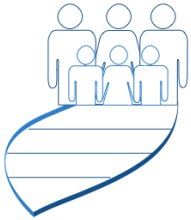


Life Sciences/HHMI

OutReach
PROGRAM




The Human Microbiome

Christine Rodriguez, Ph.D.
Harvard Outreach 2012

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

Microbes are all over us



There are millions of microbes per square inch on your body

**Thousands of different species on the skin alone
Some thrive on dry patches of the elbow, others thrive in moist environment of armpit**

It is estimated that there are more microbes in your intestine than there are human cells in your body!

http://commons.wikimedia.org/wiki/File:Man_shadow_-_upper.png

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers



What is the Human Microbiome?

Microbe: tiny living organism, such as bacterium,

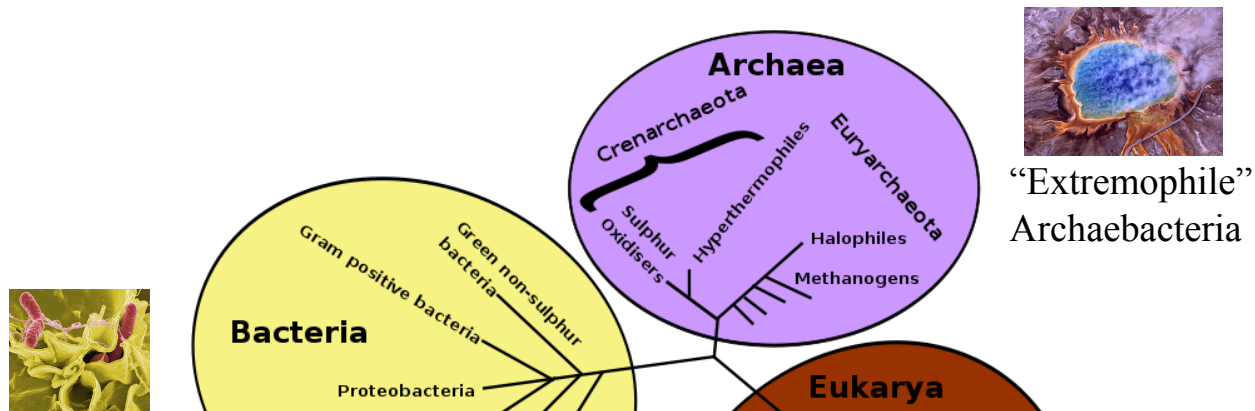
fungus, protozoan, or virus

Microbiome: collectively all the microbes in the human body; a community of microbes

Biofilm: a community of microbes that live together on a surface

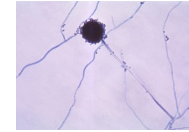
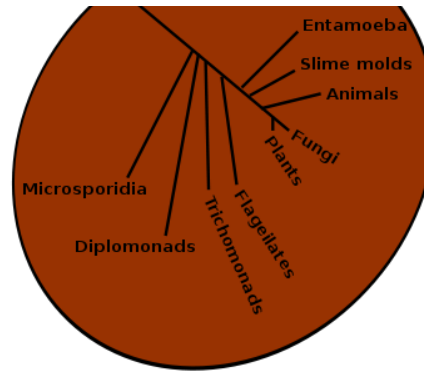
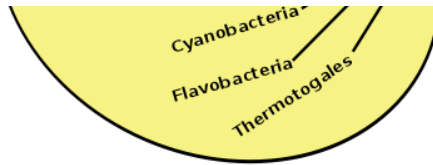
Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

Microbes in the Human Microbiome include species from each major domain





Bacteria

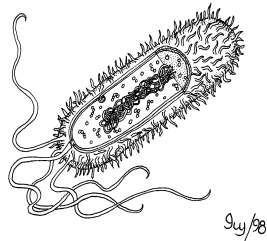


Fungi

- http://en.wikipedia.org/wiki/File:Aspergillus_niger_01.jpg
- <http://en.wikipedia.org/wiki/File:SalmonellaNA1D.jpg>
- http://en.wikipedia.org/wiki/File:Grand_primate_spring.jpg
- http://commons.wikimedia.org/wiki/File:Tree_of_life.svg

Summer 2012 Workshop in Biology and Multimedia for High School Teachers

What features distinguish the microbial domains?



Generalized bacteria and archaeobacteria cell

Bacteria

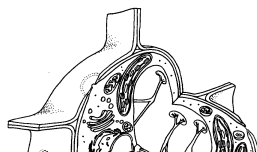
- Have no nucleus or membrane bound organelles
- Often sphere (cocci) or rod (bacillus) shape, but others as well

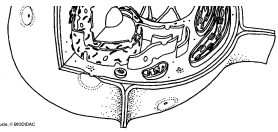
Archeobacteria

- Have no nucleus or membrane bound organelles
- Can look similar to bacteria or drastically different shapes, such as flat and square
- Have some metabolic similarities to eukaryotes

Eukaryotes

- Have a true nucleus and membrane bound organelles





-
-

Wide variety of shapes. For this presentation, we will focus on fungi
Fungi are unique since they have a cell wall and form spores during reproduction

Generalized eukaryotic cell

http://bioediac.bio.uottawa.ca/thumbnails/1/1/1/0068&file_type=GIF
http://bioediac.bio.uottawa.ca/thumbnails/1/1/1/0068&file_type=GIF

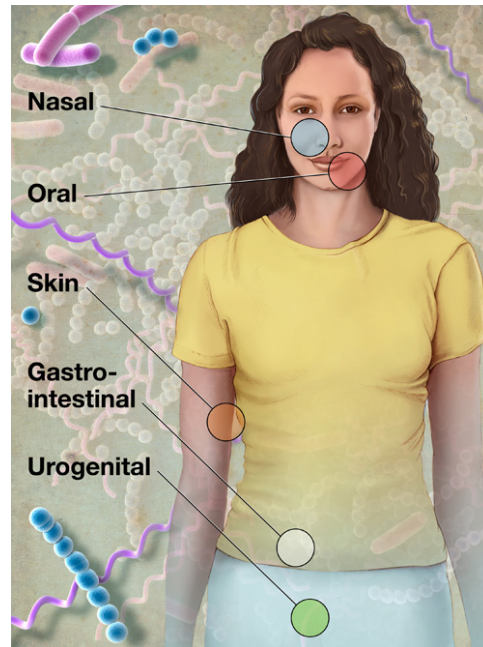
Summer 2012 Workshop in Biology and Multimedia for High School Teachers

Microbes are normally found in and on the human body

The following sites are “hotspots” for microbial life

Some microbes are **native**, normally found in the body

Some microbes are **introduced**, suddenly arriving at a new residence in the body



Let's explore these five regions

Summer 2012 Workshop in Biology and

What's Happening in the Nose?

The nose is a primary defender against inhaled pathogens

Inflammation from viral infection and allergic reactions



Cilia and mucous lining trap inhaled microbes

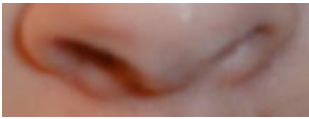
Inhaled medicines and oral antibiotics

There is a delicate balance of microbes that are maintained to keep that environment healthy. Weakened immune systems can throw off that balance and allow the wrong microbes to grow out of control.

Summer 2012 Workshop in Biology and Multimedia for High School Teachers

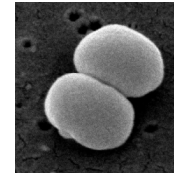


Nose

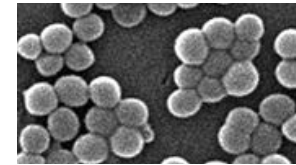


The interior lining of the nose contains mucous secreting glands. A wide variety of microbes are normally found there. Here's a few:

Staphylococcus epidermidis bacteria forms a biofilm that coats the mucosal lining



Staphylococcus aureus bacteria is fine when kept under control by a protease found in *S. epidermidis*, but if left to grow out of control, *S. aureus* can become pathogenic and cause infection



Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

<http://commons.wikimedia.org/wiki/File:Human-nose.jpg>

<http://en.wikipedia.org/wiki/File:MBSA7829.jpg>

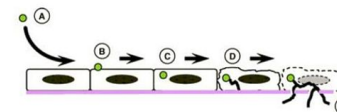
http://en.wikipedia.org/wiki/File:Staphylococcus_epidermidis_01.png



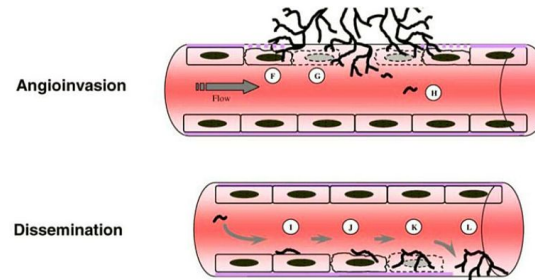
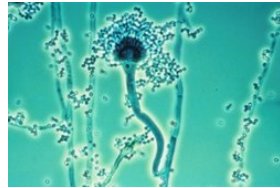
Nose

Aspergillus fungal spores are often inhaled

Alveolar Infection



through the nose. If the immune system fails to clear these, mold can grow in the lungs



Cornebacterium accolens bacteria is rarely a pathogen, but if it enters the bloodstream due to a torn blood vessel, it can cause serious infections



Summer 2012 Workshop in Biology and Multimedia for High School Teachers

http://en.wikipedia.org/wiki/File:Corynebacterium_ulcerans_01.jpg
<http://en.wikipedia.org/wiki/File:Aspergillus.jpg>
http://en.wikipedia.org/wiki/File:Aspergillus_fumigatus_Invasive_Disease_Mechanism_Diagram.jpg

http://commons.wikimedia.org/wiki/File:Human_nose.jpg

What's Happening in the Oral Cavity?

A wide variety of microbes regularly enter the oral cavity



saliva, pH,

Brushing and flossing teeth clears some built up biofilm





temperature, immune system prevent many species from surviving



Oral antibiotics inhibit growth

Symbiosis of the oral microbes that are able to survive these conditions form an elaborate scaffold that lives on the tooth enamel and at the interface with the gums. It forms a barrier for incoming bacteria.

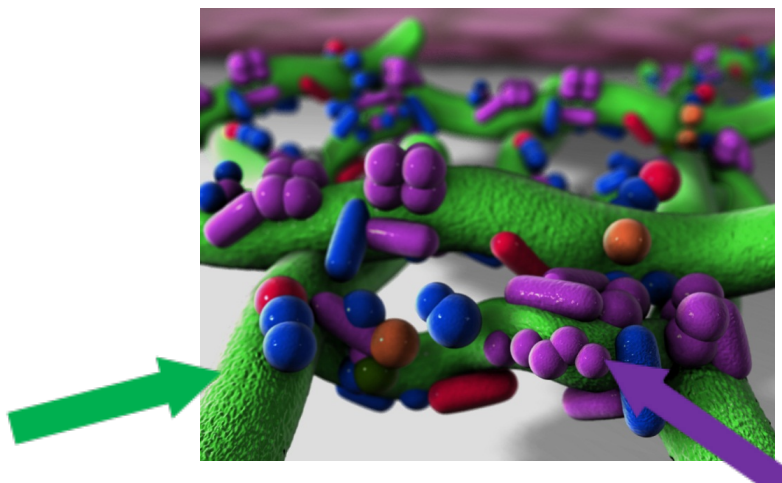
Summer 2012 Workshop in Biology and Multimedia for High School Teachers

http://en.wikipedia.org/wiki/File:Teeth_by_David_Shankbone.jpg



Oral Cavity

The oral cavity has a wide variety of microbes normally found there. Here's a few:



Streptococcus mitis bacteria typically forms a

Fusobacterium sp. bacteria is a larger bacteria that helps form a scaffold for many other bacteria in the oral biofilm

http://en.wikipedia.org/wiki/File:Teeth_by_David_Shankbone.jpg

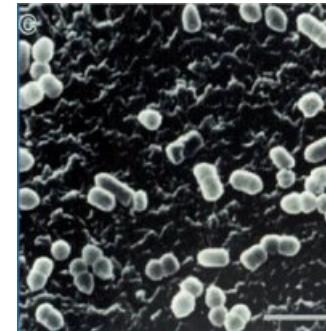
Summer 2012 Workshop in Biology and Multimedia for High School Teachers

biofilm on the hard enamel surfaces of the teeth. If gums get inflamed, it can enter the bloodstream and cause infection



Oral Cavity

Prevotella sp. bacteria have natural antibiotic resistance genes. They can attach to epithelial cells or other bacteria and cause larger infections in inflamed areas.



Candida albicans fungus can cause oral infection known as thrush



What's Happening on the Skin?

There are several skin environments: oily, dry, moist. Some microbes prefer one over another.



The skin has natural defenses including slightly acidic sweat and antimicrobial peptides.

Microbes hide in crevices to recolonize skin after washing with soap

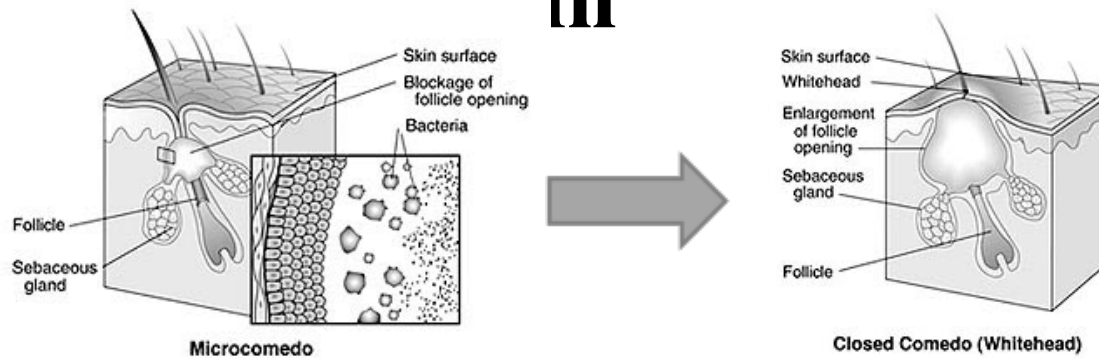
Antibiotic washes and oral antibiotics disturb normal balance of microbes on the skin

There is a normal balance of microbes on the skin that protect introduced microbes from harming us. Damaged skin gives opportunities for microbes to invade the bloodstream and cause serious illness.





Skin



- *Propionibacterium acnes* bacteria colonizes healthy pores, but if pores become clogged, it grows out of control
- *Staphylococcus epidermidis* bacteria normally colonizes on the skin. But when *P. acnes* clogs pores, *S. epidermidis* also grows out of control in the infected pores
- *Staphylococcus aureus* bacteria can also infect clogged pores like *Staph epidermidis*. Even worse, many antibiotic resistant strains of *Staph aureus* make it difficult to treat the infection.

<http://microbewiki.kenyon.edu/index.php/File:Lesionsmicro.jpg>

<http://microbewiki.kenyon.edu/index.php/File:Lesionsclosed.jpg>

http://commons.wikimedia.org/wiki/File:Anterior_view_of_male_upper_body_retoched.jpg

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers



Skin





Trichophyton and *Microsporum* fungi feast on keratin in the skin and cause ringworm fungal infections

<http://en.wikipedia.org/wiki/File:Yearinfection.JPG>

http://commons.wikimedia.org/wiki/File:Anterior_view_of_male_upper_body_retoched.jpg

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

What's Happening in the Gut?

Major barriers for microbes entering the gut:

- low pH
- Saliva and Bile
- Immune system



- Finding a place to attach to intestinal wall
- Surviving a widely varied diet

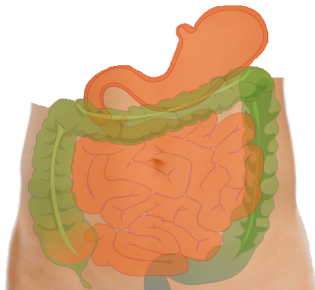


For those microbes that manage to colonize the gut:

- gut flora perform regular tasks of digestion, vitamin production, many others
- Gene transfer between the myriad of species in the gut can generate new combinations of drug resistant “superbugs”

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

http://commons.wikimedia.org/wiki/File:Intestine_and_stomach_-_transparent_-_cut.png



Gut

Bacteroides thetaiotaomicron
bacteria ferments simple
carbohydrates in the gut,
releasing hydrogen and CO₂.

+ carbohydrates



CO₂ and H₂

Methanobrevibacter smithii



CH₄ Methane

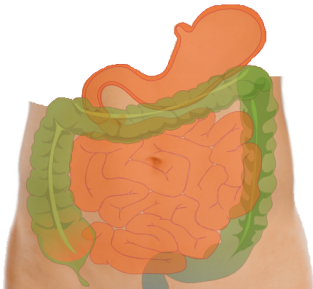
archeabacteria consumes hydrogen gas from *Bacteroides* and produces methane, which is lost from gut as “gas”



Gas

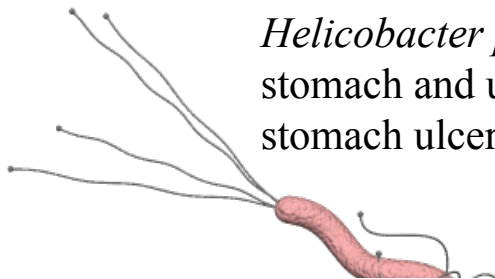
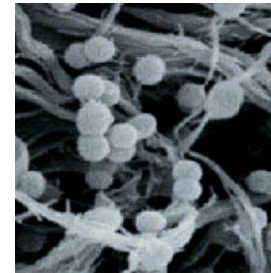
Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

http://commons.wikimedia.org/wiki/File:Intestine_and_stomach_-_transparent_-_cut.png



Gut

Ruminococcus sp. bacteria can be found in significantly high numbers in the gut flora. They break down cellulose in the gut, helping with digestion.



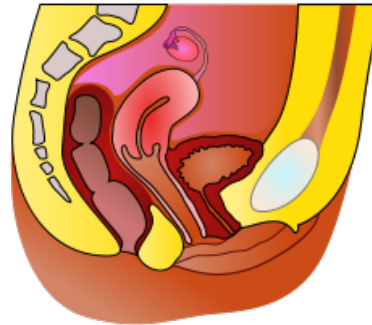
Helicobacter pylori bacteria has a helical shape and colonizes the stomach and upper G.I. tract. It is known to be a major cause of stomach ulcers, although many with *H. pylori* do not get ulcers.



What's Happening in the Urogenital Tract?

Urinary system almost
sterile due to urea and
other chemicals

Urine often flushes
out microbes that find
their way in



Introducing a catheter into
the urethra can introduce
microbes directly into the
bladder, where a biofilm can
grow and cause bladder
infection

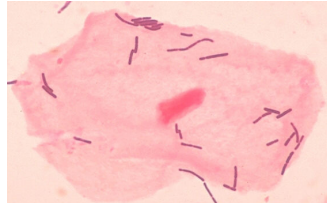
The vagina has a low pH due to *Lactobacillus* secreting lactic acid and hydrogen peroxide.
Let's explore the microbiome of this region further.





Urogenital

Lactobacillus normally maintain low pH while other species are kept in small numbers in the vagina



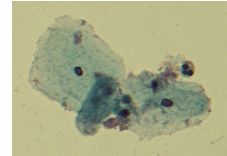
Lactobacillus and vaginal epithelial cell

If *Lactobacillus* decreases from antibiotics...



Candida albicans can take over and cause a yeast infection

G. vaginalis and vaginal epithelial cell



Gardnerella vaginalis can grow too much and cause bacterial vaginosis.

http://commons.wikimedia.org/wiki/File:Lactobacillus_sp_01.png
http://commons.wikimedia.org/wiki/File:Female_Genital_Organs.svg

http://en.wikipedia.org/wiki/File:Candida_albicans_2.jpg

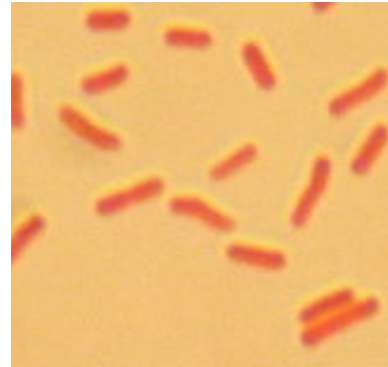


Urogenital

The urinary tract is normally sterile due to urine flushing out the tract.



Urine sample infected with *E. coli*



Urine sample infected with *E. coli*

But, *Escherichia coli* from GI tract can infect urinary tract due to poor hygiene and contamination from nearby GI tract opening.

http://commons.wikimedia.org/wiki/File:Female_Genital_Organs.svg

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

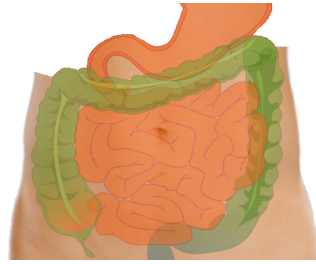
http://commons.wikimedia.org/wiki/File:E_coli_Gam.JPG

<http://commons.wikimedia.org/wiki/File:Pyuria2011.JPG>

Interplay Between Medicine and Microbes



Antibiotic
s



Chemotherapy drugs

Kills infectious bacteria but also disrupts natural flora. Can result in yeast infections, digestive problems, etc.

Gut flora has been shown to modify some drugs during metabolism. This causes many side effects, including upset stomach.

http://commons.wikimedia.org/wiki/File:Chemotherapy_bottles_NCI.jpg
http://commons.wikimedia.org/wiki/File:NOVAMOXIN_antibiotic.jpg

Summer 2012 Workshop in Biology and
Multimedia for High School Teachers

Use of Antimicrobial Products

How many do we really need?



But do we need some

Will this allow “superbugs”
that can barely survive these

natural exposure to germs to keep our normal flora around?



Products kill germs to reduce infection

treatments to grow and become more prevalent... causing problems for the future?

<http://commons.wikimedia.org/wiki/File:Afwasmiddel.jpg>

<http://commons.wikimedia.org/wiki/File:Tissue.jpg>

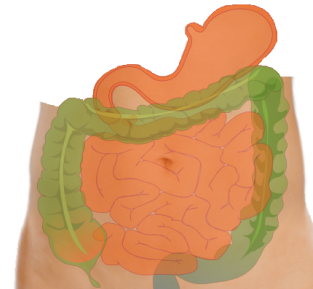
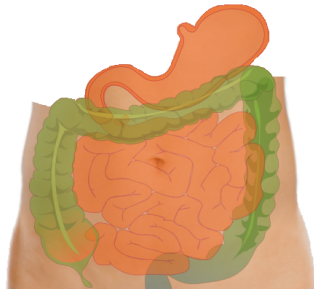
http://commons.wikimedia.org/wiki/File:Refill_soap.jpg

<http://commons.wikimedia.org/wiki/File:Toothpaste.jpg>

<http://commons.wikimedia.org/wiki/File:Hands-Clapping.jpg>

Summer 2012 Workshop in Biology and Multimedia for High School Teachers

Is My Gut Microbiome the Same as Yours?



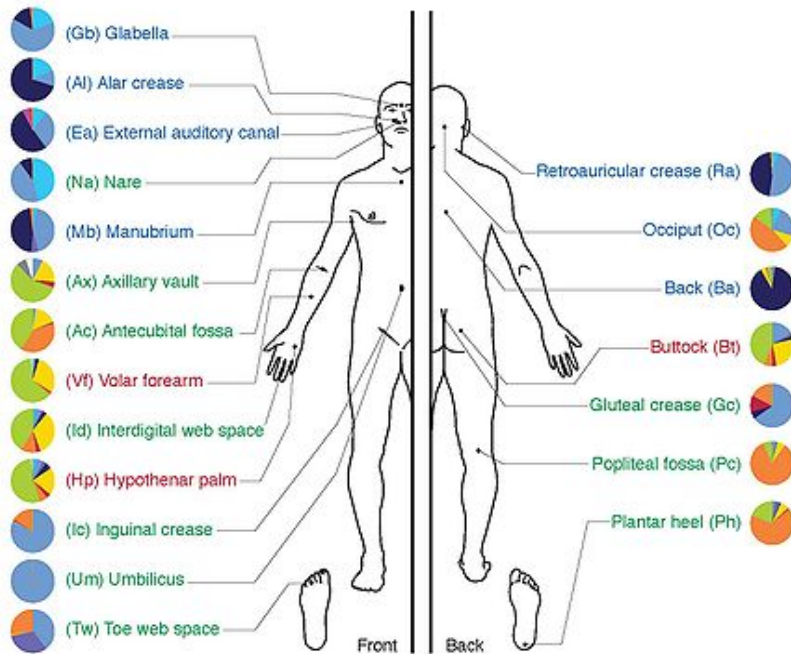
The number and amount of the many different microbes can vary greatly from person to person.



Relative amounts of species

Research in the Human Microbiome Project is starting to identify the relative amount of each microbe present at different locations in the body.

The Microbiome of one person can be different than others in species and relative amounts



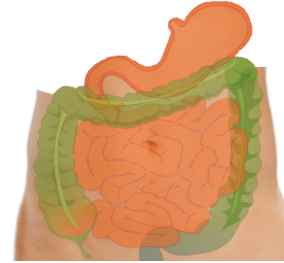
So many new questions to answer about the Human Microbiome...



How does the gut flora modify drugs, and how can we minimize side effects?



Are we making germs more resistant to antimicrobials? What happens when the germs are resistant to all of the drugs in our arsenal?



Why does my gut flora look different than yours? How does that affect obesity, food allergies, and ability to fight disease?

What do you want to know?

<http://commons.wikimedia.org/wiki/File:Hands-Clapping.jpg>

http://commons.wikimedia.org/wiki/File:Chemotherapy_bottles_NCL.jpg

http://commons.wikimedia.org/wiki/File:Intestine_and_stomach_-_transparent_-_cut.png

Summer 2012 Workshop in Biology and Multimedia for High School Teachers