Functional Genomics
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Lecture No 03
Genetics, Genomics and Epigenomics

So, welcome to the third lecture of week one of the course functional genomics. So what we are discussing in the last two lectures are how the discovery made by Mendel let it led to the emergence of the field called genetics that led to a new field called genomics and the post genomics era we are looking at the wealth of the data that is being analyzed using a new branch or either new approach of science called as bioinformatics and we said that how it is work flown out really a distinct quantity we called it as (())(00:51) genetics or molecular genetics and how it is (())(00:54) and really help us in understanding but it is not that bioinformatics is end of the field that is growing with all these understanding us to how genes functions and how the genome functions you know we are trying to understand something beyond what the DNA sequence tells us.

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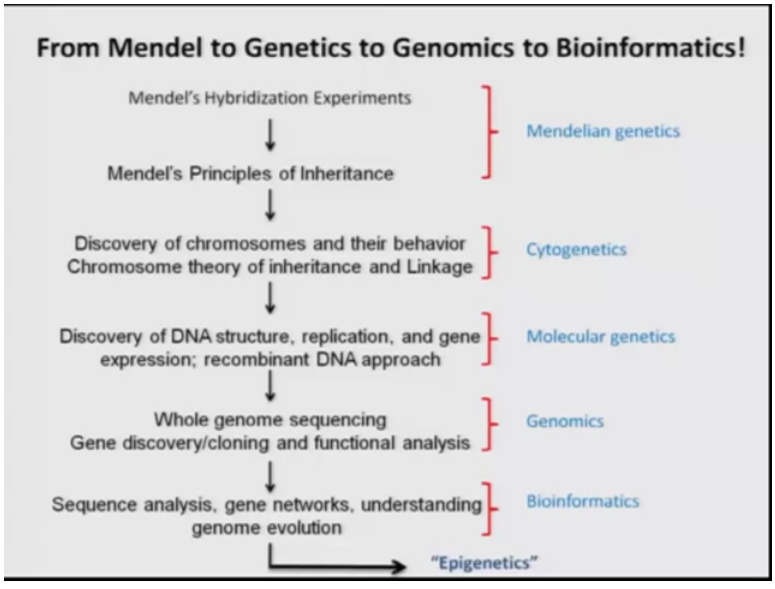

It is not simply the sequence that tell whether you are healthy or unhealthy. It is sometimes beyond your genome sequence. So that is the field in emerging field that is coming up which you called as you know Epigenetics, it is beyond your DNA sequence. So, let us look into what is Epigenetics?

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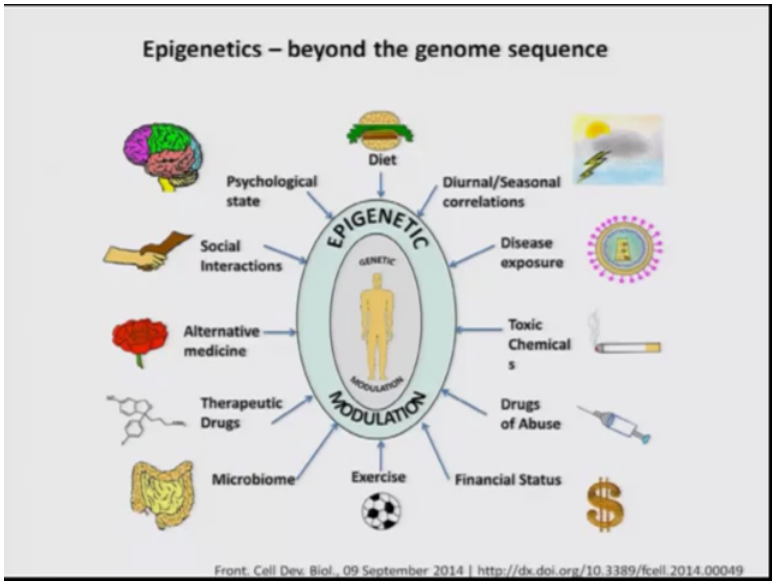

So if you look into all of us, let us say that I and my brother we are twin brothers, we have identical DNA sequence. Is it that both of us will be identical in terms of our physiology, in terms of however body functions? The answer is not necessarily, the reason being although we shall identical genome we may not have identical lifestyle, for example each individual as it is shown here in this slide or expose to different environment meaning what you eat as diet could be different, he may be eating something different than me, my I maybe liking something for example burger, he may like pizzas or he may like parathas and so on.

I may be happy person because I am into a job which is stress free whereas he is into a job which is having much more stress. So, you know your physiological or psychological state could vary or social interactions. I may be living in a country where people are more friendlier or he has gone to country where people are not that friendlier. So, he is not finding many friends, social interaction or I may be tune to the allopathy where I whenever there is problem I go to allopathy doctor which gives you the modern medicine so to 1say or he may be more a person who likes the tradition medicine and so on so the drug that I have he goes to different doctor, I go to different doctor and so on.

There going to be extremely different condition that we we grow up he may be having a condition which is very cold, I may be in tropical and so on. So I may be earning more, he may be earning less so that again gives something for you to be happy or your lifestyle or how do you

take care of yourself. So I may be not having enough time to play or (())(3:39) play whereas he goes and play. So, his exercise body activity is different so all these things can change the way your genome functions. It is kind of two way interaction whether you are able to survive an infection is something which you are genome as say in that at the same time whether if you are infected the infection also can in way change your genome how does it function, that is what you call the Epigenetics.

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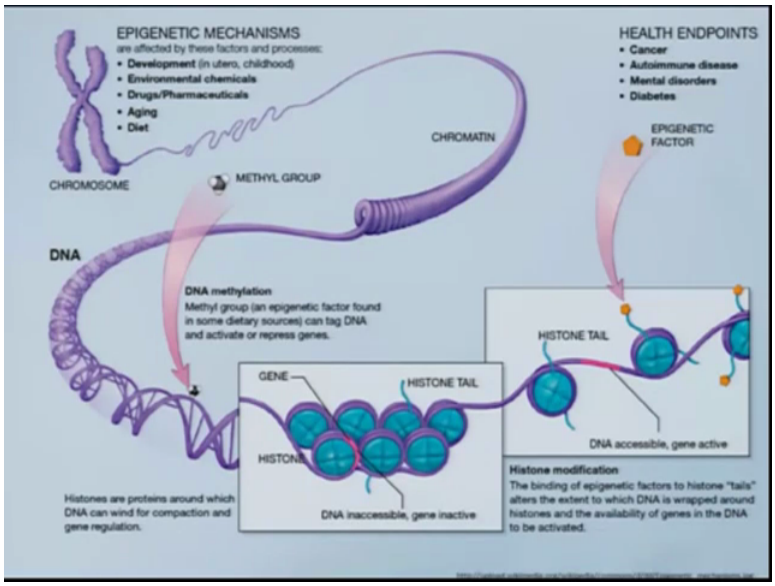

We are going to restrict our discussion to one particular you know area that is how this kind of interactions that is your body interacts with various such changes, whether it is diet, whether it is exercise, whether it is infection, whether I smoke, whether I drink. What food I have? You know they have some effect on the genome and we believe one of the way by which the genome can be altered but not necessarily at the sequence level you know we are identical twins anyway but it could be that at certain place of our genome, you know the genome maybe modified with the group for example which you called as the Epigenetics factors it could be methylation of the histone, methylation of the DNA and so on.

So this change the way your chromosome functions you know that pain normally when the chromatin or the histone gets methylated. They are you know more compact when they get acetylated, they open up so the expression level of the genes press that are present in that region again as a huge influence how the cell responds. So people believe that the at the DNA level for

example the methyl groups that are shown here in this for example here this is the methyl group that is the methyl group is added to for example cytosine, now see base of the DNA can change the way the DNA in functions or it could be for example the histone tail.

You know the amino acid sequence that form the histone tail can get for example attached with the either acetyl group or methyl group and then that reflects the way the chromosome gets decondensed or condensed that detects whether your gene is functional, less functional, more functional or not it all functional. So that's, that's one of the way by which you know system develop, so you are enrollment or the enrollment in which you are living, your life style can change the way the gene functions not necessarily by altering the sequence but how the chromosome functions like the modifications and we know now that these modifications can also have an influence on the next generation.

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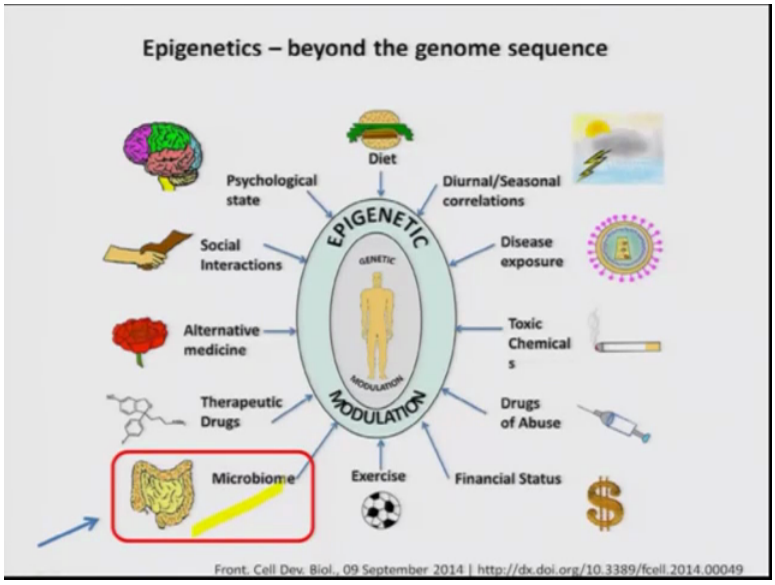

Just to give you some interesting inside into this process we will talk about what is called is gut microbiome. What you meant by gut microbiome, is very interesting because all of us have microbes living in our body. It could be your gut intestine or it could be your eye lashes, it could be your hair, could be your skin, it could be your saliva everywhere you know you have microbes thriving right and they are some of them most of them or friendlier to you, so it does not really harm you but it does and they do have influence and how you function as a organism, so that we will talk about.

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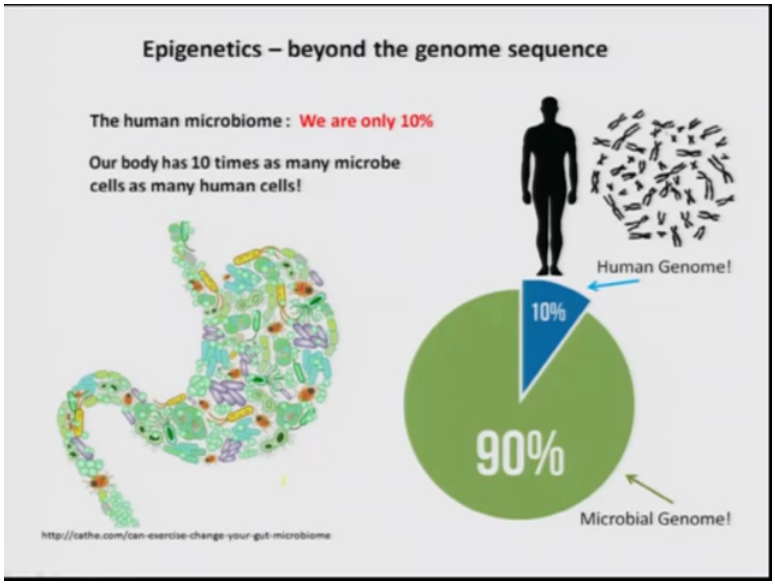

This what it is the human microbiome only if you will talk about the gut. Our body has ten times as many microbe cells as many human cells. In fact if you count the number of cells in your body and the number of microbe that are present you know it is almost their DNA is ten you know ten times more than yours. So, that is amazing concept that's what people called it as the second genomes.

The microbiome genome is called as the second genome or the other genome and if you look into that 90 percent of your DNA that is there in your body, the microbes have in terms of the cell number and so on. So that's an interesting concept if that is the case that that the number of cell that are there in your body of the microbes for exceeds the number of cells of your own then they certainly are going to have a significant influence on how your body functions right. So how really this is affected.

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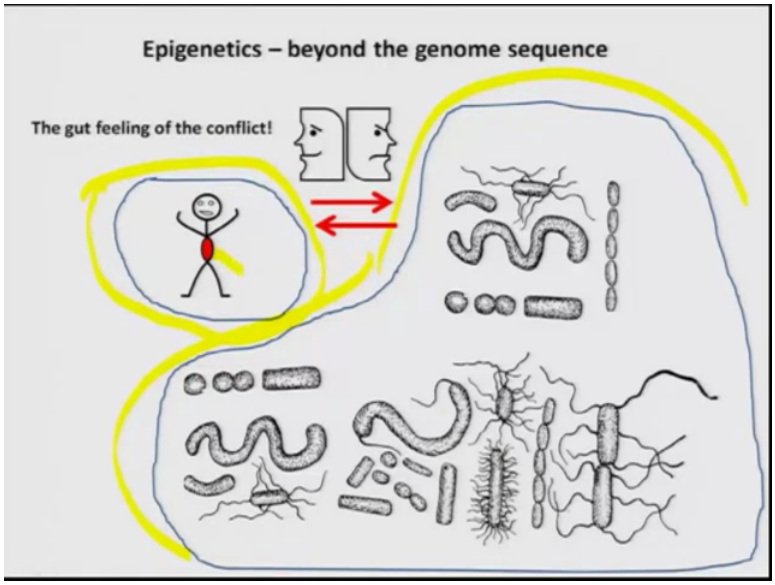

These how it is the gut feeling conflict meaning there are you know your gut has got, this is what just diagrammatical represented, these is your human you know the cell of human origin that is there in body and this is just to say that in terms of number you know they are far above in ten times as compare to the number of just microbe and we are just (())(8:41)your gut. So there is the conflict, the conflict meaning some are good for you, some are not so good for you right.

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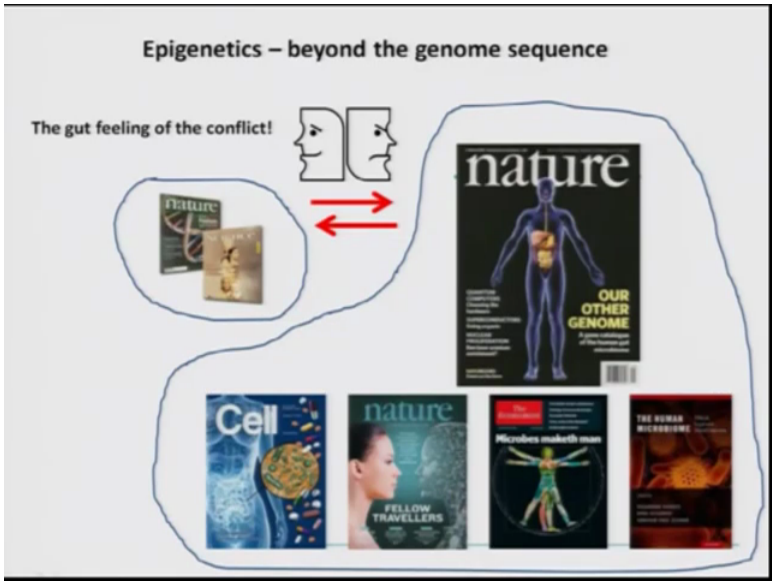

You do not realize that but the scientist have realized that the microbiome of your gut has some major influence on your wellness and is important for you to be healthy and at times it can make you feel sick or fall sick that's why there are large number of papers publish recently which talks about the importance of understanding the microbes that live in our gut because this is not same in even within a family.

You know there are five members each one will have different types of you know microbes thriving in the gut and it changes with the age. I will talk about little later. So therefore you know the microbiome is going to make a huge impact on your health, so there are half (())(9:41) a number of you know discoveries have come from the microbiome. They are looking into how you it makes you healthy or susceptible for disease and so on. So that's really really something, you know is because of the genomics revolution.

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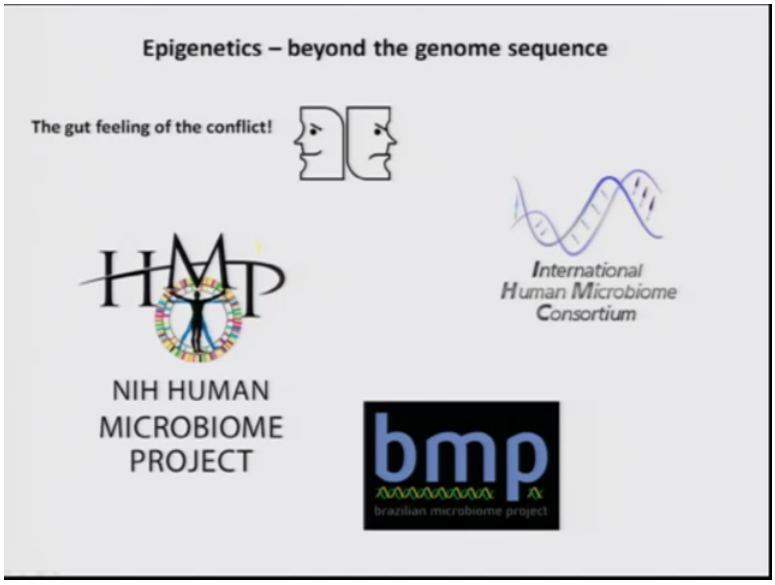

So understanding the importance of microbes the NIH National Institute of health of the US which normally (())(10:05) any new program, is come up with what is called as human microbiome project. Because it is you know it is going to be more challenging than sequencing human genome for two reasons one, it is not unique because when it talk about the number of cell that are ten times more than human the difference is that human cell the DNA is same in every cell whereas in the microbiome there could be thousands and thousands of different species that live.

So, if you take all of them now when you sequence the DNA it just kind of (())(10:38) mixture. So you don't know which sequence belong to which species even to type and classify them is going to be difficult because these microbes cannot be cultured outside because these they all can leave only inside your body possibly right so even classifying them is going to be difficult. The even governments like Brazilian government has come up in a microbiome project even the Indian government is trying to in put together a consortium project to understand the gut microbiome.

Indian population (())(11:10) this whatever the use government that's for its population may not applicable to India are you know even in India every state has a different lifestyle and food habit's right. So you you go to Punjab you will get of food that is very different from the food that you will get from for example Tamilnadu or Maharashtra. So you know the microbe that thrive or grow in your body depends on what kind of food that we eat so it's going to be extremely challenging to understand what are the different types of microbes present in the populations right.

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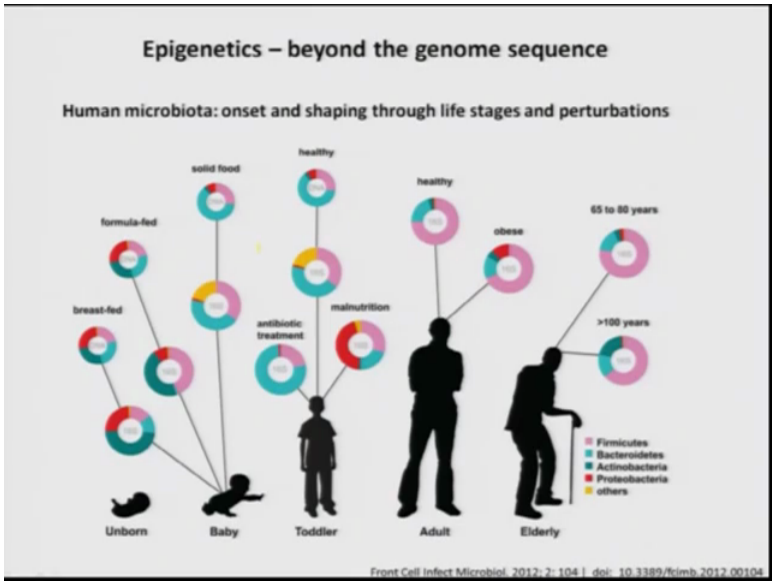

But what is interesting is the following. The human microbiota are the biome, you know it changes the the number of species the variety changes as you age. This is mostly to do with the kind of food that you eat alright. So that's we can see that the unborn baby is free of any microbiome because as long as the baby is inside, the mother's womb he or she is completely

protected from any microbiome and when this born is free. But he or she gets the microbiome into you know the intestine when they feed on you know when they the mother breast feed, so along with the milk from the skin the microbes get in right.

This is also study with suggest that the microbiome of the babies differ between a normally born babies as compared to the babies that are born out of, for example cesarean section when they you know make small slit in the uterus take the baby out, so it's different because the kind of exposure they a underwent when they are born right. So that in fact give some protection or make them susceptible there are beautiful paper chicken go and you know read we will post it when the course is online. So you can see that for each whether a baby, toddler, adult or elderly.

You know this is one study wherein they have shown how for example each you can see that this donate like thing is a this is talks about you know the different types of microbe. Each colour represent a particular group microbes so let us not worry about what microbe it is let us assume that a colour in a donate represent a particular group of microbe and you can see for example, this dark green that that is seen here the baby when in that that's is almost 50% when breastfeed right.

But it goes down that particular microbiome number goes down if the baby is on formula food for example lactogen, cerelac and whatever it is that that when mother cannot feed them there are supplemental comes but the movement is shift to solid food. You see that that's that dark green is disappeared that means these microbes thrive on you know the metabolite that come from mothers food or some milk supplement right and that that change and then you have another you know light blue colour whatever, a new group of microbe that come into your gut as you switch to solid food.

And of course you know you go and you have some fever and your doctor gives you heavy dose of antibiotic it is going to wipe out most of the microbe that live in your guts. So you can see that antibiotic treatment let to, you know a majority of them all being this light blue colour group. The pink and red has completely disappeared and you see that you know a healthy individual who is not under any antibiotic treatment you know you there is a difference has compare to somebody who is under antibiotic treatment.

What is also interesting is that individual that are malnourished for example people or children from marginally section who are not really having healthy food nutrient food. Their microbiome mic gut microbiome is very different. You have this light blue colour microbe is almost the number is come down and they have this colour this called as the the reddish or orange that group has really really you know outnumber the other. So that's you know proteobacteria, right.

So we don't know the significance but what we know is there is a correlation between your profile of gut microbiome as compare to your lifestyle or the food that you intake and off course if you are healthy adult you have the pink colour that is predominant, obesity. You know the red again comes down whether it is malnutrition or you have excessive fat because of you eat a lot you know you have the red coming up right and as you age you know things change. So, how do you know this that there are different groups of microbiome and that change is as your age or the kind of food that you have.

We know because of the genomic tools, so basically you isolate the DNA or RNA you basically here what you do is twice rate the DNA look at certain signatures in the DNA with which you are able to group the microbes into one or the other groups that what is shown here for example firmicutes, bacteria, actinobacteria and others. So you are able to classify them and then you are able to classify according to the lifestyle age and so on.

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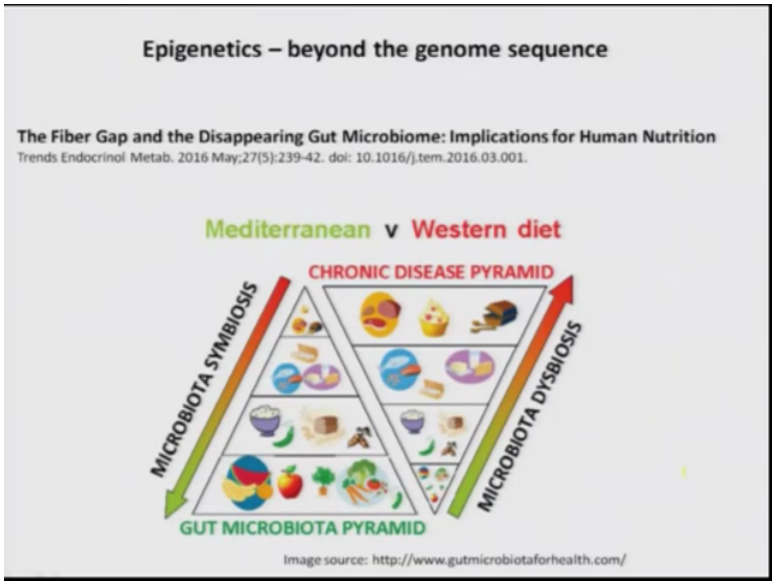

What does it really give you is very interesting this is one study which talks about how your food the diet can help or can change the gut microbiomes. So for example fiber gap and that disappearing gut microbiome. This is a paper this is you know you can go and access this paper it is available if you give this reference you will be able to read that what it says is that the food habit changes the way this microbiome is there.

So this is microbiota like you see that if you have a good system is something like this then you have more of fruits and vegetables and and less of this junk food, it gives you a microbiota combination which is a very good signature for healthy living but if you get into more of this western diet where more of pizzas and fast-food and others then it cuts and less of this vegetables and others it tills the balance to what is called as dysbiosis which is probably a pattern which is not you know in sync with a good healthy life that is how does it really help.

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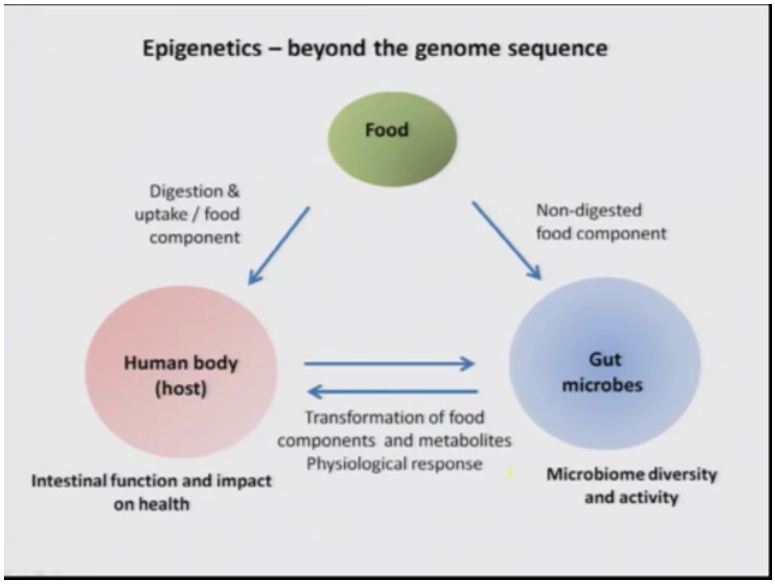

This is what is your food can really make you healthy or not so healthy even your genome other is gives you protection again something. So this is the food that you know you take in and of course the food is digested, broken and then all the components you know are distributed to your body where circulation and that makes you for example your intestinal function to function better and of course better health right. But what happen there could be certain fluid which you are unable to digest or that could be component of the food which your body cannot absorb and

that's where is going to influence what are the bacteria that that thrive in your gut. So it is going to change so if you change the food cell your gut microbiome will change.

So this change in the non-digested food or the metabolites or the components is going to really change the microbiome diversity and activity and if the combination is such that they make lot of metabolites because they also feed on this food that is available in your stomach. From then they release certain metabolites and and they interact with your intestine so as so on because they also release many chemicals that would affect or influence your physiology and can make you either healthy depends on what combination of microbiome you have or can make you susceptible or put you at a risk of developing certain disease. It is not simply anything do to with your digestive track or digestive disorders it can affect every part of your body.

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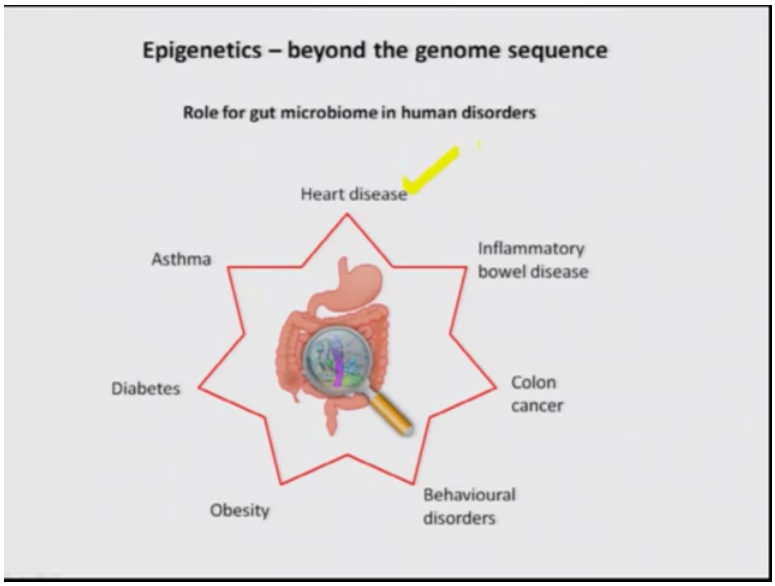

For example there are microbiome, it particular combination of each is known to you know increase the heart disease or what is called is inflammatory bowel disease where digestive process is compromise. You will not be able to sleep, you have stress and so on, colon cancer there are studies that I have shown clear correlation between your microbiome diversity and susceptibility or risk of having colon cancer, behavioural disorder even depression, autism people are shown to be associated with the kind of microbiome you have. So it influences obesity, diabetes, asthma you you name it any of the common disorder that you see are all influenced by the microbes that are present in your gut okay.

So you know all these thing because of the tour of genomics. you are able to analyze the sequence of the microbes, so you are able to classify them and tell individual A is different from individual B with regard to what kind of microbes that live in his or her gut and we are coming up the signatures which tell you okay this combination is not good so you change your food, you change your lifestyle and make you know a condition where in your biome is sort of plot back to the normal pattern therefore you risk of developing something goes down.

So it is really you know is is translating into medicine because by typing what kind of biome you have, variable to tell an individual whether he or she is at risk of developing certain disease and since the biome microbiome is dependent on the kind of food that you have and the lifestyle that you leave in. You can suggest changes as a result you know your microbiome will change. If that changes the risk is going to go down. So it it has a translation, application and that is possible only because the genomic technologies that helped in in a classifying the microbes typing them which otherwise practically impossible using conventional procedures.

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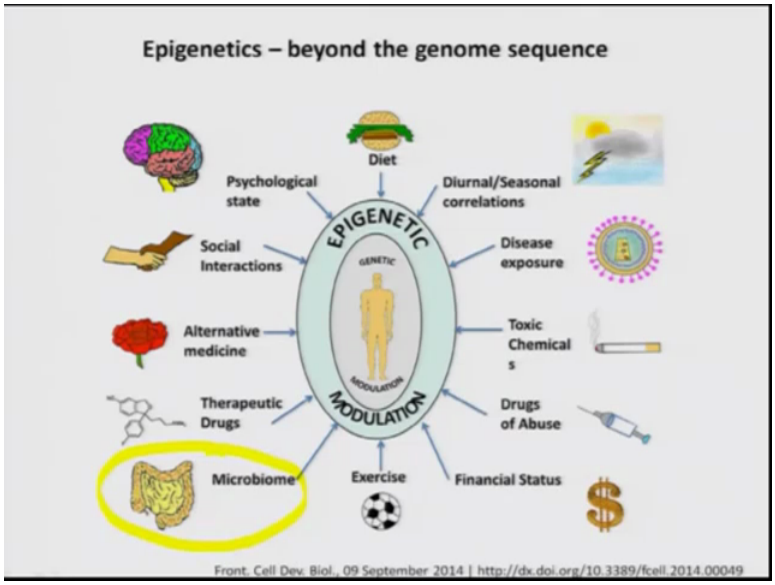

So, what I spoke about is just one that is microbiome but in the microbiome after all goes and influence the way the genome functions which you call as a epigenetics but the epigenetics is not restricted to microbiome. It could be the season, exposure to disease you know infection whether you are smoke, drug abuse, financial status, your lifestyle whether you have exercise, psychological state, social interactions so on. But these are not independent for example you

have money or not having money can affect how your brain functions whether you happy or not happy. Sometimes if you are kid you know whether you get your food that you wanted or not wanted. You know (())(22:57) is going affect your inner brain.

Social interaction again whether you are able to talk to your friend are not any given day is going to affect your brain. You are happy or not happy so thinks like that this all these are linked and it is a combinational these they are influence your genome as to how they are altered in terms of methylation, acetylation and so on and that can have (())(23:23) inflused on how we live and this is something just we are beginning to understands. So really we don't have all the tools to understand. You are beginning to understand to see how the change is happening because we know only one that is methylation or acetylation that could be many other modification that happens the genome which have not understood and how that influence the functional your genes have not been understood. This is something that you need to study.

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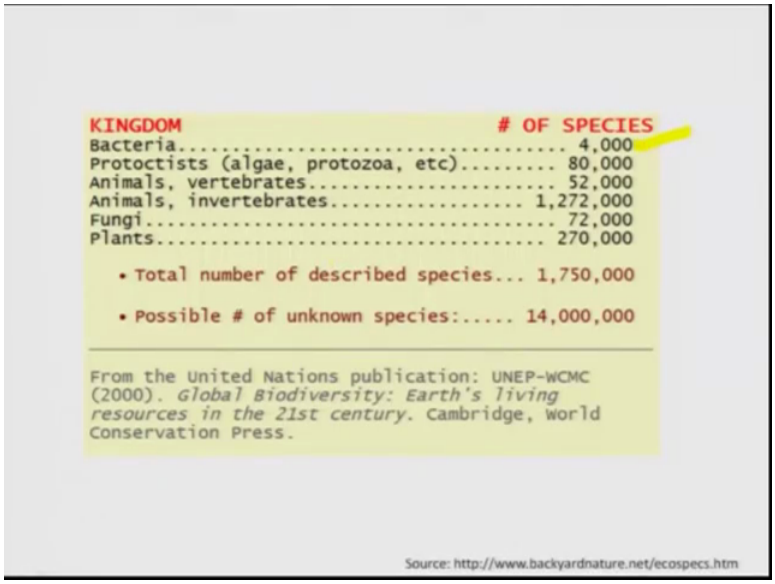

But beyond humans is not as I told you, you know the humans are small less than one percent of all the species that live on the earth. There are many many successful species and that could be of profound used to the human kind and you can see that if you look into the number of species bacteria as four thousand something shown here, protozoans, animals and vertebrates including everything is small invertebrates enormous number and so on and what is not include here is the unknown species which include many of your gut microbiomes, skin microbiome because they

cannot be cultured in the lab it cannot be tested, it cannot be classify the unknown species mostly in the microbial in a communities pretty large right.

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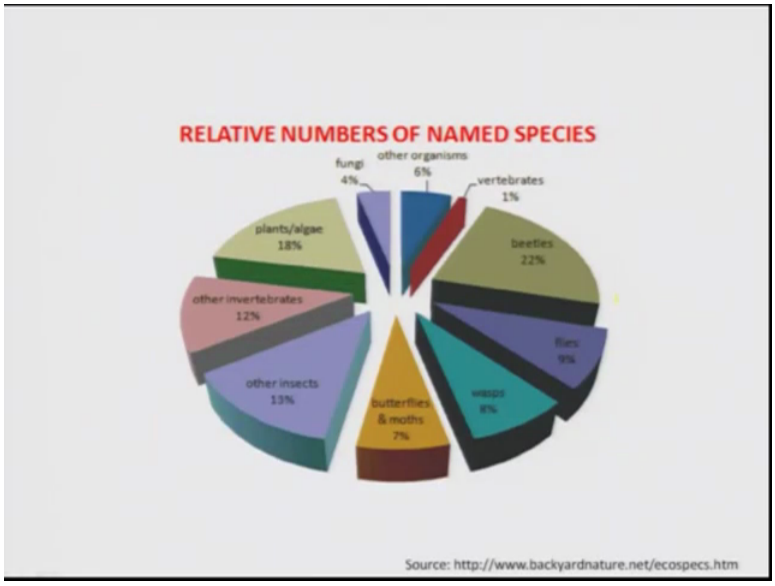

But if you look into only the known organisms if you look the relative number of species that are named, identified, classified. You will find the vertebrates which includes humans is pretty pretty small. You have so many other organisms. They all successful they leave in different condition many of them all of much help to the human welfare and and and if you look in to that you know then it is important to classify, understand and the DNA of the sequence because that is one way we can come up with certain understanding as to how they function (())(25:17) and be successful right.

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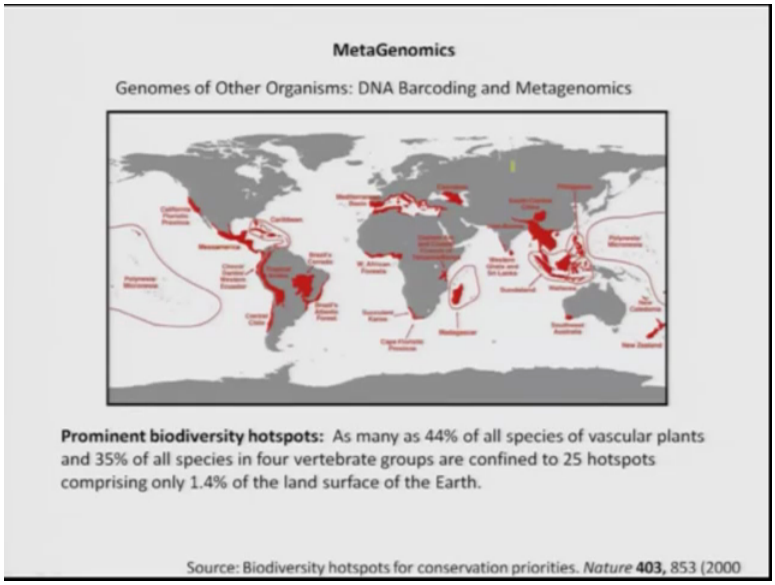

So if you see again the prominent biodiversity meaning the number of plants species and animal species you know their all restricted to certain region of the world. This is world map the red the red you know colours indicate the hotspots where have a large number of plants and animals that are living not all of them have been studied fully right. So, absolutely these are important and you can see for example India in are the western ghats from Maharashtra to Kerala and the Srilanka you know most of these fall in the tropical you know rain forest you know so as you have a huge biodiversity and its extremely important to understand what the genome of this organisms and how different they are out similar they are and so on.

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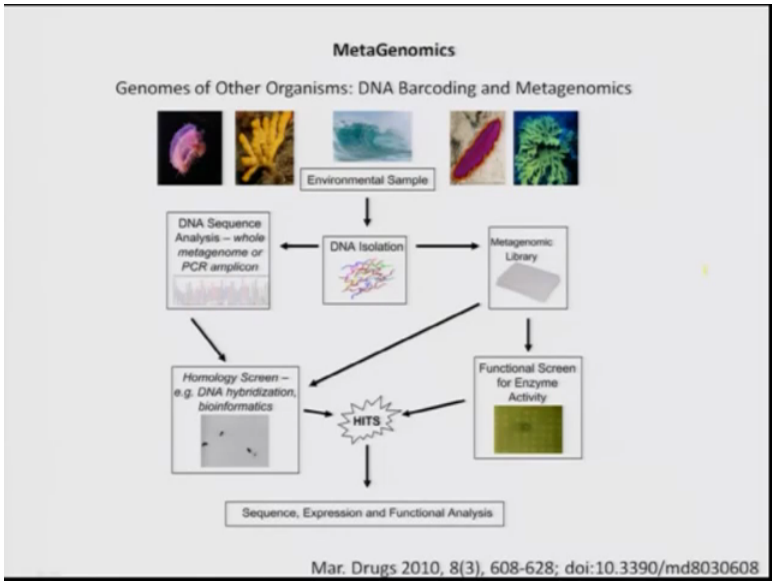

Therefore you know this is the recent phenomenon in new field is evolved is called as Metagenomics. Here in the goal is to you know sequence the DNA of a large number of species that are otherwise not studied could not studied cannot be cultured in the lab because these are not lab organisms so you need to understand them because they have tremendous impact on the human welfare I will talk about little later.

So these what the mean proposed and being carried out is to isolate the microbes or species from different parts it could be deep down under the ocean or in the mountain cliff, or from the sea shore, riverbed, dessert you know living organisms are everywhere go and collect them, isolate their DNA, sequence them and look at certain patterns and come up with in understanding you can go on to do some expression studies, functional analysis what new genes they have how that made them to survive that.

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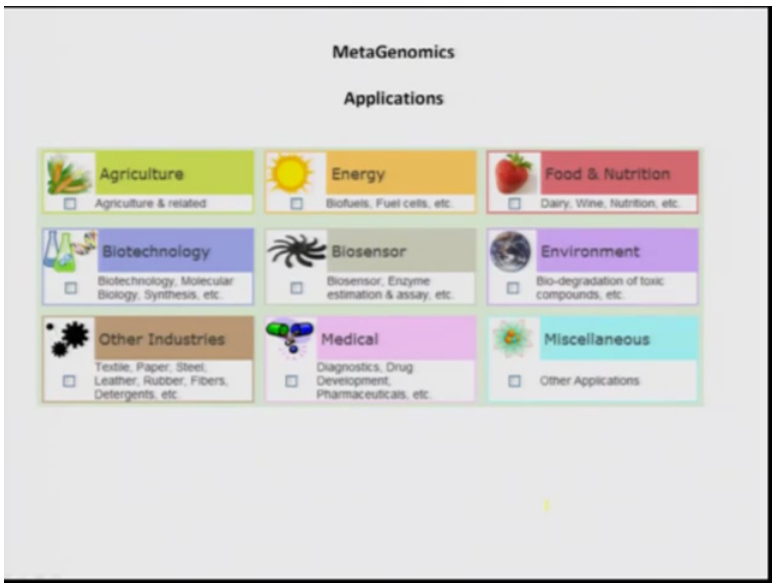

These are very very important because they have a tremendous application in terms for example agriculture may be certain microbes can tell you the soil texture so simply looking at microbe will be able to tell how healthy the soil is or the microbe in term gives back something to the soil right or it could be for example biotechnology they may have certain proteins and enzyme which are industrial application or for example they could be help us you know in paper production or leather conditioning, rubber, fiber you name it you have huge industrial application, medicine for example, diagnosis and others biosensors they means simply tell what is the enrollment that are there is it more mercury there is more iodine there.

You know there are certain microbe that thrive on that so it will immediately tell you what is energy for example biofuels, food and nutrition. You can talk about everything and these all them microbe that really going to help us so, understanding the genome is extremely important that's why there is new emphasis on Metagenomics where people trying to classify bugs or microbes based on the DNA profiling, understand how they evolve, how do they function and use their knowledge for betterment of the planet, betterment of human in welfare. So, with that we will end the third lecture of this week and we will see you again the next class.