



"You live in intimate association with bacteria, and you couldn't survive without them." ~Bonnie Bassler

# Definitions

#### What are Microbes?

They are single celled organisms too small to be seen by the naked eye. The most numerous and diverse organisms on earth. 10x more microbial cells on earth than stars in the universe! The total mass of living things consists primarily of microbes.

# What is the Human Microbiome?

It's the entire genetic material of 100 trillion microbes that live in and on the human body. The microbiome genes are 100x greater in number than our own genes. It weighs about 3 pounds - about the same as our brain.



The microbiowhat? Is that the new science-fiction thriller movie that everyone is talking about? No, but it could be.

In fact, this topic makes me think of one of my favorite science fiction movies called "<u>Fantastic Voyage</u>".

Released in 1966, this movie takes its viewers on a... umm...fantastic voyage...through the human body.

A team of four male scientists and their assistant [who just happens to be 26 year old Rachel Welch] pile into a specially designed submarine. Their mission: destroy a blood clot in a patient's brain. The whole kit-n-kaboodle is shrunken down to one micron and injected into the patient. However, their miniaturization is only temporary. They have just sixty minutes to complete their mission before they revert to original size or get attacked by the patient's immune system. Oh the drama! Click here to watch the theatrical trailer.

OK, let's leave science fiction behind for now and move on to some science-fact. They say - *fact is stranger than fiction*. I think you'll be fascinated by the information in these videos.

While research has been taking place for a decade, science has only uncovered the tip of the iceberg. I think they will unlock the secrets to many of our health problems once they know more about the entity we call our microbiome.

OK, strap yourself in and get ready for a fantastic voyage of your very own! Fear not, no miniaturization is required. All I ask is that you have an open mind. Here we go...

Al Klapperich, Branch Manager Gluten Intolerance Group of East Central Wisconsin

# **Definitions**

#### What is the immune system?

It's a network of cells, tissues, and organs that protect us against attacks from bacteria, viruses, parasites, and fungi. Think of it as our "armed forces".

This amazing mechanism must recognize and remember millions of enemies.

A healthy immune system recognizes it's own cells (known as "self cells"). Normally, self cells are seen as friendly and left alone.

Foreign cells (known as "nonself cells") can be tagged as enemies. These cells are hunted down and killed.

Sometimes the friendly, self cells are seen as enemies and thus attacked and destroyed. This is known as an autoimmune disease. Source

# Where is the immune system

**located?** In organs such as tonsils and adenoids, lymph nodes, the thymus, the spleen, bone marrow, appendix.

About 70% of our immune system is housed in the gut [intestinal tract]. <u>Source</u>



## Play video (5:28): <u>http://bit.ly/21miass</u>

The Invisible Universe provides an excellent and easy to understand explanation of what the microbiome is and what it does. Below, you'll find notes from the video.

We are more microbe than human. Ten times more microorganisms cells in and on our body than human body cells.

Most microorganisms are not bad - most are good. Without them we are not as healthy.

Where do they come from? Initially from our mother as we pass through the birth canal. Also via breast milk.

Over the years we build our own set of microbes we pick up from family members and the environment around us, however they remain very unique to us, much like a finger print.

Microbes educate our immune cells - teaching them things they should fight [bad bugs that make us sick] and good bugs that aren't a threat.

They become or first line of defense when fighting off invading germs. They even release their own antibiotics.

Like different eco systems in nature, different species of microbes adapt to their environment depending on where they live. Wet places like mouths, noses, and arm pits. Oily places like scalps and backs. Dry places like our forearms.

The gut is the biggest and most important collection of microbes. It is the most complex and most diverse. They are fighting off infections, revving up and dampening down our immune system, and signaling cells. They even help regulate our metabolism.

### **Definitions**

What are Probiotics? They are live microorganisms that are intended to have health benefits. Probiotic products include fermented foods (such as yogurt, kefir, aged cheeses, kimchi, sauerkraut) and dietary supplements.

Two of the most common groups of bacteria found in products are Lactobacillus and Bifidobacterium. Each of these groups includes many types of bacteria. <u>Source</u>

**Be aware** - In 2015, The Celiac Disease Center at Columbia University found 55% (12) of the 22 popular probiotics contained detectable levels of gluten. 13 of the 22 were labeled as "gluten-free". 18% (4) of the tested products exceeded the FDA limit of 20 parts per million - 2 of them were labeled "gluten-free". <u>Read More...</u>

<u>Gluten-Free Watchdog will be</u> <u>testing 31 different probiotics</u>. Test results will be available to GFW subscribers.

What are Prebiotics? Nondigestible food ingredients aka fiber. They are food for our bacteria. <u>Source</u>

# Invisible Universe Continued

If they are not functioning properly due to antibiotics, what we eat - it can lead to diseases like: colon cancer, colitis, perhaps even diabetes and obesity.

Some scientists believe the increase in diseases is because we have lost key gut microbes. Our microbiome is far less diverse than undeveloped countries and early generations.

Babies delivered via C-sections are not exposed to very important microbes. Not enough breast feeding, exposure to antibiotics, and obsession with cleanliness. All alter the microbiome. It may explain the increase in asthma and allergies, maybe because the microbes never taught our immune system to work properly.

Maybe taking good microbes (probiotics) and prebiotics could help prevent and treat some diseases.

This information is new and there is still a lot to learn, but scientists are finding the microbes that make up our microbiome are essential for our health and happiness.

#### Home is where the microbes are

For six weeks, The Home Microbiome Project followed seven families consisting of eighteen people, three dogs, and one cat.

They discovered the families drastically affect the microbial communities already established in the house.

When three of the families moved, their own unique microbial community completely erased the

previous inhabitants microbial signature in less than day.

Read more ....

# Who is Rob Knight?

Currently he is a Professor in the Department of Pediatrics, with an additional appointment in the Department of Computer Science, at the University of California San Diego.

He was chosen as one of 50 HHMI Early Career Scientists in 2009, is a Senior Editor at the ISME Journal, a member of the Steering Committee of <u>The Earth Microbiome</u> <u>Project</u>, and a co-founder of the <u>American Gut Project</u>.

A bit more of Rob's history can be found in a 2012 Nature.com article: <u>http://</u> <u>bit.ly/1nLXBsk</u>.

More of Rob's videos can be found here: <u>http://bit.ly/</u> <u>1R74Hjv</u>

...and author: <u>Follow Your</u> <u>Gut: The Enormous Impact of</u> <u>Tiny Microbes</u>





Play video (10:29): <u>http://bit.ly/1LZkeF7</u>

Rob Knight gives us a deeper, inside look at the microbiome and how it affects us.

Science has revolutionized how we see our place in the universe. Copernican revolution revealed that our planet is not the center of the universe. Darwinian revolution made us realize we are not the top of beings, but merely just a twig on the tree of life. Dark Matter revolution made us realize all of the stars/galaxies we see around us makes up only 4% of the entire universe. 96% is Dark Matter/Dark Energy that we do not understand. Microbial revolution makes us realize our body contains 10 trillion human cells. Living in and on us there are 100 trillion microbial cells -

many of them too small to see with the naked eye. Human genes add up to about 20 thousand. Our microbial genes range from 2 to 20 million in number. We could consider ourselves as less than 1% human.

99%+ of our genes come from our microbes

The Human Microbiome Project mapped the healthy human microbiome of 250 healthy volunteers.

Tremendous amount of diversity found between the volunteers. Each of us have a completely different microbiome from the person sitting next to us. Our human genome we share is 99.9% the same. When healthy - the functions of the microbes perform are similar.

Not surprising, the same is seen in larger eco-systems. Grasslands from South Africa and New Zealand and Rainforests from Zimbabue and New Zealand. They look similar even though they

#### Rob Knight on celiac disease & the microbiome...

"Celiac disease is related to inflammatory bowel disease and also involves an immune system component: when celiac sufferers eat wheat products, the natural gluten proteins in wheat activate the immune system, which attacks the lining of the gut, shredding it.

There has been intense interest in whether celiac is linked to the microbiome, but at this point, the dozen or so studies have found essentially no consistent trends associating microbes with celiac.

Although many studies are able to find differences between the microbiomes of celiac patients and healthy people, the bacteria in the celiac patients differ from study to study.

Clearly the pattern is complex, and more work is needed to understand whether gut bacteria contribute to celiac or simply respond to the altered, gluten-free diets of celiac patients."

Source: Ideas.TED.com http://bit.ly/1TXO1RJ

# Being Human Continued

are on different continents, yet they do not share the same species.

When unhealthy, the microbes are linked to different diseases like Inflammatory Bowel Disease to Rheumatoid Arthritis. In mouse testing - autism and depression.

Strictly by looking at microbiome, scientists can tell with 90% accuracy if a person is lean or obese. Doing the same with the human genome accuracy drops to 58%.

Mice can be raised with no microbes of their own. They are introduced to microbes from lean or obese mice. The amount of weight they gain is based on whose microbes they received.

Behavior is also affected. A mouse can be made more anxious by giving them microbes from an anxious mouse or less anxious is microbes come for a less anxious mouse. They can also induce an autistic-like behaviors [hoarding marbles] and subsequently reverse them.

Remarkable findings because obesity is generally attributed to will-power or human genes. These microbes can affect these traits that affect how we think of who we are.

Remember this is mouse model work, we do not know how it will apply to humans but the potential for this research will affect a wide range of diseases that you might not have thought were linked to the gut.

If you think of the gut microbiome as an organ, it's the only organ you can transplant without doing surgery. Doctors can use medical grade stool to replace the microbiome on a patient with <u>Clostridium difficile</u> infection [C. Diff] - a life-threatening kind of diarrhea that kills 14,000 people a year in the USA alone.

C. Diff can be cured with 95% efficacy by translating a healthy microbiome [also known as <u>Fecal Matter Transplant</u>]. Antibiotic treatment has only worked 20-30% of the time.

How many other diseases linked to the microbiome can achieve similar success rates by manipulating the microbiome?

#### Who is Dr. Alessio Fasano?

A world-renowned pediatric gastroenterologist, research scientist and entrepreneur

He is the chief of Pediatric Gastroenterology and Nutrition at MassGeneral Hospital for Children

He directs the <u>Center for Celiac</u> <u>Research</u>, specializing in the treatment of patients of all ages with gluten-related disorders, including celiac disease, wheat allergy and gluten sensitivity.

Dr. Fasano also directs the Mucosal Immunology and Biology Research Center.

Under his leadership, investigators are studying the molecular mechanisms of autoimmune disorders including celiac disease, and other-gluten-related disorders.

He authored the groundbreaking study in 2003 that established the rate of celiac disease at one in 133 Americans and a 2014 book titled - <u>Gluten Freedom</u>.





# Play video (17:01): <u>http://bit.ly/rTVWXqN</u>

Dr. Fasano gives us even more details on how our microbiome and our environment shapes who we are.

A few centuries ago life expectancy was 32 years. Now in industrialized countries it's 80+. This was all driven by proper nutrition. The next generation - for the first time ever - will have a lower life expectancy than our current generation. Again, it's driven by nutrition.

There is now a better understanding of the recipe that transforms people from a state of health - to a state of disease. Talking about immune-mediated diseases - not just celiac disease or a problem with gluten - cancer, behavioral issues, cardiovascular issues,

"You eat junk - you bave a microbiome out of balance."

infections and of course auto-immune diseases. These conditions are all commonly linked by the process of inflammation.

We knew that genetics would impinge on your final final destination.

Environment is important - in that - nutrition is a key element. Nutrition is much more than just fuel.

The two worlds of who we are genetically and the environment need to physically interact. The gut - the largest interface we have - the port of entry where the environmental triggers come in and will eventually lead to a clinical outcome. Of course the immune

#### Celiac Disease & Microbiome

A study published in the Cleveland Clinic Journal of Medicine - March 2016.

The microbiome in celiac disease: Beyond diet-genetic interactions

#### http://bit.ly/1MtOsLu

Evidence points to the mix of bacteria that make the gut their home, collectively called the microbiome.

Although genetic factors and exposure to gluten in the diet are proven to be necessary for celiac disease to develop, they are not sufficient.

Additional environmental factors must be contributing to disease development, but these other factors are poorly understood.

In germ-free rats, long-term feeding of gliadin, but not albumin, from birth until 2 months of age induced moderate small-intestinal damage. Similarly, germ-free nonobese diabetic-DQ8 mice developed more severe gluten-induced disease than mice with normal intestinal bacteria.

These findings suggest that the normal gut microbiome may have intrinsic beneficial properties capable of reducing the inflammatory effects associated with gluten ingestion. Notably, the specific composition of the intestinal microbiome can define the fate of gluten-induced pathology.

#### **Continued on Next Page**

# Gluten & Gut Microbiome Continued

system is important.

Today we discuss the microbiome and how nutrition can really impinge on it.

Hygiene Hypothesis - Twenty years ago they looked at the 50 year time frame we went after the major killers of human kind infections. This effort was very effective. However, we set the stage for the epidemics of immune mediated diseases like MS, Crohn's Disease, Type I Diabetes, Asthma. These epidemics are accelerating. Happening only in industrial countries. If someone from developing counties migrate they will suffer the same kind of phenomenon. Hygiene Hypothesis - we are too clean for our own good..and now we are paying the price.

Autism is the most frightening epidemic. Time frame is not 50 years. In 25 years autism rates when from 1 in 5,000 to 1 in 68. Male/female ratio is 4 to 1. Next generation, 1 out of 4 boys will be lost to autism. The timeline cannot blame genetics for these epidemics. We are changing the environment way too fast for our bodies to adapt. The same goes for food allergies. There is an escalation in a short amount of time of these kind of consequences.

It used to be - you develop a cow's milk allergy by year one, the vast majority will grow out it. People develop cow's milk allergies later in life. Type I Diabetes was called Juvenile Diabetes - must drop that terminology because Type I can develop at 40 or 50. Celiac Disease was considered a childhood disease - it can develop in your 70s. What's going on?

"In the US, the incidence of celiac disease doubles every 15 years" In the US, the incidence of celiac disease doubles every 15 years. We were under the impression if you were genetically predisposed for celiac disease and you ingest gluten grains, you have the two key elements to

develop celiac disease. The target organ is not small - 20 feet long in an adult - and must have a critical mass of damage in order to develop symptoms.

#### Celiac Disease & Microbiome - Continued

Taken together, these studies support the hypothesis that the intestinal microbiome may be another environmental factor involved in the development of celiac disease.

Many questions still remain and further study is required to get a better understanding of how the puzzle pieces fit together.

Special thanks to my friend and Gluten Intolerance Group of Central Arkansas Branch Manager, Anne Luther for sharing this study.

Role of the Microbiome in Celiac Disease Dr. Alessio Fasano - May 2015

#### http://bit.ly/1T1akEJ

Does the Gut Microbiome Play a Role in Autoimmune Disease? Amy Nett, MD - Dec. 2014

#### http://bit.ly/25bqGPR

The Microbiome and Celiac Disease: A Bacterial Connection Amy Burkhart, M.D., R.D. Dec. 2014

#### http://bit.ly/1pT7czf

# Gluten & Gut Microbiome Continued

Hygiene Hypothesis is being challenged. In countries (South America, North Africa, some Middle Eastern counties) where hygiene is not implemented - they don't see these epidemics. Hygiene Hypothesis cannot explain it all.

[Dr Fasano says this is the most important information from his talk. I have transcribed it - verbatim - to the best of my abilities]

"If you are lucky, you were born as mother nature decided we should be born with vaginal delivery, I can't emphasize enough - proper nutrition you've been feed they way we evolved as a species, no infections, very little/ no use of antibiotics - if you did that, the outcome is to really develop an eco-system of microorganisms that we now know live in symbiosis [beneficial to each party] with us from birth to death - i.e. the microbiome in good balance. This is not my interpretation, this is factual.

The microbiome is the trainer in the first 3 years of life of how we really unleash our weapons when we are under attack. The immune system is trained mainly by the microbiome. The immune system - developmentally speaking were developed to fight one single enemy - infections. As a species, classically, were used to dying either because a predator will eat us or infection will kills us. It is only recently that the immune system has to fight many other enemies never been seen during evolution - pollution, chemicals, radiation.

If you do the job right - you train the immune system right - the threshold where you unleash these tremendous weapons with the collateral damage we call inflammation that create an unfriendly environment for microorganisms to grow - will be set very high. When really, really we are under danger. If we do that and train the immune system properly we stay healthy and mainly because not matter what kind of genes we have - we unleash this inflammation when we really have no alternative.

You are out of luck if you are born by cesarian section, you got God knows what in your mouth - but not food. You go to the freezer section of the super market and buy the dinner tray - we have no idea what's in there. You got multiple infections, bombarded by antibiotics - this leads to a total imbalance of your eco-system of microorganisms - what we call dysbiosis. Now this, will train the immune system to set that threshold very very low. So you unleash inflammation even when it's not needed. What is the price you pay? Depending on the genetics, you will develop those immune

### Gluten & Gut Microbiome Continued

mediated that I told you - even when the minisculist stimulus comes from the environment.

Of all these elements that dictate the composition of the microbiome - the way you're born is a one shot, that happens once in a life time. Infections and antibiotics use occasional elements. You eat three - four times a day. The microorganism that makes the microbiome - they need to eat - they eat whatever we eat. You eat junk - you have a microbiome out of balance. You eat wealthy and healthy, you will be definitely in better shape. Now you can go to sleep..." "You eat wealthy and healthy, you will be definitely in better shape."

Microbiome is a such a buzz word, we been studying it for decades - the interplay between us and microorganisms - it came out as a surprise. We didn't know there was this hidden world. 95% of the organisms that live with us are not culturable, therefore we didn't know they existed.

They talk with us. There's a cross talk that has a tremendous impingement on who we are. If we develop cancer or obesity may depend on the microbiome. Our behavior - animal models suggest - may be dictated by the microbiome.

While studying celiac disease we learned something inexplicable. The fact you have the genes for breast cancer, Alzheimer's, high blood pressure, heart attack, celiac disease - it doesn't mean it's destiny. You got the short stick of evolution by inheriting those genes from your parents. If you do or do not develop those diseases - genetics or not - totally depends on the microbiome.

If you are born by C-Section your chances of developing an autoimmune disease - celiac disease - are 5 times greater. Why? The microbes from the mother's birth canal are highly selective - they are meant to stay with you. C-Section birth only transfers skin microbes - they are casual - "all comers" - from people in the delivery room - some of those microbes are not good.

Human genome is very rudimental. We are at the bottom in terms of genetic complexity. We have only 25,000 genes. The worm we use for fishing - 75,000. Wheat has 150,000. How do we explain the complexity of who we are?

Early childhood nutrition on health in adults is not cliche any more. The way we feed the generations to come will determine if they lead a long and happy life. We have preventative medicine - preventing rather than fixing.

"Prenatal, Perinatal, Postnatal factors - they all impinge on who we are and the cross roads is again - nutritionally influence the microbiome."