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Examining genomics and your health, Part 2: Genomics of your microbiome and your health

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Genomics and Your Health

Part II: Genomics of your microbiome and your health

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In case you ever feel lonely… You are really not alone, ever.

- Basically, 9 out of every 10 cells in your body are not human cells…. What a thought.
- A typical person has 10 trillion human cells
- But, 100 trillion cells that belong to microscopic organisms
- We have evolved to co-exist over the eons
- The details of those relationships have very interesting implications for disease and even development and behavior

Dr. Suess and *Horton Hears a Who*

We are starting to hear what we cannot see!

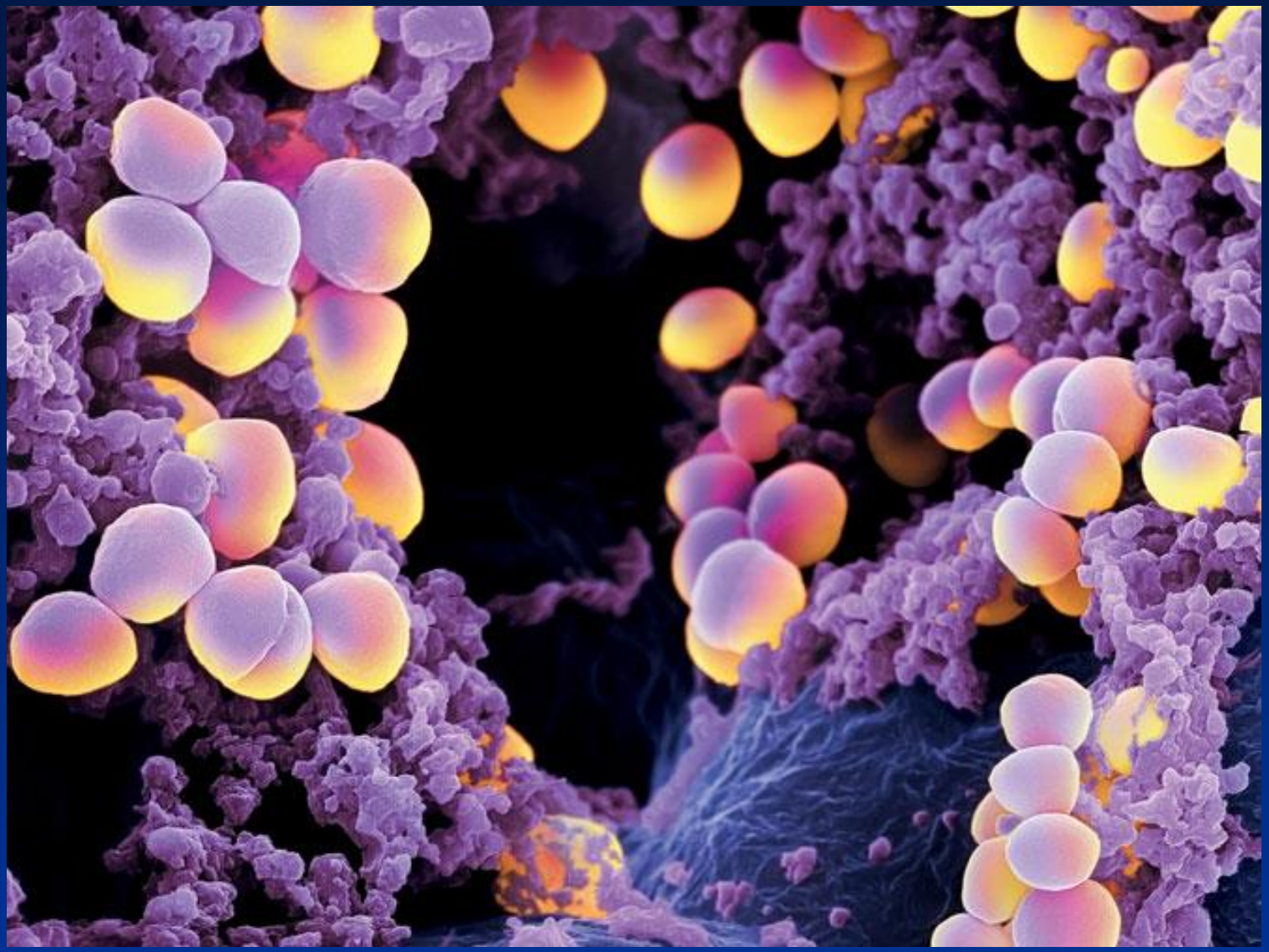
Very Timely Topic

- Documentary coming on May 4, 2013 to the Smithsonian Channel…
- You may never think about your body the same way again…
- www.Smithsonian.com/microbes
- Cover story in Smithsonian Magazine, May 2013

Photograph by Martin Oeggerli, with support from School of Life Sciences, FHNW; Taken from: http://ngm.nationalgeographic.com/2013/01/microbes/oeggerli-photography#/09-mouth-microbes-670.jpg

MOUTH MICROBES

The human mouth hosts a panoply of microbes, some taking up residence on the mouth lining (blue) within days after birth.

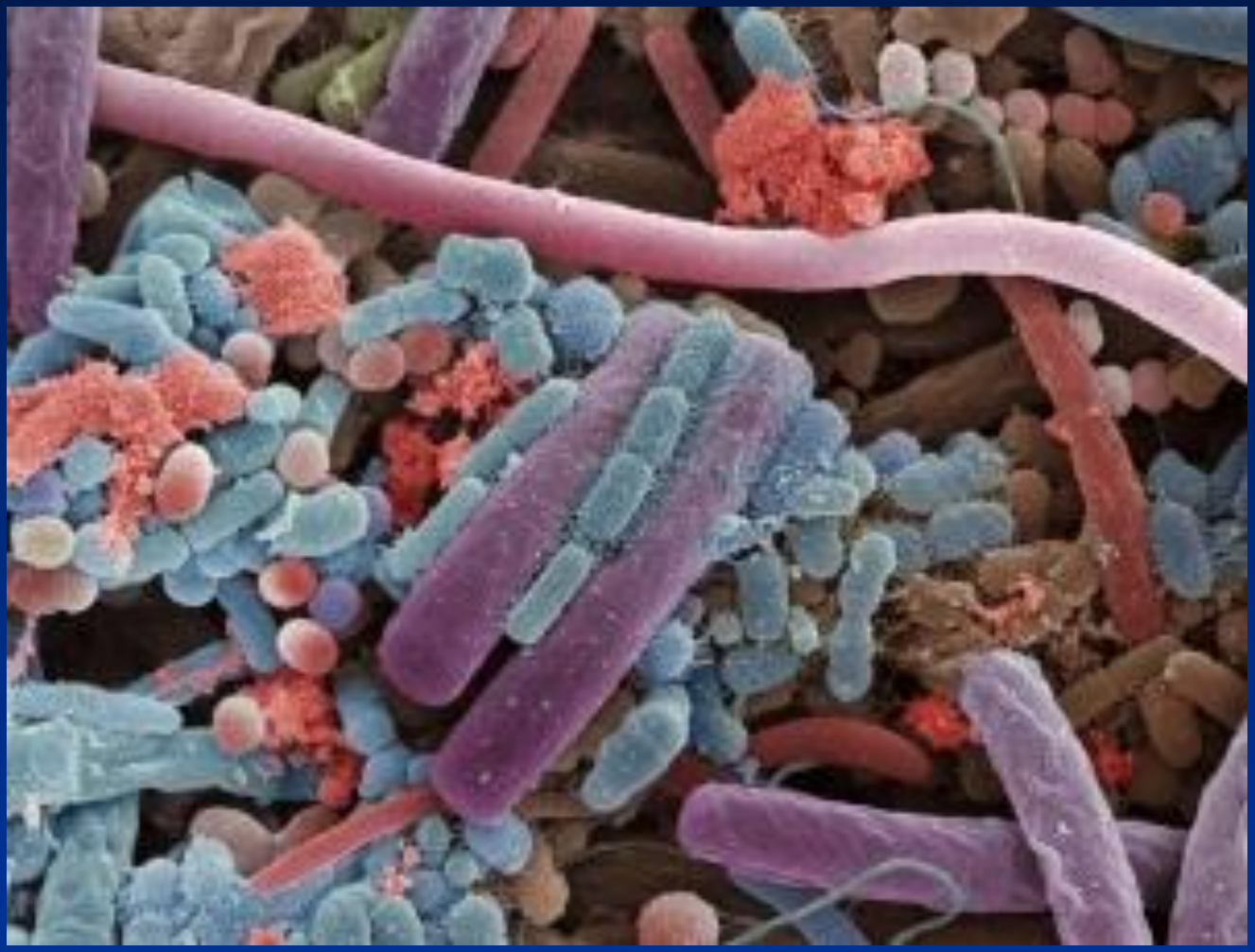


Photograph by Martin Oeggerli, with support from School of Life Sciences, FHNW; Taken from:http://ngm.nationalgeographic.com/2013/01/microbes/oeggerli-photography#/10-staphulococcus-aureus-670.jpg

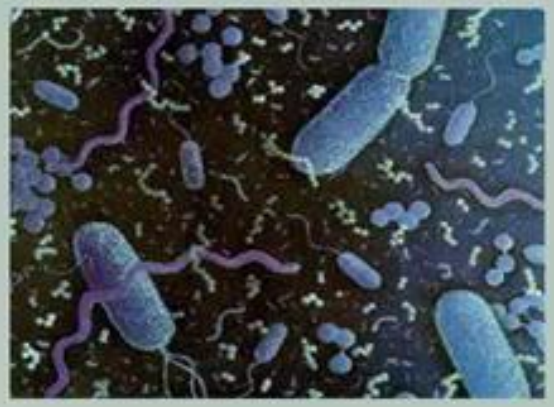
STAPHYLOCOCCUS AUREUS

The bug lives harmlessly in the noses of about a third of us.

Human Tongue Bacterial Community



Taken from: http://www.nature.com/news/microbiome-sequencing-offers-hope-for-diagnostics-1.10299



Though many diseases are caused by microbes:

cholera, tuberculosis, AIDS, malaria, measles, food-borne disease, etc.

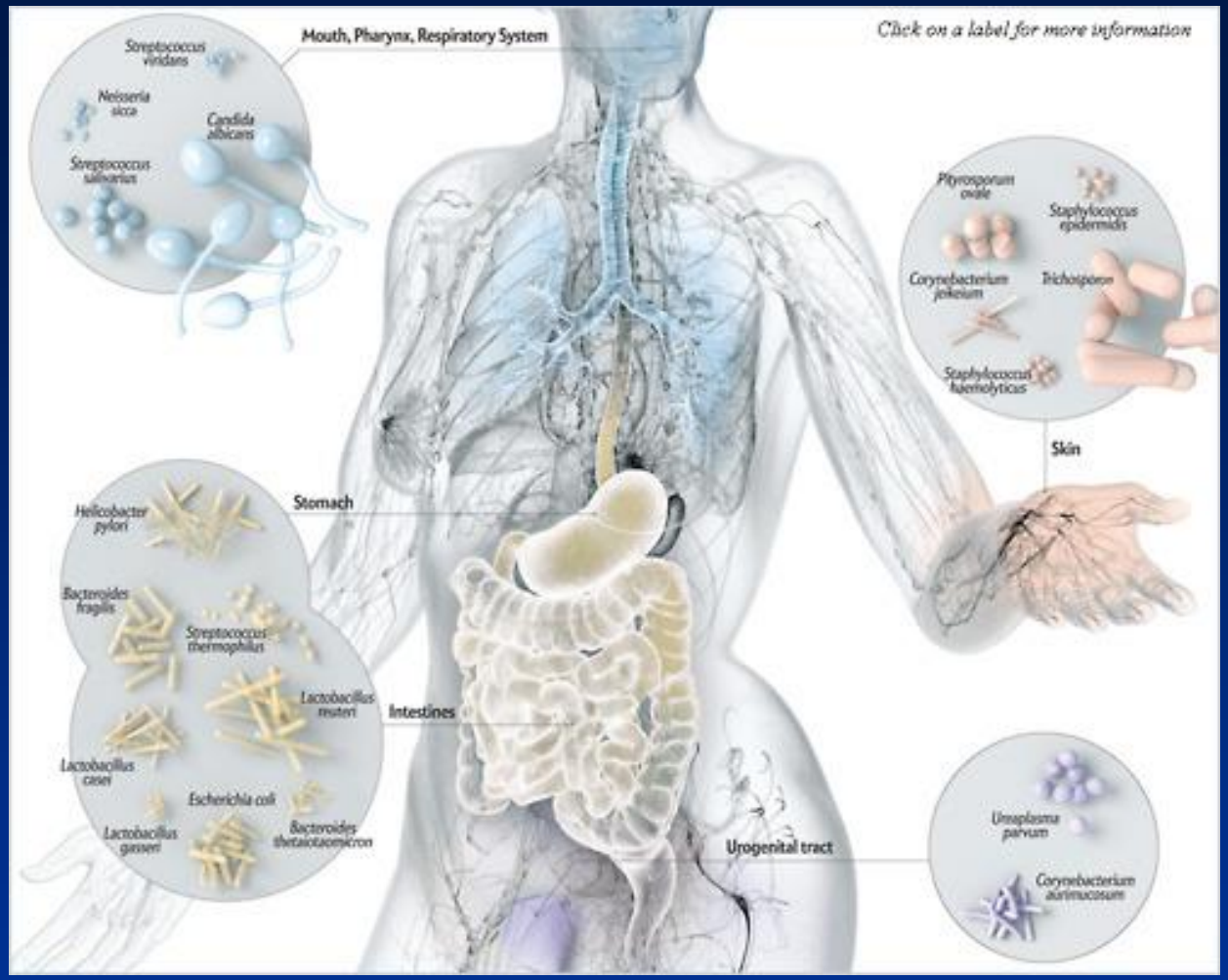
The MAJORITY of microbes do not cause disease. Rather, they contribute to:

- ► Food production (bread, cheese, yogurt, beer, chocolate, coffee, etc.)
- ► Soil production/regeneration
- ► Pollutant/toxin degradation
- ► Oxygen production
- ► Human health

Taken from: http://vimeo.com/24221417

Have you ever heard of the Human Microbiome Project (HMP)?

- http://www.hmpdacc.org/
- Funded mostly by National Institutes of Health (NIH); started in 2007; $140 million
- 2008; the European Commission; $29 million for MetaHIT; Metagenomics of the Human Intestinal Tract Project
- National Human Genome Research Institute (NHGRI)
- Census project for the organisms that live with us



Taken from: http://rationaldiscoveryblog.com/post/23136159768/explore-the-human-microbiome-the-human-microbiome

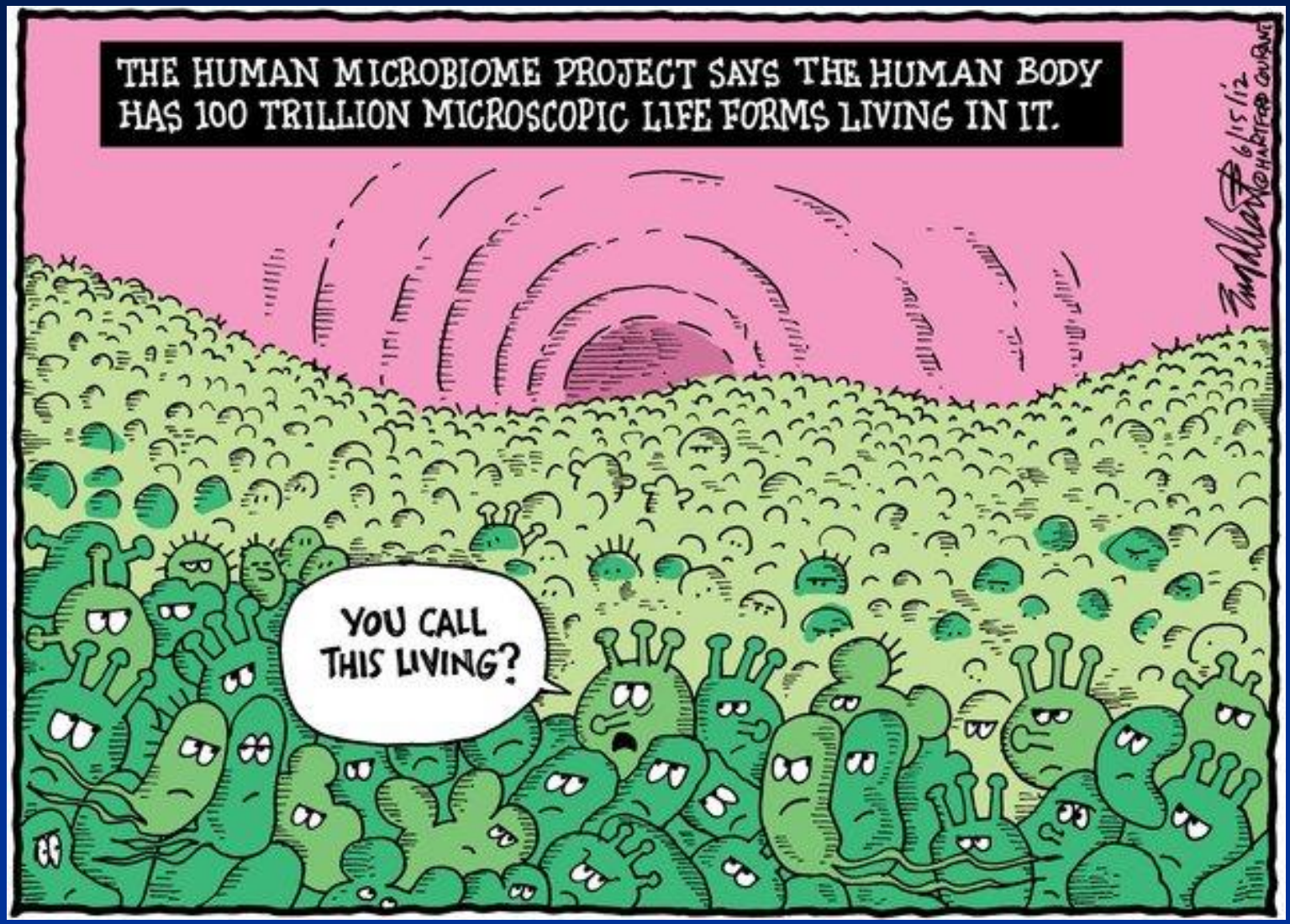
Human Microbiome Project

- 200 scientists; 80 Institutions, 5 year project
- To map the microbiome in 242 healthy people; ages 18-40
- This is the first real human microbiome census
- Your own genetics is in interplay with the genetics of your microbes
- How might the microbiome change when you are sick?
- We exist within our own little ecosystem
- We need to study our own community interactions

Human Microbiome Project

- Women were sampled in 18 places, including 3 sites in the vagina
- Men were sampled in 15 places
- The people were resampled three times throughout the sample, generating a total of 11,174 samples
- Sequenced the bacterial DNA to find the unique genes in the microbiome
- Now the challenge…How does the microbiome affect health and disease and try to improve health by manipulating the microbiome.

Taken from: http://www.quantumrevolution.net/wp-content/uploads/2013/02/microbiome.jpg



A New Way to Study Human Health

- Only about 10% of the microbes living on people have been surveyed/studied→ First microbiome census
- How different are the microbes from site to site in the same person and from person to person?
- How much do these communities change in our life time?
- How can these communities keep us healthy or make us sick?
- Probably not a good idea to be too “clean”.

Cover Art for the Journal Nature
June 2012

Self-Portrait: the Human Microbiome" by Joana Ricou
Illustration by Steven H. Lee

June 13, 2012 – Landmark Papers

- 16 papers published simultaneously reporting on the first wave of findings from the HMP
- Some highlights from the research:
  - Which is more different? Microbial communities within different regions of your body or between you and another person?
  - Microbial communities on a person change over time

  (fewer microbes in vagina just before birth): temperature, pH, other environmental effects
  - Different species assemblages may be able to do the same kind of job (variation in microbial diversity)

Taken from: http://www.newser.com/story/148082/10k-microbial-species-inhabit-you.html

Thought to consider…

- We have about 21,000 or so human genes,
- But our resident microbes possess another 8 million or so genes, many of which are collaborating behind the scenes handling food, being involved with the immune system, influencing our behavior and manipulating the human genes.
- “Man is not an island or a peninsula, but more of a metropolis.” (Conniff, 2013)

Consider the following series of Great Visuals by Perrin Ireland

Graphic Science, June 19, 2012

http://www.wagsrevue.com/thewag/?q=content/graphic-science-1

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

THE RESEEARCHERS FOUND

1,000 STRAINS OF BACTERIA ON EACH PERSON!

THE MICROBIOME STARTS AT BIRTH. AS BABIES PASS THROUGH THE BIRTH CANAL, THEY PICK UP THE BACTERIA FROM THE MOTHER'S VAGINAL MICROBIOME.

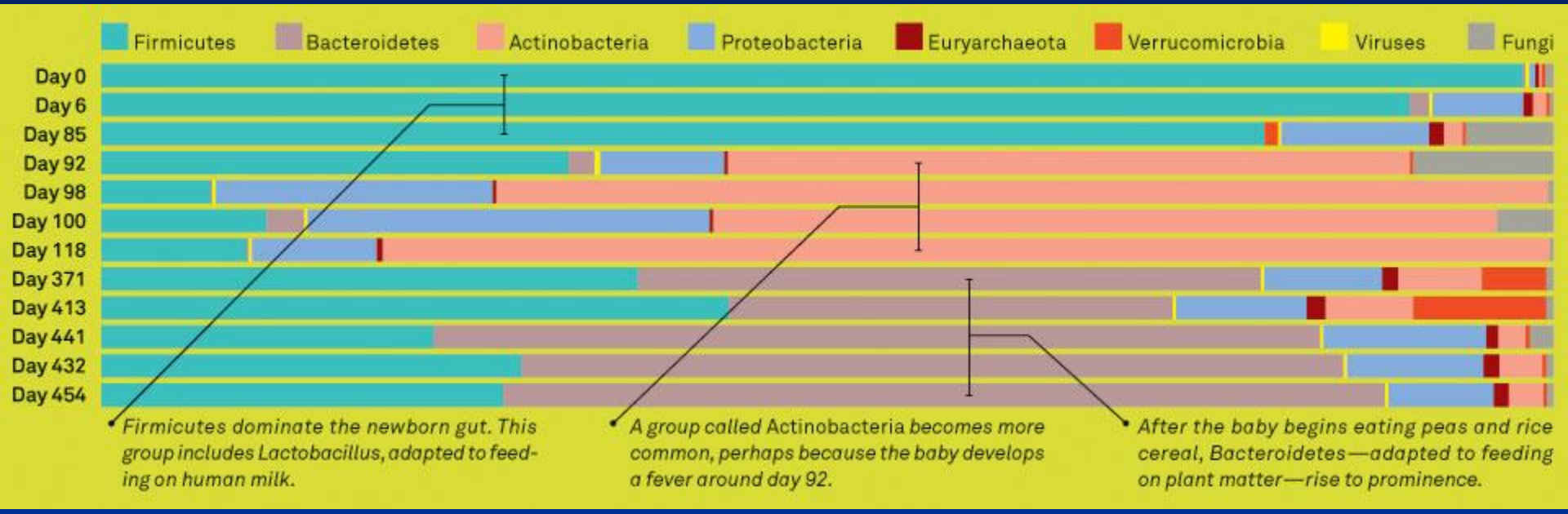
PRI

BABIES ARE MICROBE MAGNETS.

FOR 2-3 YEARS THEIR MICROBIOMES GROW WHILE THEIR IMMUNE SYSTEMS DEVELOP, LEARNING NOT TO ATTACK FRIENDLY BACTERIA.

PRI

Overview of the human microbiome development (in the large intestine) for the first 15 months

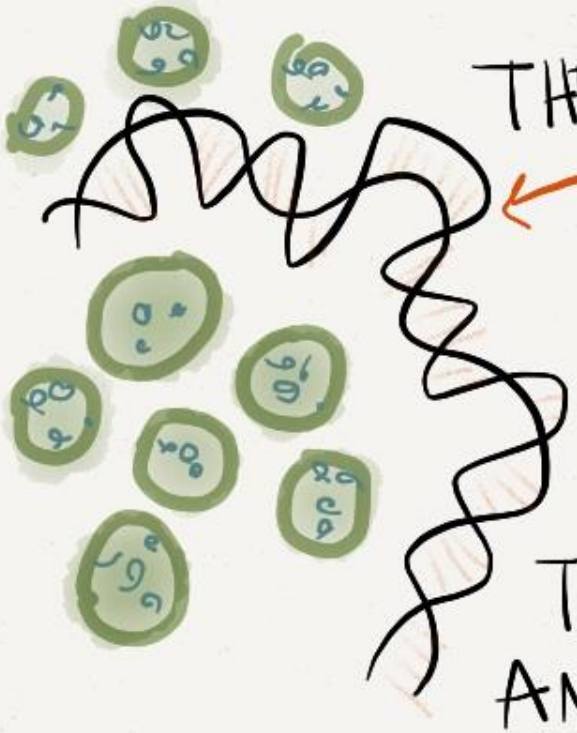


Taken from: Zimmer, 2011

WE ALL CARRY 2-5 LBS OF BACTERIA...

HUMANS ARE LIKE CORAL: AN ASSEMBLAGE OF LIFE FORMS LIVING TOGETHER

PRI



THERE ARE GENETIC SIGNATURES OF DISEASE-CAUSING BACTERIA LURKING IN EVERYONE'S MICROBIOME...

THEY LIVE PEACEFULLY AMONG THEIR NEIGHBORS.

HALF OF YOUR STOOL IS NOT LEFTOVER FOOD.

IT'S MICROBIAL BIOMASS

Without even realizing it, we have been changing our microbiome through the use of modern medicine

- For more than 70 years, we have been using antibiotics.
- A typical child in the developed world receives 10 – 20 courses of antibiotics by the age of 18.

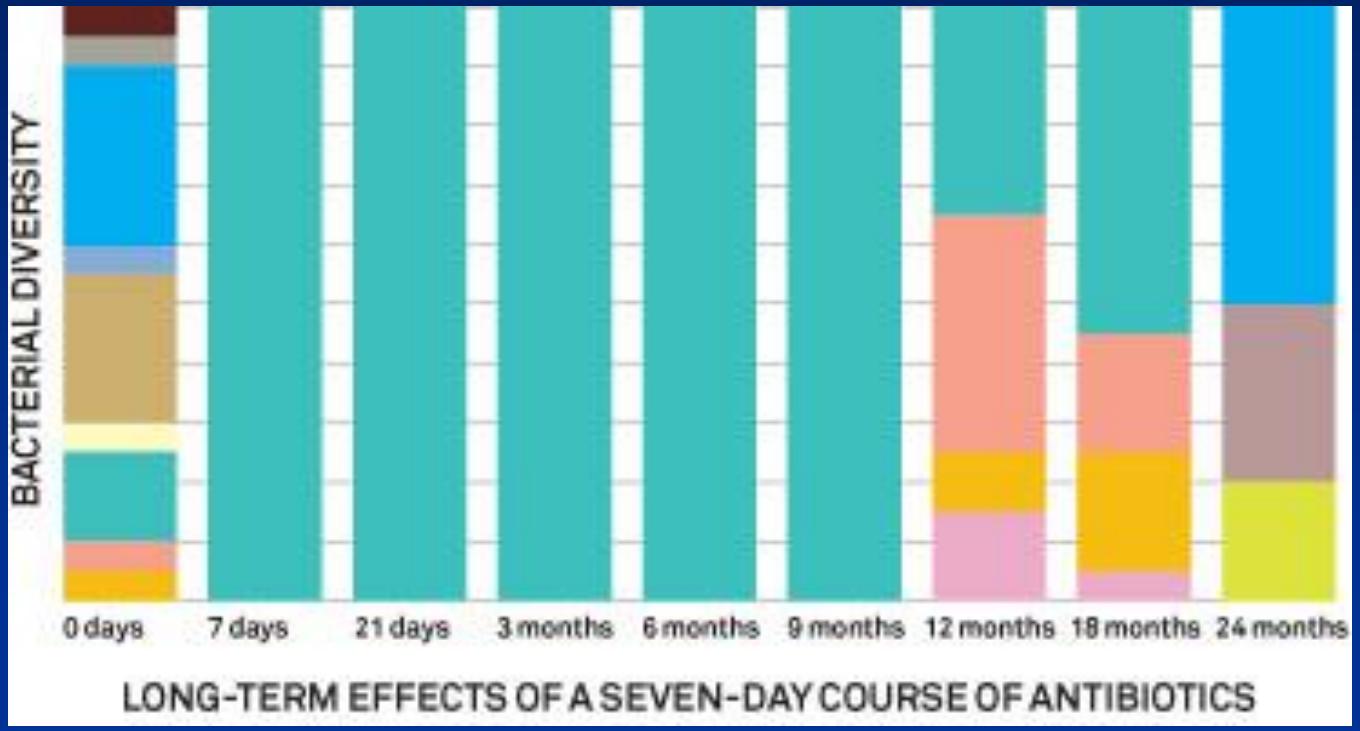
According to Dr. Martin Blaser, New York University's School of Medicine…

"Here's the point. You have 10-12 diseases that are all going up dramatically, more of less in parallel – diabetes, obesity, asthma, food allergies, hay fever, eczema, celiac disease. They're not going up 2 or 3 percent, they're doubling and quadrupling, Each one may have a different cause. Or there could be one cause that's providing the fuel, and my hypothesis is that it's the disappearing microbiota."

Taken from: Conniff, 2013

Effects of a weeklong course of antibiotics, clindamycin, on microbial diversity in genus *Bacteroides;*

Colors represent different species



Taken from: Zimmer, 2011

Some Human Microbiome News from the past week

- April 24, 2013→ role of our own bacteria in heart disease
- April 25, 2013 → role of bacteria in Autism symptoms
- More work needs to be done… Do the bacteria help to cause the medical condition or do they show up in response to the medical condition? Can we use this knowledge to make better medical treatments?

"Gut Bacteria's Belch May Play a Role in Heart Disease" April 24, 2013

- http://www.npr.org/blogs/health/2013/04/24/178407883/gut-bacterias-belch-may-play-a-role-in-heart-disease?sc=ipad&f=1128
- Waste product left behind by bacteria (TMAO) plays a role in heart disease and stroke
- May be one reason to explain why some people with high cholesterol never go on to develop heart disease while others do.

"Vaccine May Help Control Autism Symptoms" April 25, 2013

- http://www.dnaindia.com/health/1826762/report-first-vaccine-developed-to-help-control-autism-symptoms
- Vaccine would target bacteria that play a role in the most severe Autism symptoms
- Patients with Autism have a higher than average percentage of *Clostridium bolteae*
- Vaccine targets these "abnormal" bacterial communities

Some other discoveries

Taken from: Young, 2012

- Gut microbial genes may be a better predictor of Type II Diabetes that other usual measures such as waist-hip ration, or body mass index
- Better way to classify inflammatory bowel diseases
- There is a 0.1% difference among human genomes, but there is an expected 50% difference in our metagenome (microbes).
- May be easier to target or control bacterial than our genes; This will be more sophisticated than “eating yogurt”

Some other discoveries

Taken from: Zimmer, 2011

- Obesity, heart disease, and anxiety can be linked to our microbial diversity
- In many cases it is not the presence or absence of species but how they interact together; their diversity
- We may eventually have a microbial based mouthwash to promote healthy oral microbiota to fight disease-causing oral microbes. A new approach to Gingivitis???

Some other discoveries

- In cases of skin acne, healthy people have additional strains of the pathogenic bacterial species that appear to be keeping them healthy-→ current treatment practice kills most of the bacteria on the skin, maybe there can be a better option? (Yang, 2013)
- Mice grown in a relatively sterile environment had different microbiota than the control mice and developed very strange behavior, normal behavior was restored when the environment went back to normal (New Scientist; vol., 214, Iss. 2860 p. 7)

Some other discoveries

Taken from: Blaser et al, 2013

- Fecal Microbiota Transplantation (FMT); fecal transplants… Have had a > 90% success rate and are starting to be posited as a first-line therapy for colitis caused by *Clostridium difficile*
- Gastroenterologist, Dr. Colleen Kelly at Rhode Island Hospital sprays a fecal cocktail (from a patient's relative) into the operating room and allows the patient to inhale the microbiota as part of treatment (Conniff, 2013).
- "There is no yuck factor for people who are this sick."

The concept behind FMT

Taken from: Conniff, 2013

- Dr. Kelly states that the procedure is to "seed them through the colon planting a healthy microbiome like a landscaper installing a new garden."
- Of the 94 *C. difficile* patients she has treated, Dr. Kelly says that all but three have overcome the infection. Now she is participating in a double-blind clinical trial against a placebo with the National Institutes of Health
- Lab-based formulations may eliminate the need for a human donor → RePOOPulate is already being developed as an experimental version

A new treatment following birth by C-section

Taken from: Conniff, 2013

- When a baby does not pass through the birth canal, the baby is not exposed to the normal microbiota found there and may be pre-disposed to certain medical complications.
- New treatment involves wiping the baby down with the mother's vaginal microbiota

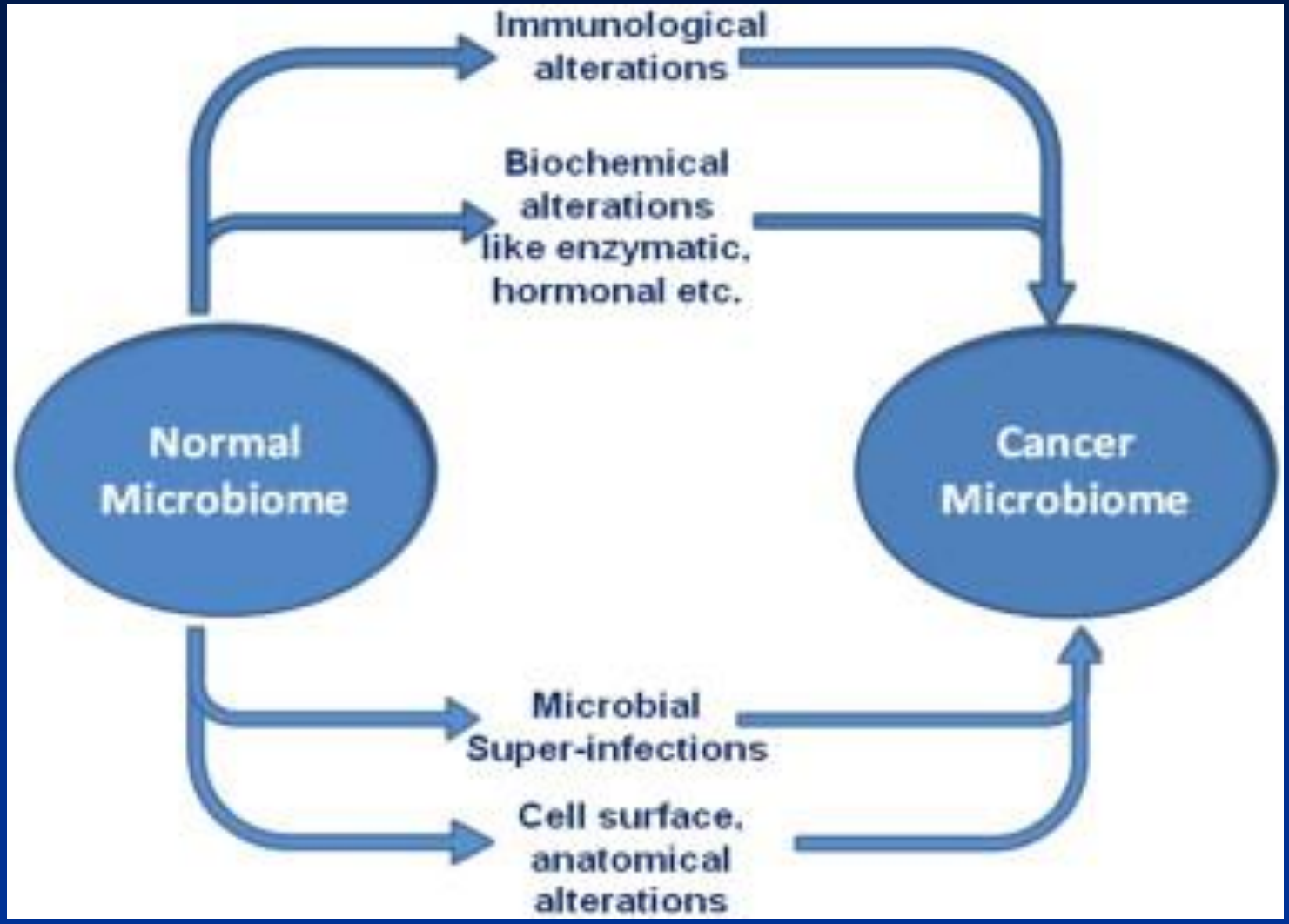
Quest to find ancient human microbes

Conniff, 2013

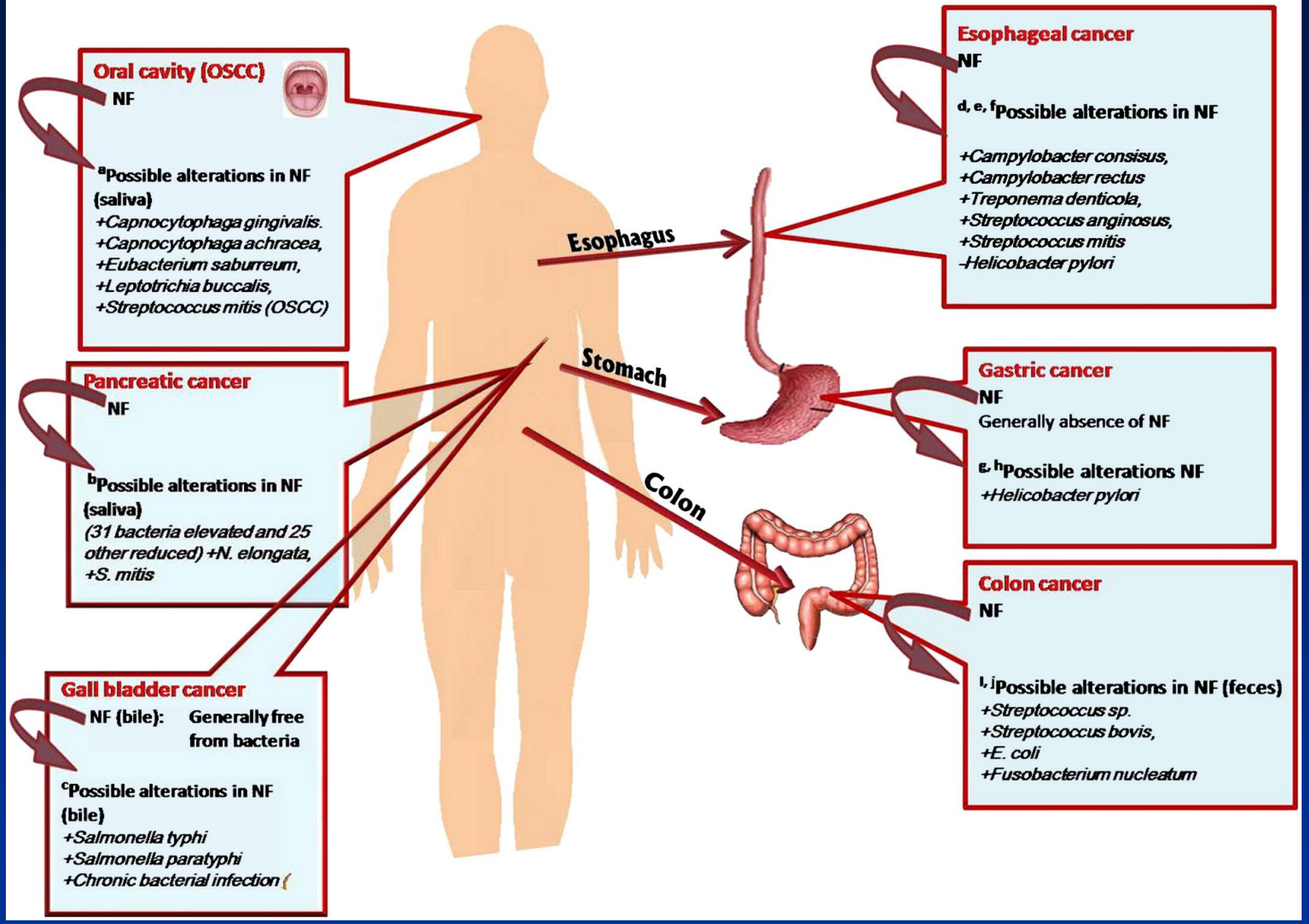
- Did our ancestors have some helpful microbiota that we have since eliminated?
- Dr. Maria Gloria Dominguez-Bello and team are searching among people in the Amazonian rainforest.

The Microbiome likely plays a role in cancer

Role of Microbiome in Cancer



Taken from: Khan, Shrivastava, and Khurshid, 2012



Taken from: Khan, Shrivastava, and Khurshid, 2012

Ways that you can participate – Citizen Science

- Your wildlife http://www.yourwildlife.org/
- The Belly Button Biodiversity Project

"Bacteria in belly buttons are highly diverse, but predictable."

Taken from: http://kidshealth.org/kid/talk/yucky/bb_inside.html

Some other public efforts

- American Gut; You can get much of your microbiome sequenced for about $100!; http://www.indiegogo.com/projects/american-gut-what-s-in-your-gut--7?website_name=americangut
- Ubiome – can sequence your gut over three time points (about $300)!; http://ubiome.com/shop

Microbiome → Start-up Companies

- Second Genome; $10 million seed money; "The most important genome in your body may not be your own."; http://www.secondgenome.com/
- It may be easier to manipulate this second genome than our own…

These are exciting times…

"Coming to understand our microbes not as enemies but as intimate partners could change our lives at least as dramatically (as the advent of antibiotics and vaccines) with time and proper testing". (Conniff, 2013)

So, Do you want to know your microbiome?

More things to consider and resources to explore

Bonnie Bassler, Ph.D. found molecular communication between bacteria cells

In 2002, bearing her microscope on a microbe that lives in the gut of fish, Bonnie Bassler isolated an elusive molecule called AI-2, which showed not only that **almost all bacteria can communicate — but that they do so all the time**. (Watch her 2009 TEDTalk!)

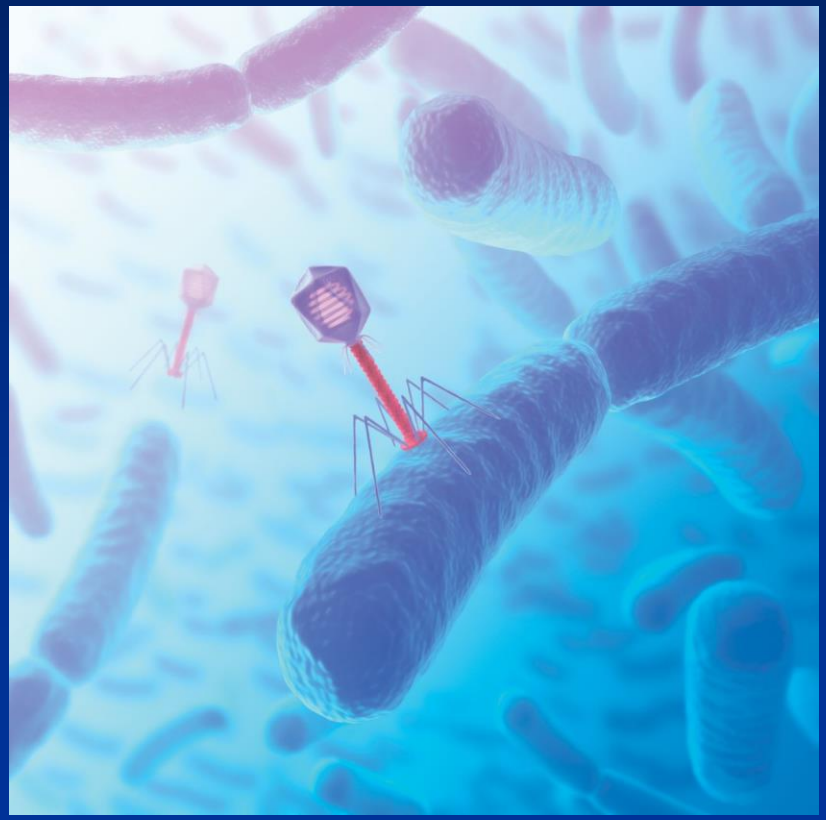
- Jonathan Eisen – Meet your Microbes
- TED Talk
- http://www.ted.com/talks/jonathan_eisen_meet_your_microbes.html

A new genetic map that could make your skin crawl
PBS News Hour
June 14, 2012

- http://www.youtube.com/watch?v=Vawqhe8OxBI

What about the other human microbiome…

- The viruses…



Taken from: Williams, 2013

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