

LUNCH AND LEARN

PUGET SOUND BUSINESS TRAVEL ASSOCIATION – FRED HUTCH

➤ Tara Palumbo Egan
Assistant Director,
Corporate Engagement,
Philanthropy



Connected

Home to **3,000+** staff,
including more than
250 scientific faculty

Located in Seattle's
vibrant South Lake Union
neighborhood



➤ Emilie Seydoux
Staff Scientist
McGuire lab
Vaccine and Infectious Disease Division



➤ WHY DOES A CANCER RESEARCH CENTER HAVE VIROLOGY EXPERTISE?

- Many cancers are caused, either directly or indirectly, by viruses and other pathogens
 - Bone marrow transplantation was discovered as a treatment for blood cancers
 - This work led to the development of immunotherapies
 - People with compromised immune systems are vulnerable to viral infections
- ➔ More than 20% of Fred Hutch researchers have had active projects in COVID-19

<https://www.fredhutch.org/en/news/center-news/2021/03/Five-reasons-why-cancer-research-center-has-virology-expertise.html>

COVID-19 IS CAUSED BY THE CORONAVIRUS SARS-CoV-2

- This is the 3rd coronavirus to jump from animals to humans since 2003 (after SARS-1 and MERS)
- COVID-19 is a tricky disease!
 - Incubation time can range from 1 to 14 days
 - Can be infectious before you show symptoms
 - Approximately 20% of asymptomatic patients
 - Evidence for airborne transmission
 - Super-spreading: wrong place, wrong time



The New York Times

Why the Coronavirus Is More Likely to 'Superspread' Than the Flu

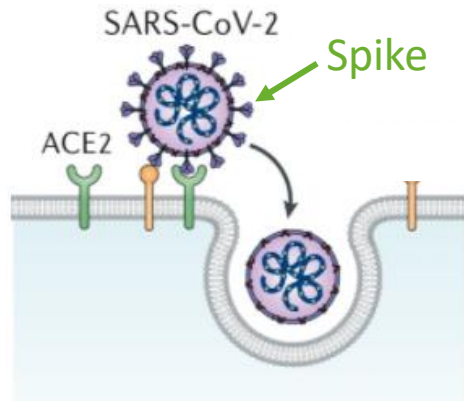
Most people won't spread the virus widely. The few who do are probably in the wrong place at the wrong time in their infection, new models suggest.

The Coronavirus Can Be Airborne Indoors, W.H.O. Says

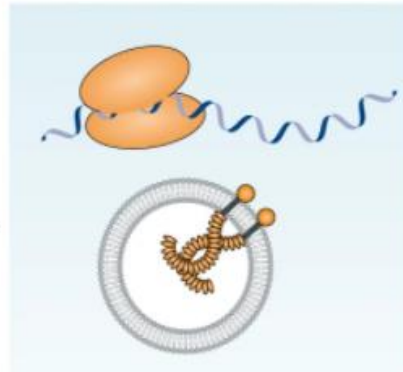
The agency also explained more directly that people without symptoms may spread the virus. The acknowledgments should have come sooner, some experts said.

➤ IMMUNE RESPONSE TO NATURAL INFECTION

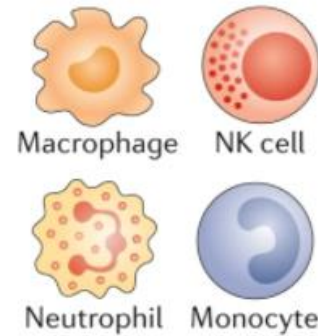
1. Virus entry



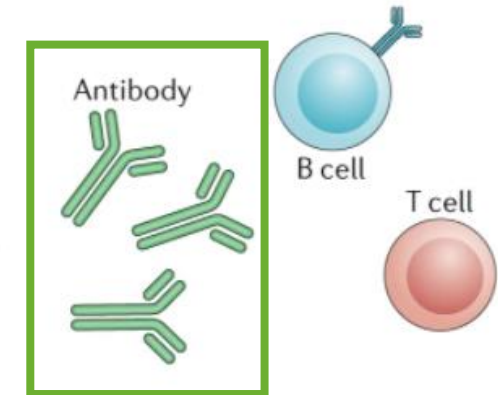
2. Oh oh, there is something wrong



3. Innate immune response

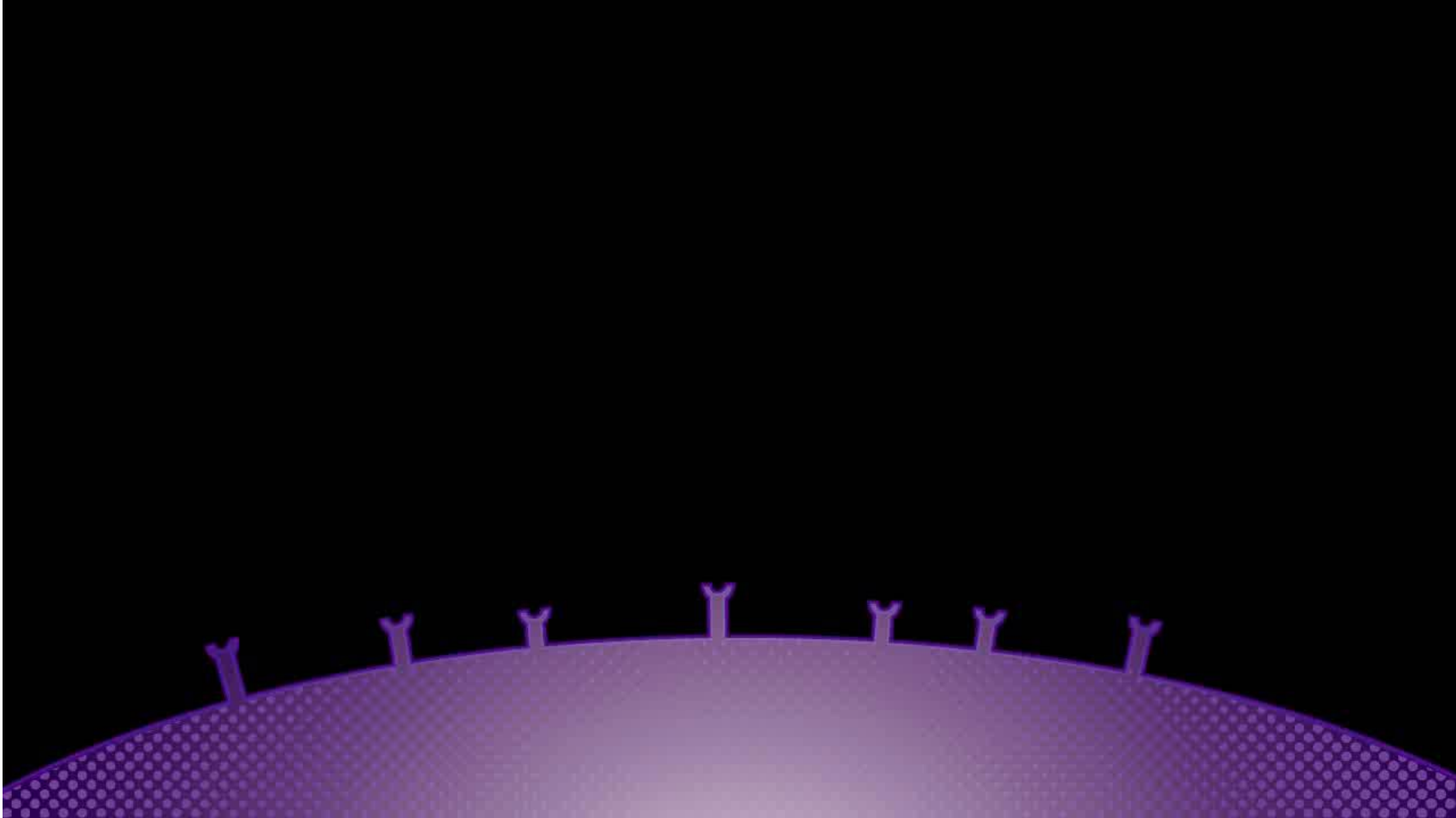


4. Adaptive immune response



➔ Successful vaccine: have that same response!

➤ HOW CAN ANTIBODIES NEUTRALIZE THE VIRUS?



DIFFERENT VACCINE PLATFORMS ARE BEING DEVELOPED AND USED

Pfizer/BioNTech

mRNA vaccine
Approved in the US

Moderna

mRNA vaccine
Approved in the US

Janssen/J&J

Viral vector
Approved in the US

Oxford/AstraZeneca

Viral vector
Approved elsewhere

Gamaleya Centre

Viral vector
Approved elsewhere

Novavax

Protein subunit
Not yet approved

Sinovac

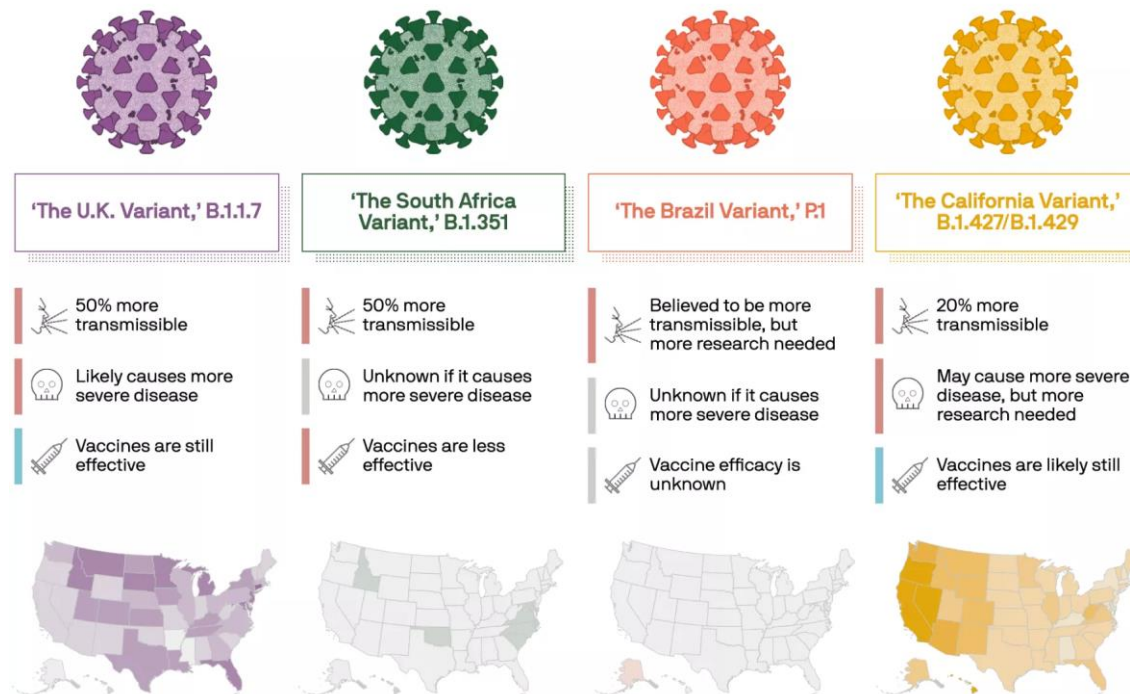
Inactivated
Approved elsewhere

Type of vaccine		Licensed vaccines using this technology	First introduced
Live attenuated (weakened or inactivated)		Measles, mumps, rubella, yellow fever, influenza, oral polio, typhoid, Japanese encephalitis, rotavirus, BCG, varicella zoster	1798 (smallpox)
Killed whole organism		Whole-cell pertussis, polio, influenza, Japanese encephalitis, hepatitis A, rabies	1896 (typhoid)
Toxoid		Diphtheria, tetanus	1923 (diphtheria)
Subunit (purified protein, recombinant protein, polysaccharide, peptide)		Pertussis, influenza, hepatitis B, meningococcal, pneumococcal, typhoid, hepatitis A	1970 (anthrax)
Virus-like particle		Human papillomavirus	1986 (hepatitis B)
Outer membrane vesicle		Group B meningococcal	1987 (group B meningococcal)
Protein-polysaccharide conjugate		Haemophilus influenzae type B, pneumococcal, meningococcal, typhoid	1987 (H. influenzae type b)
Viral vectored		Ebola	2019 (Ebola)
Nucleic acid vaccine		SARS-CoV-2	2020 (SARS-CoV-2)
Bacterial vectored		Experimental	—
Antigen-presenting cell		Experimental	—

WHAT ARE VARIANTS OF CONCERN?

Viruses mutate all the time! Mutations can lead to variants of interest, variants of concern, or variant of high consequence.

Variants of Concern



'The Indian Variant,' B.1.617

Believed to be more transmissible, but more research needed

Unknown if it causes more severe disease

Vaccine efficacy investigations are ongoing

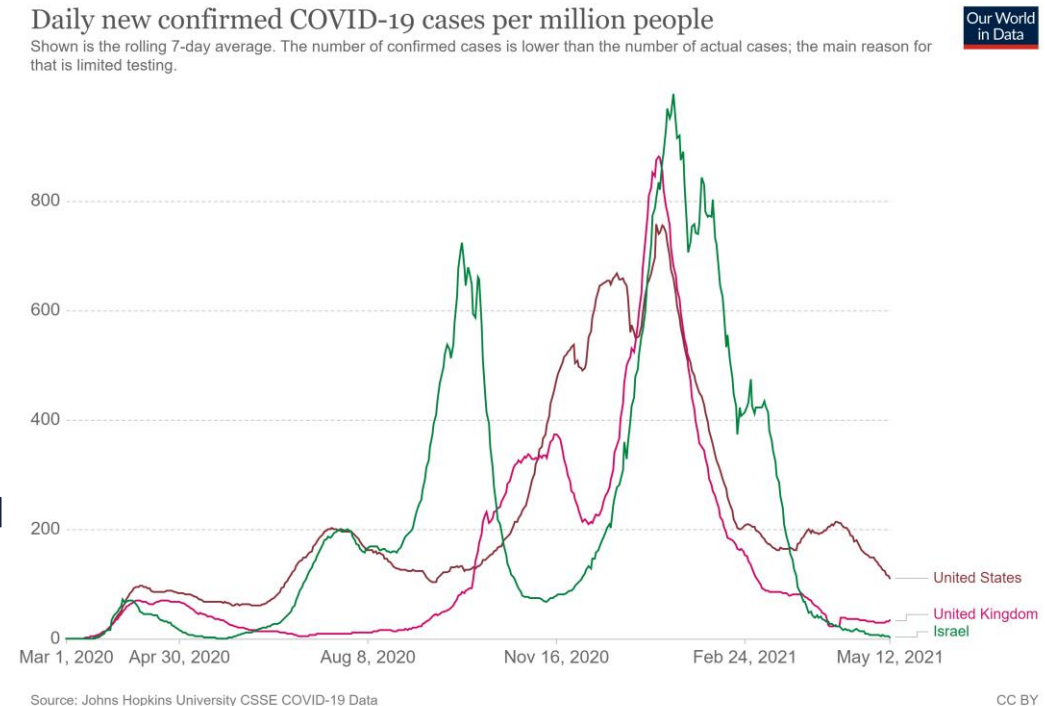
VACCINE EFFICACY AGAINST PREEXISTING VIRUS AND VARIANTS

Efficacy against any documented COVID-19 disease

	Preexisting variants	B.1.17 [UK]	B.1.351 [South Africa]	P.1 [Brazil]	B.1.617 [India]
Pfizer/BioNTech	95%	89.5% ["real world" study in Qatar]	75% ["real world" study in Qatar]	?	?
Moderna	94%	?	Booster dose in preparation	Booster dose in preparation	?
J&J	66%	?	57% [clinical trial in SA]	?	?
Oxford/AstraZeneca	67%	75% [clinical trial in UK]	10% [clinical trial in SA]	?	?
Novavax	89%	86% [clinical trial in UK]	60% in HIV negative 49% in HIV positive ["real world" study in SA]	?	?

DO THE VACCINES PREVENT TRANSMISSION?

- Clinical trials showed that vaccines prevented the disease, but **they didn't track infections** → Can vaccinated people have asymptomatic infections?
- Potential mechanisms: **stop infections** or **less infectious**
- Early data suggest that:
 - Fewer asymptomatic infections occurred in the vaccinated groups compared to the placebo groups [data from Moderna, J&J]
 - Viral loads 20 times lower in vaccinated people in Israel compared to unvaccinated, infected people
 - Reduced infection in fully vaccinated healthcare workers in US, UK and Israel
- New CDC guidelines
- Study managed by the Hutch: **Prevent COVID U**



↗ Questions?

➤ Amitabha “Guppy” Gupta
Scientific Content Strategist,
Donor Communications
Philanthropy



MICROBIOMES DEFINE US



30 Trillion Human Cells

39 Trillion Microbial Cells

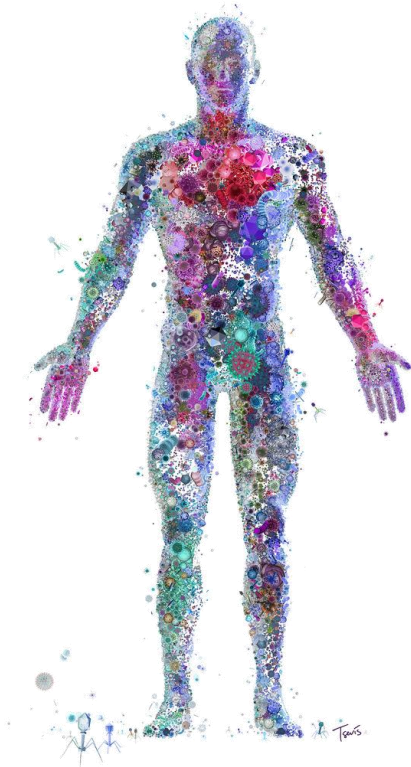
≈25,000 Human Genes

2-20 Million Microbial Genes

Charlis Tsevis / Science News Magazine

Our Microbiota Contribute ≈ 1-3% of our Body Mass

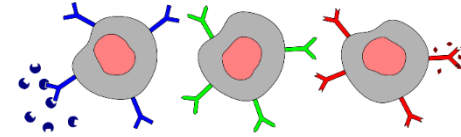
MICROBIOMES DEFINE US



Charlis Tsevis / Science News Magazine



Pathogen
Resistance



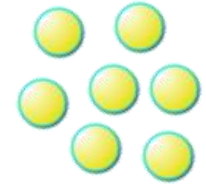
Immune System Function



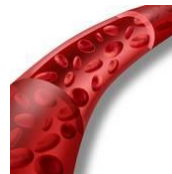
Vitamin Production



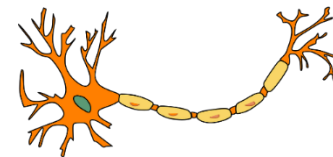
Drug
Metabolism



Fat Storage



Blood Vessel
Formation

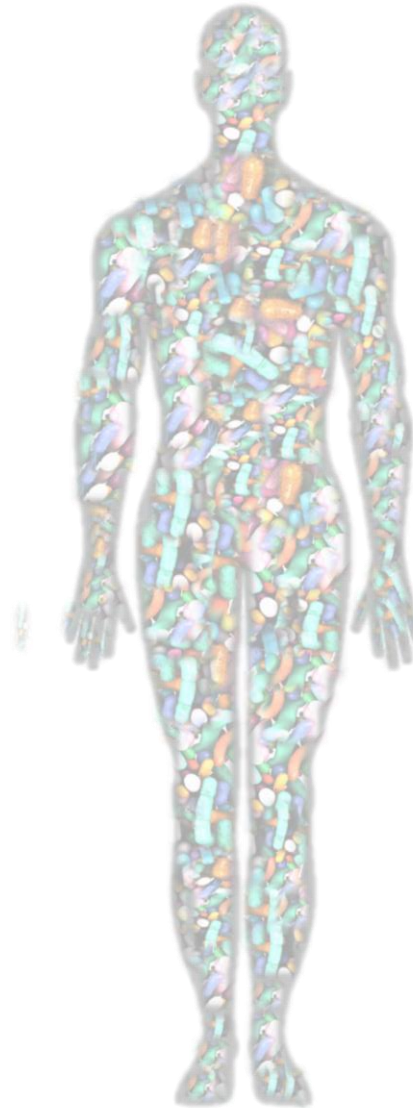
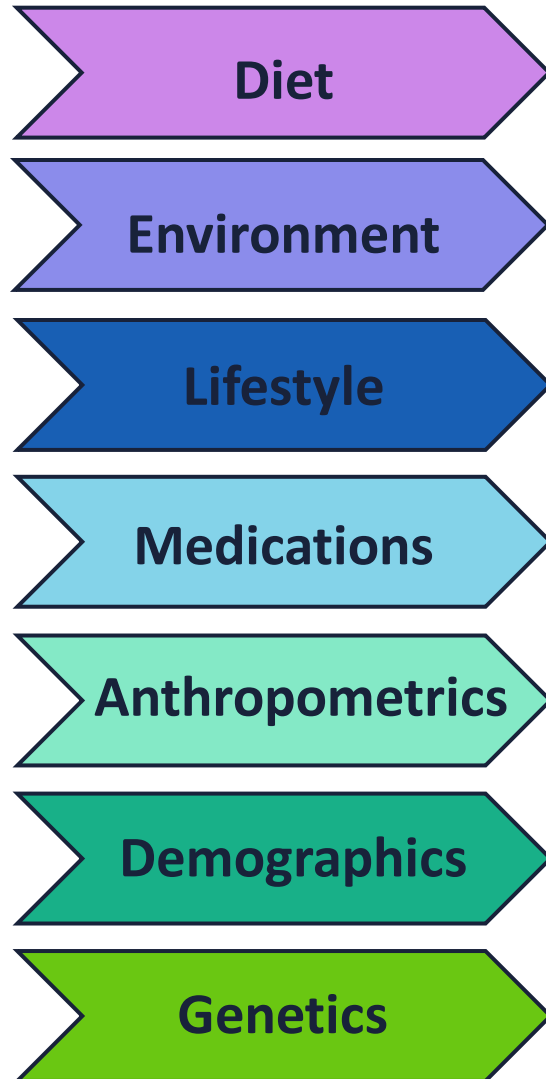


Nervous System Function



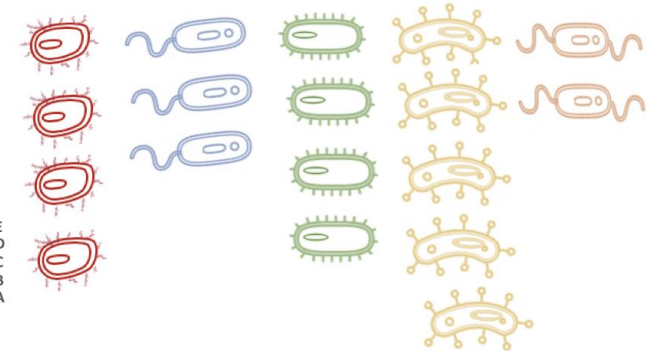
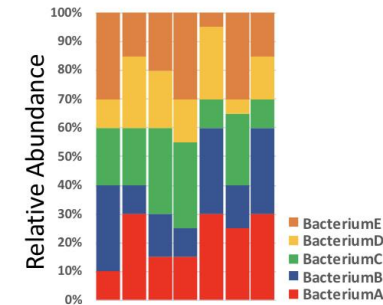
Food Breakdown

WHAT SHAPES OUR MICROBIOTA?



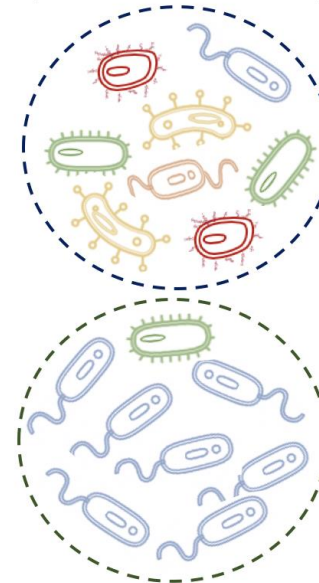
Composition

“Who” is there and in what proportion?



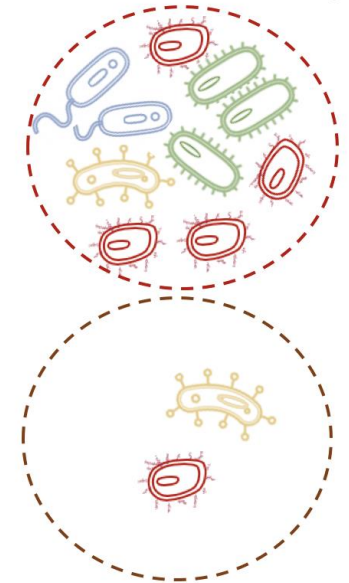
Diversity

Alpha and Beta-Diversity



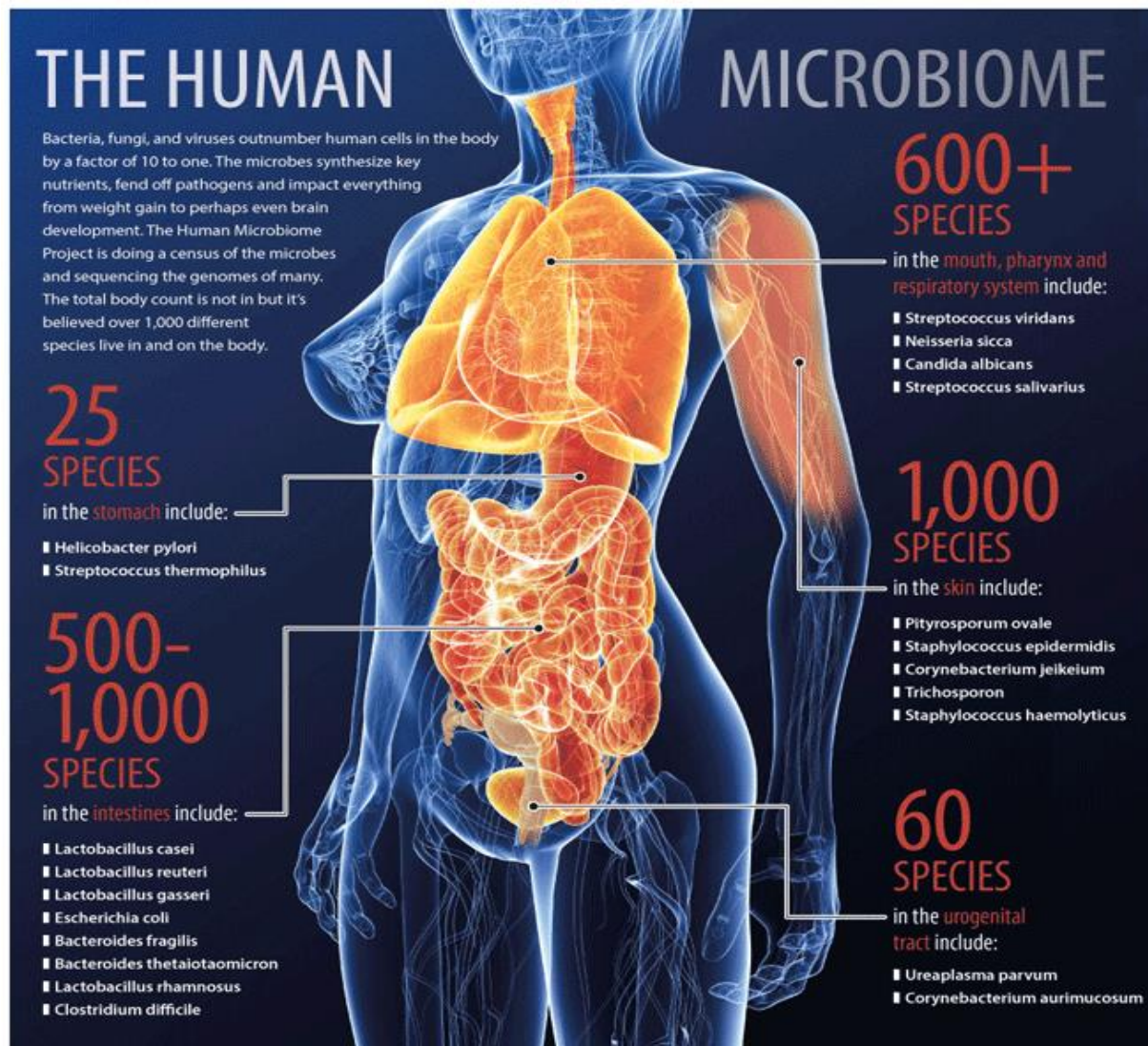
Load

Relative to human cells/housekeeping gene



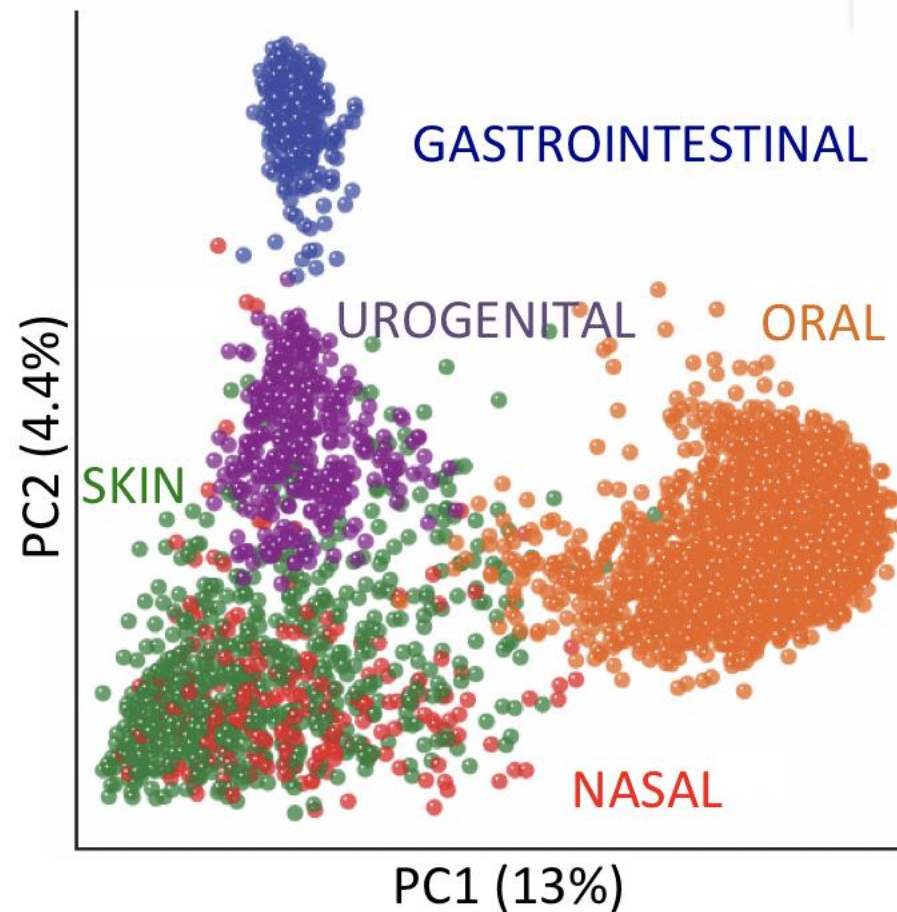
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INCREASING ASSOCIATIONS BETWEEN MICROBIOME AND DISEASE



SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN; HUMAN MICROBIOME PROJECT

Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

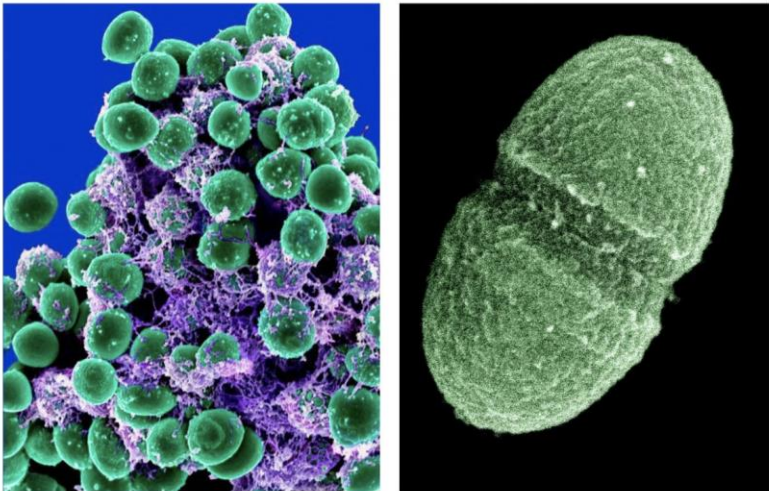


INCREASING ASSOCIATIONS BETWEEN MICROBIOME AND DISEASE

The Washington Post
Democracy Dies in Darkness

Health & Science

A closer look at the microbes that live on — and in — us



An NIAID image shows a clump of *Staphylococcus epidermidis* bacteria (green) in the extracellular matrix, which connects cells and tissue, taken with a scanning electron microscope, showing. At right, a handout image provided by the Agriculture Department showing the bacterium, *Enterococcus faecalis*, which lives in the human gut, is just one type of microbe that will be studied as part of NIH's Human Microbiome Project. (AP)

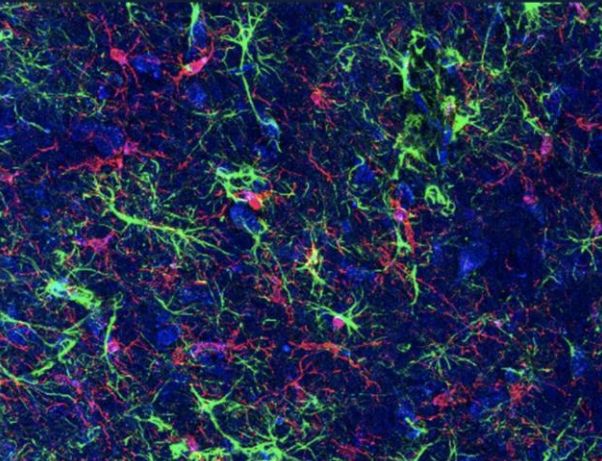
By **Alyssa A. Botelho**
June 13, 2012

- *Escherichia coli*
- *Bacteroides fragilis*
- *Bacteroides thetaiotaomicron*
- *Lactobacillus rhamnosus*
- *Clostridium difficile*

NEWS

HEALTH NEWS

Gut Bacteria May Affect Parkinson's, Study Finds



— Gut microbes can initiate activation of microglia (brain-resident immune cells), which leads to the neuroinflammation that is characteristic of Parkinson's disease. S. Mazmanian Lab/Caltech

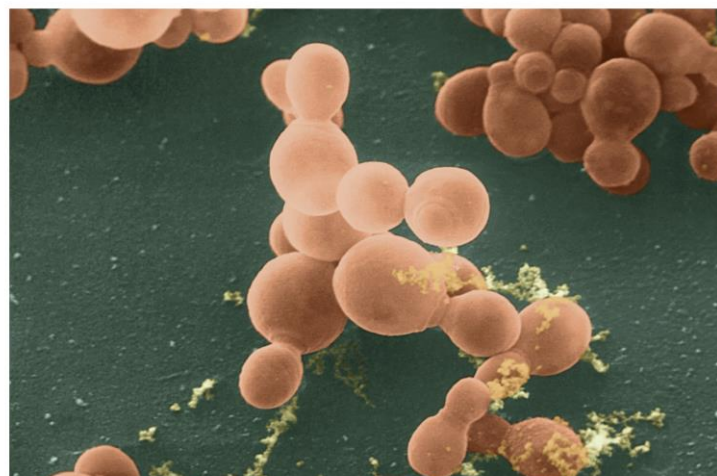
Dec. 1, 2016, 3:26 PM PST / Updated Dec. 2, 2016, 5:08 AM PST

By **Maggie Fox**

The New York Times

In the Pancreas, Common Fungi May Drive Cancer

A new study found that certain fungi can settle in the pancreas, where they spur the growth of tumors.



The abundance in the pancreas of the yeast *Malassezia*, more commonly found on the skin of humans and animals, surprised the scientists. Science Source

By **Knvul Sheikh**

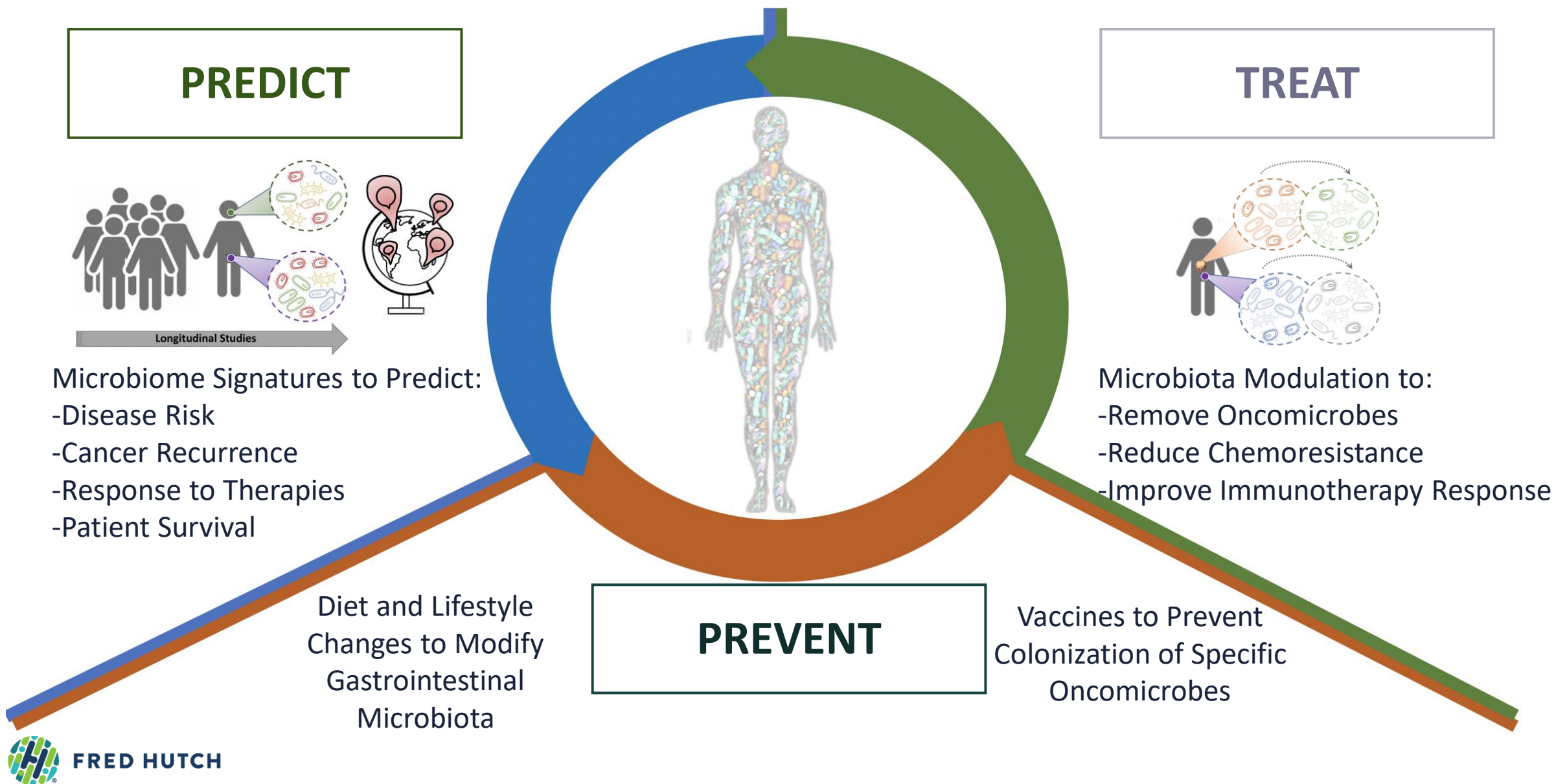
Oct. 3, 2019

f t e r 52

SOURCES: NATIONAL INSTITUTES OF HEALTH, SCIENTIFIC AMERICAN, HUMAN MICROBIOME PROJECT

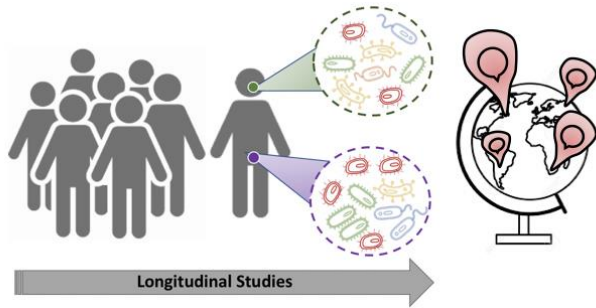
Dean Tweed • POSTMEDIA NEWS / IMAGE: Fotolia

MICROBIOTA AND DISEASE: THE PROMISE



MICROBIOTA AND DISEASE: THE PROMISE

PREDICT



Microbiome Signatures to Predict:

- Disease Risk
- Cancer Recurrence
- Response to Therapies
- Patient Survival



TREAT



- Microbiota M
- Remove Onco
 - Reduce Chem
 - Improve Immunotherapy Response

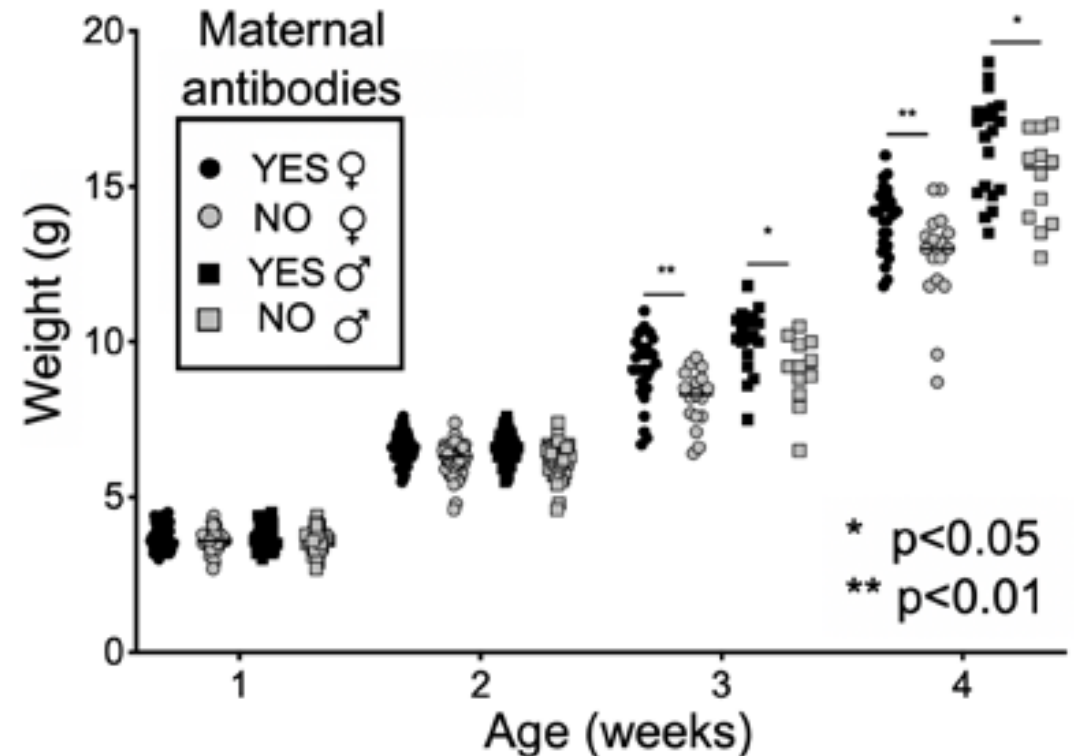
PREVENT

Vaccines to Prevent
Colonization of Specific
Oncomicrobes



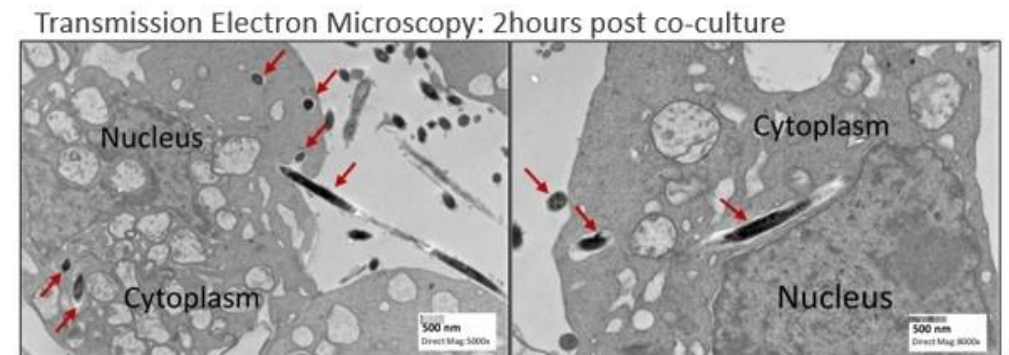
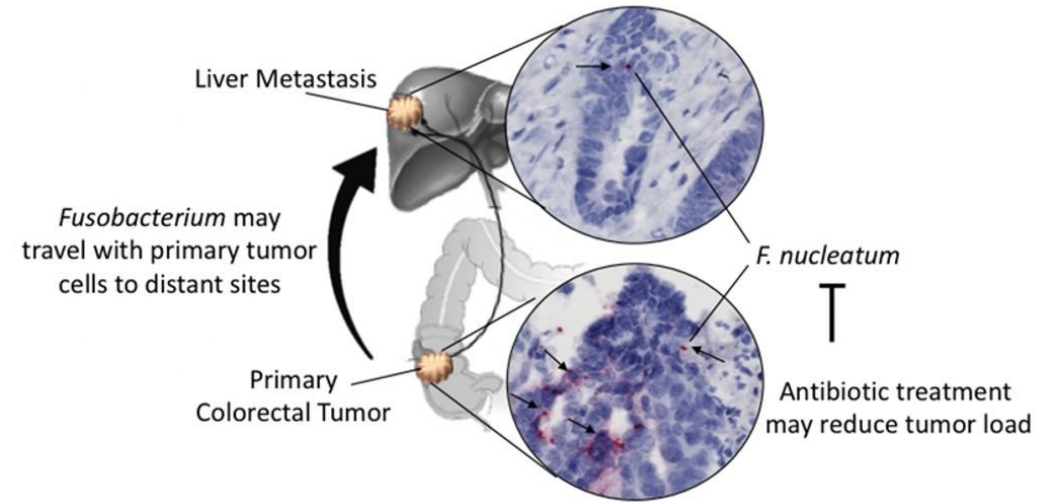
IMMUNE-MICROBIOME INTERACTION FOR HEALTHY GROWTH

- “Growth faltering” in newborns: In the US, ~15% of infants born at term and ~30% of pre-term babies experience “growth faltering”, once called “failure to thrive”.
- Microbiome at birth: At birth, the mother passes on their microbiome to the newborn.
 - This includes microbes that are beneficial as well.
 - Newborn immune system cannot distinguish friend from foe.
- Antibodies passed in breastmilk may be critical to teach the new immune system not to destroy some of these bacteria.
- Dr. Meghan Koch and her team are trying to identify if a certain type of antibody is more beneficial, or a specific antibody-microbe pair.
- This work can have a tremendous impact on infant feeding strategies



UNDERSTANDING THE EFFECT OF F. NUCLEATUM ON COLORECTAL CANCER

- **Colorectal cancer:** Colorectal cancer [CRC] is the 4th most common cancer diagnosed in the US.
 - Black people make up a disproportionate number of new cases.
 - Black and Native American/Indian people die more frequently from this disease than other races.
- **Fusobacterium nucleatum:** Dr. Susan Bullman and others have found a strong association between the bacterium and CRC
 - The bacterium travels with tumors when they metastasize
 - Her work has shown the bacteria infiltrating the region where our genomes are housed
- Drs. Bullman and Johnston are aiming to understand how the bacterium may be affecting our cells.
- This can change how we treat CRC forever.



THANK YOU!

- Take care of yourselves and each other
- Sign-up for e-news, volunteer, donate, and more at fredhutch.org/signup
 - Follow us @fredhutch on Twitter, Facebook, LinkedIn, and Instagram.
- Join a virtual Science Says event at fredhutch.org/science-says
 - Save the Date – June 15, 9-10 a.m. PDT
- Visit Fred Hutch's COVID-19 Information Hub: fredhutch.org/coronavirus



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CURES START HERE®

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Obliteride 2021

The details:

- ☑ 2021 registration is just \$35 and includes a T-shirt.
- ☑ No fundraising minimum; set your own goal for fundraising!
- ☑ Pick any activity you'd like to complete by Saturday, August 14.
- ☑ 100% of participant-raised funds support research at Fred Hutch.
- ☑ Team up — or start a team of your own! Fred Hutch has amazing Obliteride spirit and lots of friendly (and healthy) competition. Dr. Nina Salama's **Helicobikers** go all in every year; Business Development & Strategy's own Kristi Sullivan and her **Fizards Forever** bring the sweat; and Dr. Jerry Radich and his **Le Tour De Fred** aren't to be messed with — and that's just a start!



Get started!

- Register at obliteride.org
- Participant Guide, Social Media Toolkit, Participant Bibs, & more!
- **Questions? Contact: Tara Egan,**
tpegan@fredhutch.org



THANK YOU



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