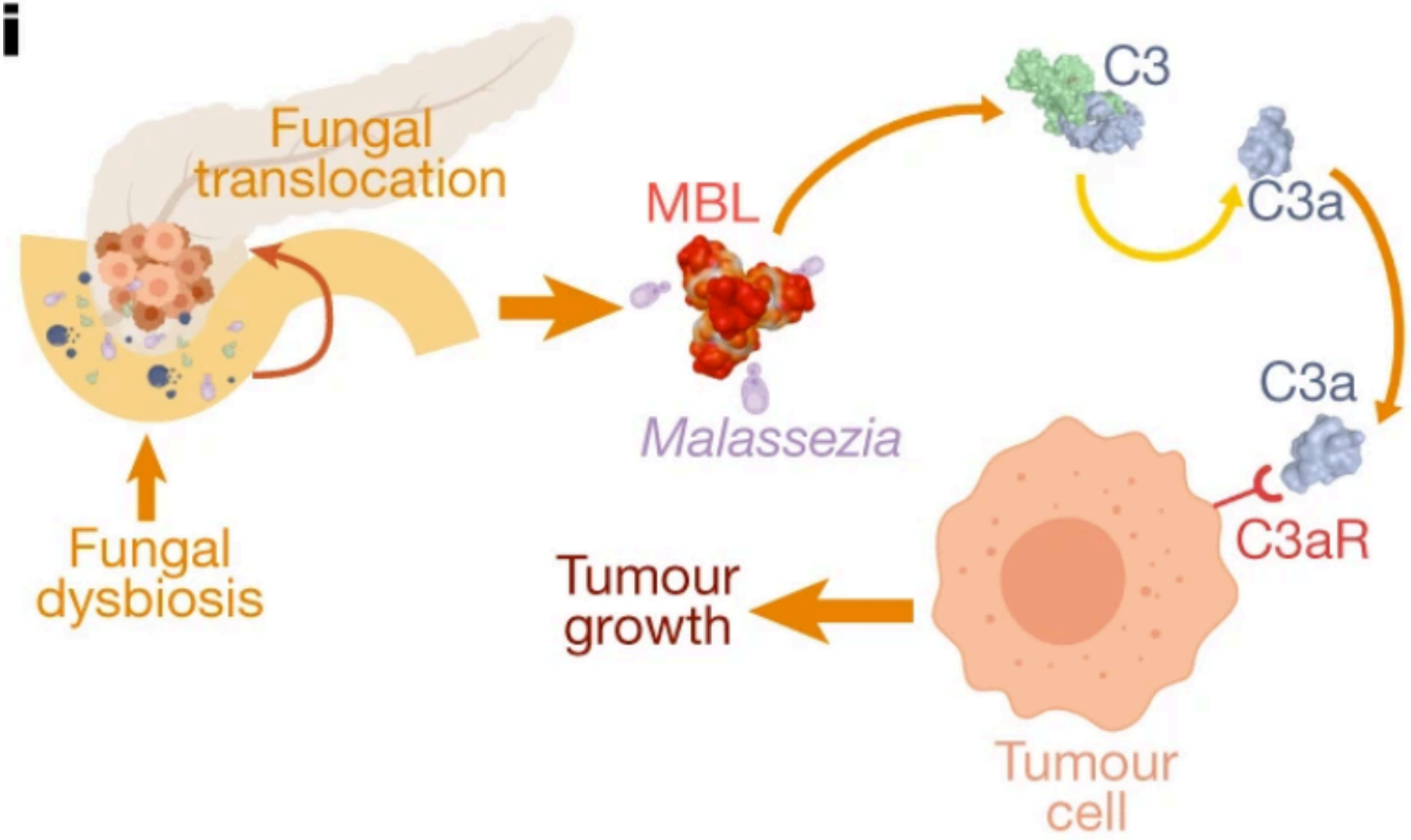


Polyketide synthase–expressing (pks⁺) *E. coli* may influence carcinogenesis through the generation of potentially mutagenic DNA adducts.

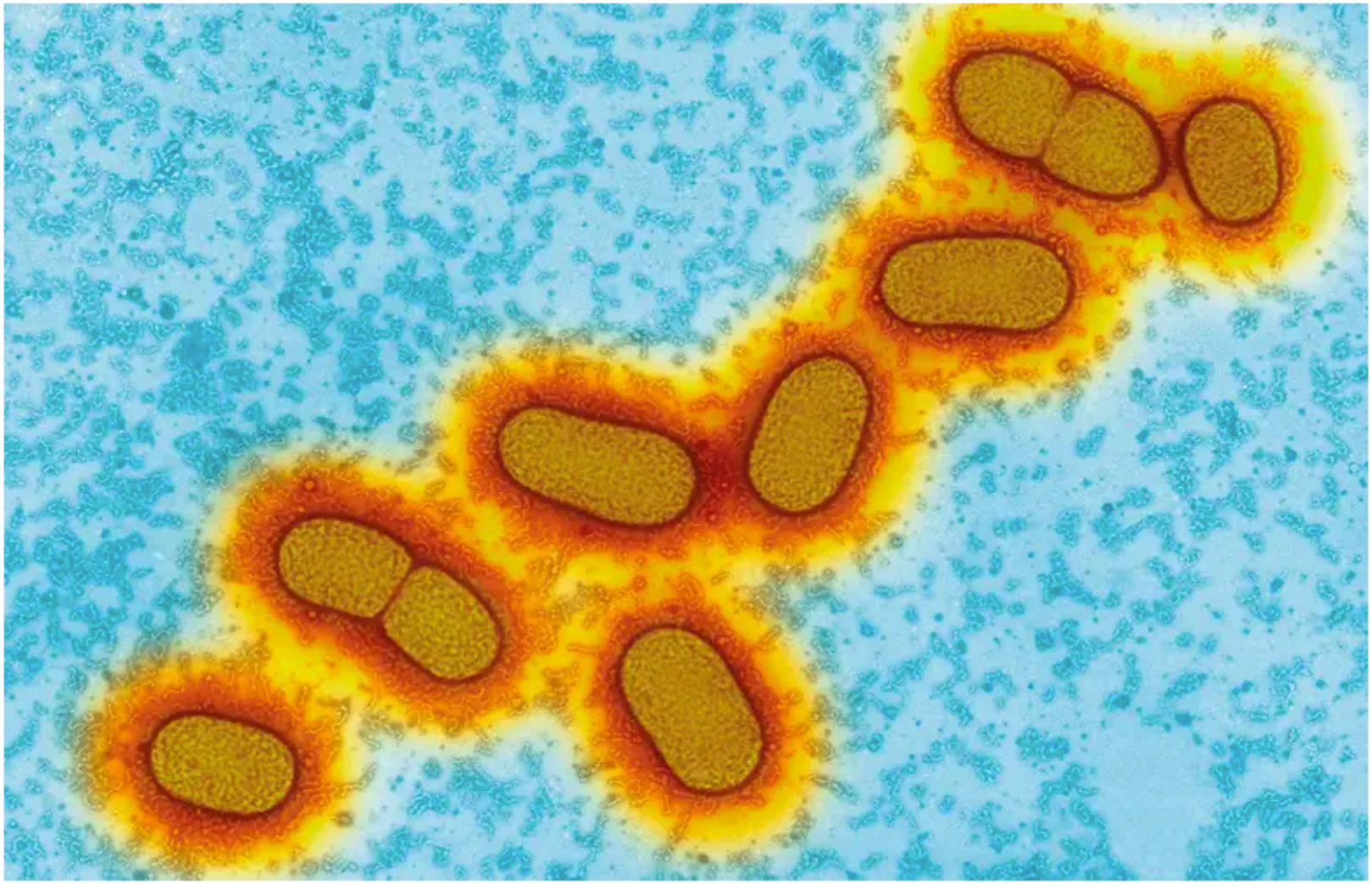
Bugs and bladder cancer



Mycobiome and pancreatic ca.

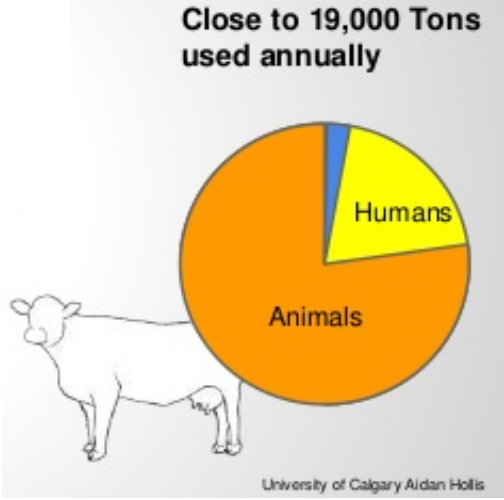


Alzheimer's disease & P. gingivalis



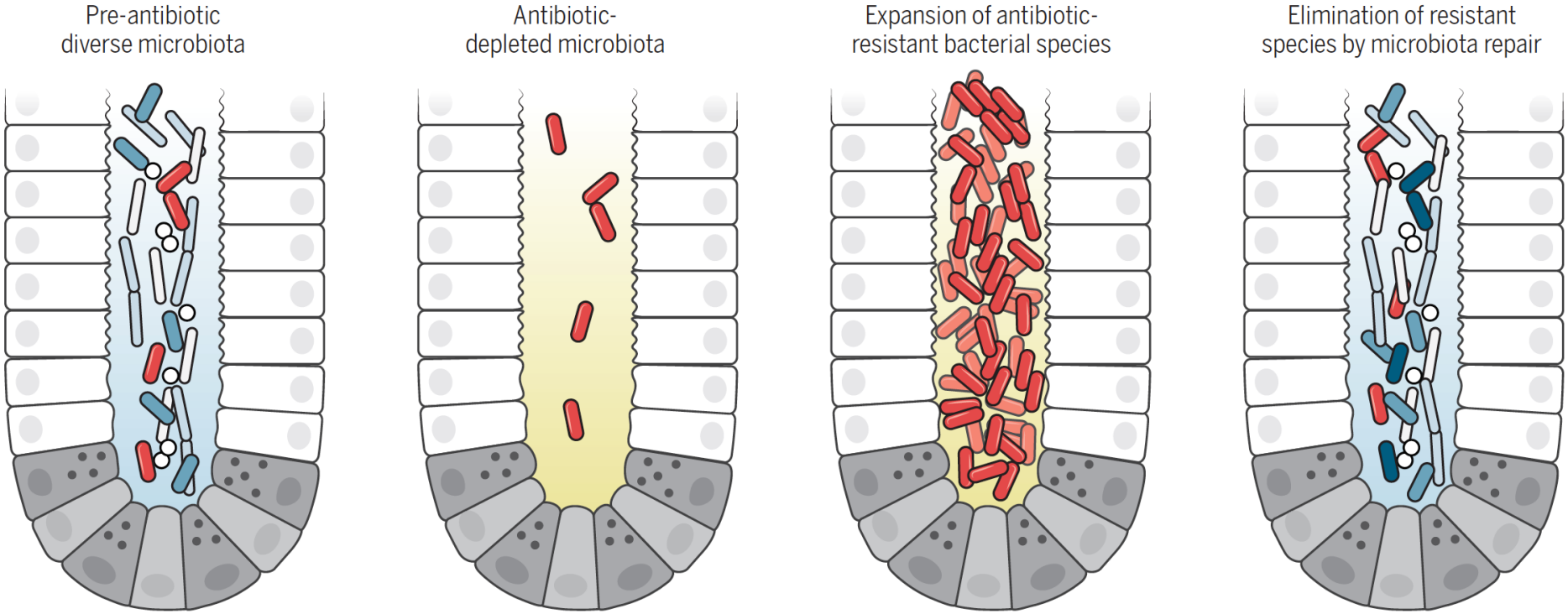
The Porphyromonas gingivalis bacteria that can cause gum disease
A. Dowsett, Public Health England/Science Photo Library

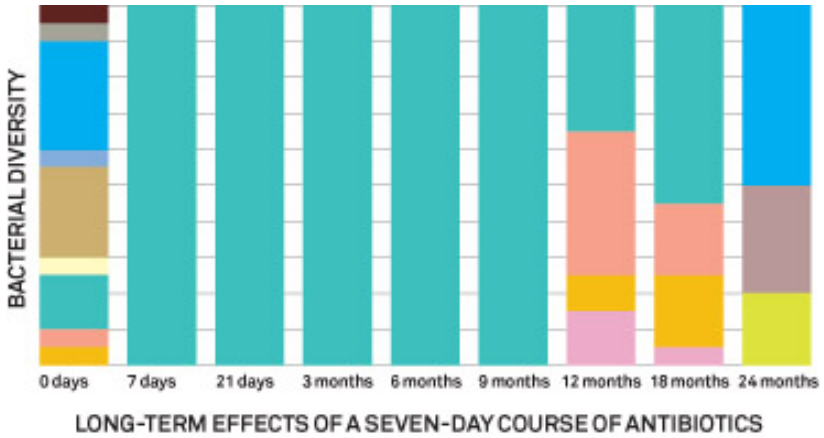
Antibiotics
(Annualy 19 000 tons into enviroment!)

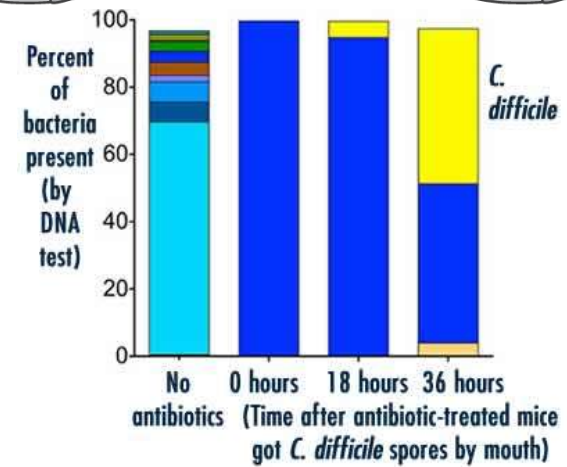


- Unselective use of antibiotics reduces bacterial diversity
- Most of the antibiotic use (over 80%) is in meat industry, to prevent infections and stimulate animal growth
- Soil fertilizers and human waste are contaminating plants
- Springs, rivers and oceans are containing more chemicals including antibiotics

Role of antimicrobial therapy







Probiotics

- Global sale in 2015. was 36.6 bilion USD and it is expected to rise to 45 bilions in 2019.
- Fastest growing segment of dietary supplements
- People are looking for ”natural” way of staying healthy and treating disorders

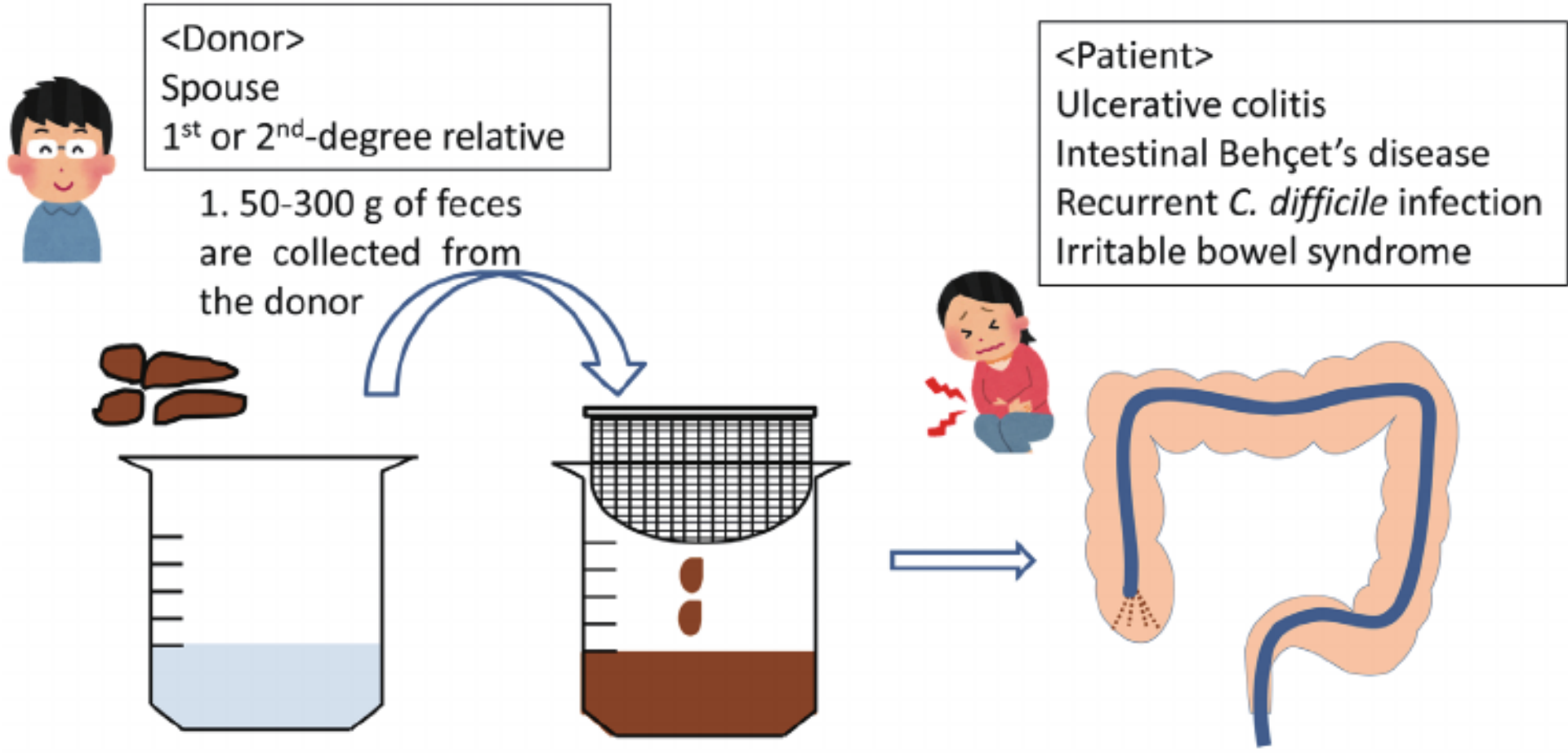
Diarhorhea after antibiotic consumption

	Probiotic	Control	p
Diarrhea			
Yes	12%	34%	*.007
No	88%	66%	
C. Difficile			
+	0%	17%	*.001
-	100%	83%	

Hickson et al. *BMJ* 2007;335:80

Fecal microbiota transplant (FMT)

Procedure


<Donor>
Spouse
1st or 2nd-degree relative
1. 50-300 g of feces are collected from the donor
<Patient>
Ulcerative colitis
Intestinal Behçet's disease
Recurrent C. difficile infection
Irritable bowel syndrome
2. Feces are dissolved in 50-100 ml of normal saline.
3. Fecal materials are filtered through a metal strainer.
4. Fecal slurry is administered through colonoscopy

FMT

- TransIplantation of fecal bacteria from healthy donor into recepient
- Clisma, orogastric tubes, per–os (capsuls with liophilized bacteria)
- It was designed to treat Clostridium difficile infection
- Treating other gastrointestinal conditions (like colitis, irritabile colon) and some neurological disorders (multiple sclerosis and Parkinsons

Enterococcus faecalis & alcoholic hepatitis & PHAGES

How does immune system differentiate pathogenic from comensal and non-pathogenic microorganisms?

Co-evolution of microbe and adaptive immunity

- We are born sterile.
- Vertical transmission of mothers microorganisms during delivery
- Adoptive immunity ”learns” to live with comensals

Maturation of babys immune system

- Neonatal gut microbiome is changing until three years of age
- Immunologic system maturate under microbiome influence
- Starts with passive transfer of mothers IgA

Importance of IgA

- Microbial antigens recognized by IgA are processed by innate immune system in ”tolerogenic” way.

Why?

IgA weakly activates complement thus favoring regulatory immune respose

Germ-free mice

- Reduced numer and size of cells in secondary immune organs
- Changed number and diversity of immune cell population
- Abnormal response to infection and injury
- Absent Th17 cells
- Reduced Treg cells

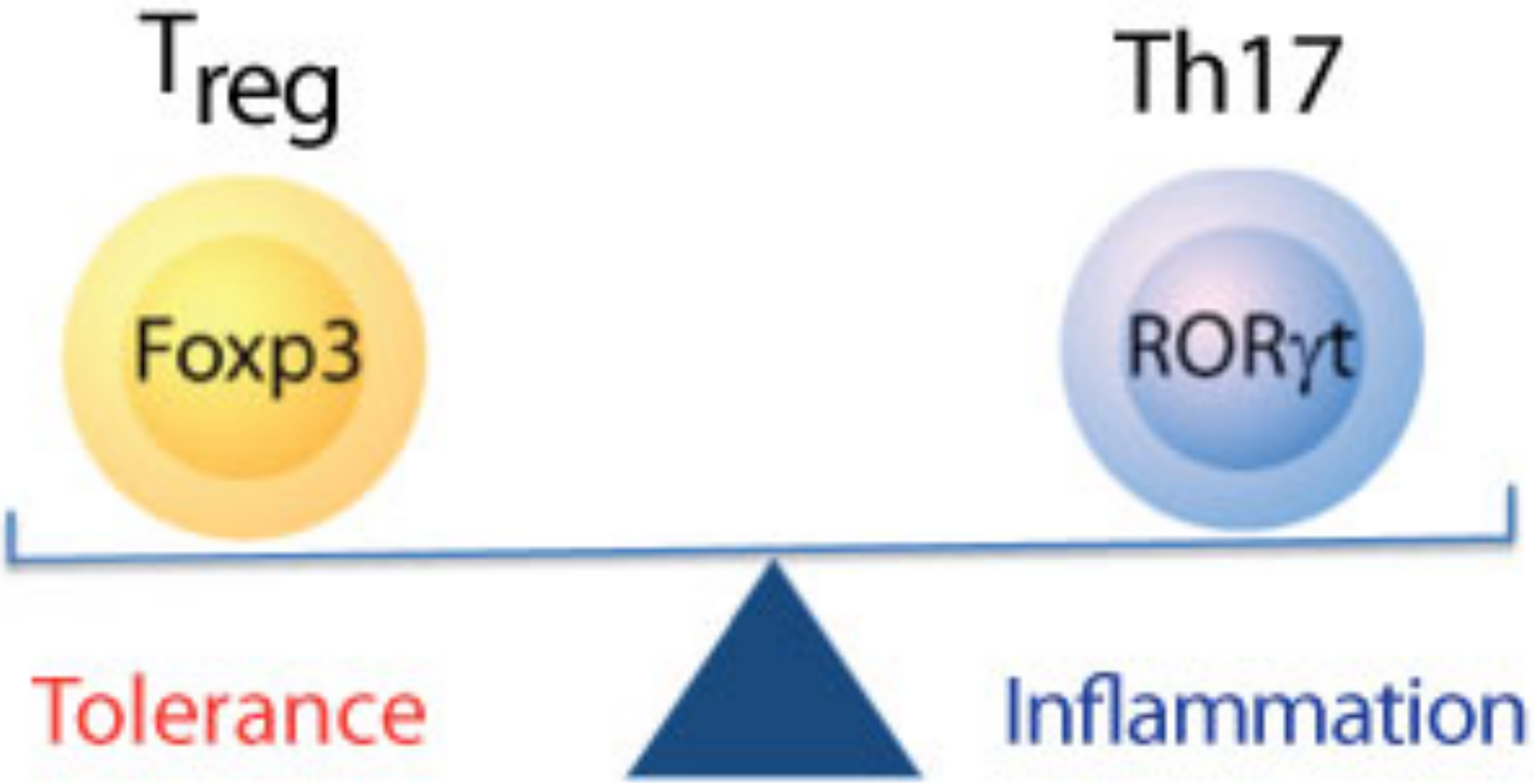
Bad from good?

- ”Good” microbes are less capable to activate TLR and NLR
- ”Bad” microbes have virulence factors
- ”Good” microbes are capable to inhibit NF–kB signaling pathway (by reducing intracellular signaling)

Reacting on ”good” bacs

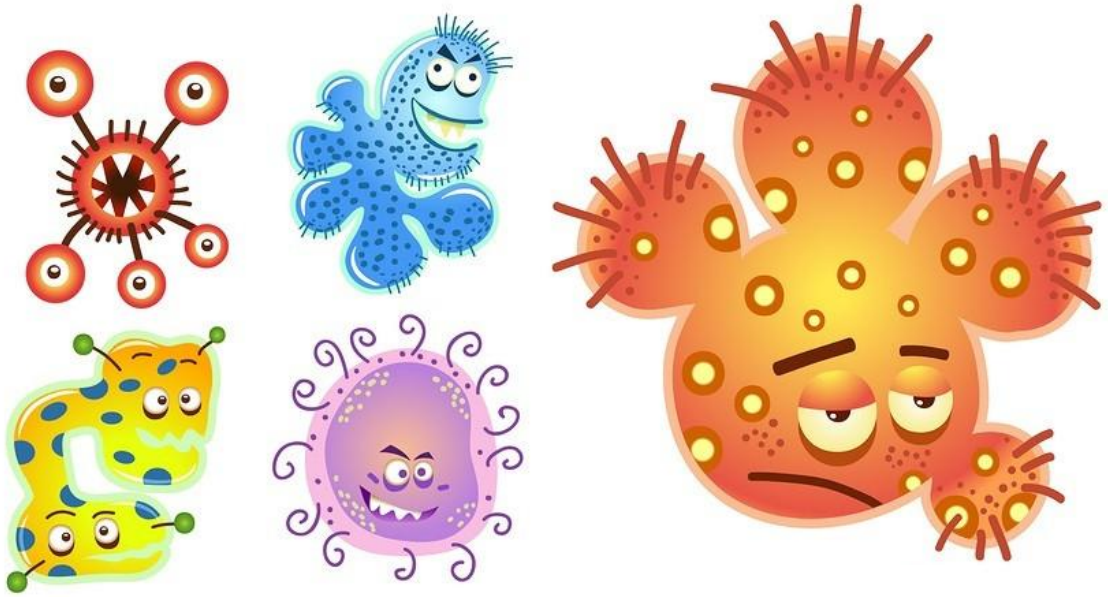
- Macrophages & dendritic cells are expressing less receptors
- Many Treg cells are being developed
- Intestinal epithelial cells are producing TGFβ to supress NF-κB dependent pro-inflammatory signals in macrophages and DC and is stimulating development of Treg and IgA-plasma cells
- Th17 protects from pathogenic bacs

Balance



More popular reading at:

- http://learn.genetics.utah.edu/content/microbiome/



Thank you!